DRUG PRODUCT SELECTION

Staff Report to the

Federal Trade Commission

BUREAU OF CONSUMER PROTECTION

JANUARY 1979

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CHAPTER I. INTRODUCTION

On July 7, 1976, the Federal Trade Commission opened an investigation into the sale of multisource prescription drugs.[1] Staff of the Bureau of Consumer Protection submits this report on whether price competition for multisource prescription drugs is unduly restricted by state antisubstitution laws that prohibit pharmacists from selecting lower-cost sources of drugs prescribed by brand name, and whether the Commission should attempt to remedy any existing problem. We have completed our investigation[2] and have concluded that antisubstitution laws impose substantial unwarranted costs on consumers[3] by unduly restricting price competition in the multisource prescription drug market.[4] We further conclude that the repeal of antisubstitution laws would produce significant consumer benefits without compromising the quality of health care.[5] To remedy the situation and facilitate pharmacists' selection (also called "substitution" or "brand

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1 Resolution Directing Use of Compulsory Process in Nonpublic Investigation, File No. 762-3124, July 7, 1976.

2 During the course of our investigation we sought comments and documentation from, inter alia, the major brand-name drug manufacturers; brand-name and generic manufacturers' associations; pharmacy and medical associations; the drug wholesalers' association; the Deans of each of the nation's colleges of pharmacy; and from consumer groups. We further obtained information from the academic community, including experts in biopharmaceutics; state pharmaceutical boards, associations and formulary commissions; other federal agencies, including the Food and Drug Administration; business organizations; and from individual pharmacists, physicians and consumers. We hired four economic consultants, representing a range of views, to provide their assessments of the potential impact of drug product selection on manufacturers' research and development incentives (see Ch. IX.A., infra). And in addition to collecting existing studies, we hired an independent market research firm to conduct a multistate survey of pharmacists' attitudes toward their state's drug product selection law (see Ch. VII.C.3., infra).

3 See discussion of potential consumer benefits in Ch. VIII., infra.

4 See discussion of the role of antisubstitution laws in insulating brand-name manufacturers from price competition, Ch. II.D., infra.

5 See analysis of alleged disadvantages of drug product selection at Ch. IX., infra.

interchange") of drug products therapeutically equivalent to but less expensive than products prescribed by brand name, we recommend that the states adopt the Model Drug Product Selection Act discussed in Ch. X.A., infra.[6]

A. The Problem

Prescription drugs, which seldom are covered by insurance plans, cost American consumers over eight billion dollars in 1977.[7] Persons over age 65, who comprise 11 percent of the population, pay 25 percent of the national drug bill, and often must do so on limited fixed incomes.[8] A considerable portion of this expenditure could be saved if the market fostered the purchase of low-cost equivalent drug products.

The basic problem is that the forces of competition do not work well in a market where the consumer who pays does not choose, and the physician who chooses does not pay. Patients

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6 This Report generally adopts the term "drug product selection" rather than "brand interchange" or "substitution." "Brand interchange" may mistakenly imply that the pharmacist is limited to selecting another branded drug product for the one prescribed, rather than an unbranded product. "Substitution" may mistakenly imply that the pharmacist is allowed to select an entirely different drug entity for the one prescribed, rather than merely a different manufacturer's formulation of the same drug, or to do so surreptitiously. (In fact, as documented in Ch. VII.A., infra, antisubstitution laws developed at a time when substitution generally did refer to deceptively dispensing a different drug entity.) "Drug" is used in this Report to indicate the active chemical ingredient or drug entity. "Drug product" means a particular manufacturer's formulation of that same drug entity. Thus, for example, "Miltown" and "Equanil" are two drug products distributed by Wallace Laboratories and Wyeth Laboratories respectively, each containing the identical drug--meprobamate. Meprobamate also may be prescribed alone or in combination under the following brand names, among others: Meprospan, Meprotabs, SK-Bamate, Tamate, Appetrol, Bamadex, Cyclex, Deprol, Equalysen, and Pathibamate. USAN and the USP Dictionary of Drug Names (M.C. Griffiths ed. 1976), at 172-173.

7 Pharmacy Times, April 1978, at 41, 48. See Ch. V.A., infra, for a discussion of drug costs.

8 Drug Topics, Sept. 1, 1977. See discussion of the special problems of the elderly at Ch. V.B., infra.

have little influence in determining which products they will buy and what prices they must pay for prescriptions.

Chemically (and therapeutically) equivalent versions of "multisource" prescription drugs (drugs available from more than one manufacturer) are frequently sold at widely disparate prices. For example, ampicillin trihydrate, a commonly-prescribed antibiotic, is available at wholesale prices ranging from $18.74 to $6.00 per hundred capsules.[9] This wide price disparity is evidence of the low priority placed on drug prices by prescribing physicians. In fact, most physicians have little knowledge of drug prices. One recent study[10] asked physicians from a diversity of practices to rank their knowledge of drug prices on a scale from one (very informed) to five (uninformed). Of the 144 physicians responding, over 32 percent replied that they had "no idea" of the prices of commonly-prescribed drugs, and over two-thirds of the remainder assessed themselves at a four or five. When the same study measured physicians' knowledge of the prices of drugs prescribed in their specialties, it found that two and a half times as many physicians underestimated as overestimated the price.

The reason for this lack of price awareness is that there is little incentive for physicians to shop around for the least expensive drug products. Patients do not choose their physicians on the basis of the cost of the drugs the physician prescribes. Indeed, probably only a small percentage of patients currently know enough about comparative drug prices or the availability of less expensive generic equivalents to ask physicians to prescribe low-cost drug products.[11] Furthermore, it is time-consuming and therefore costly for physicians to acquire comparative price information. Busy physicians understandably are concerned when choosing drugs primarily with the relative performance, benefits and risks associated with the use of a particular drug. Price considerations necessarily take on a secondary importance, if

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9 See Table 6: "HEW's MAC Savings on Ampicillin Trihydrate 250 mg. caps." in Ch. VIII., infra.

10 Fink & Kerrigan, "Physicians' Knowledge of Drug Prices," 1 Contemp. Pharmacy Prac. 18 (1978). See Ch. III.C., infra, for a discussion of this and similar studies. Except where otherwise indicated, we have not attempted in this Report to analyze the statistical validity of the various surveys cited. Where support is not available from other surveys with consistent findings, we have attempted to indicate that fact or to cite opposing studies.

11 See Ch. VII.B.4 and C.3., infra, for evidence that patients seldom ask pharmacists about the availability of low-cost products.

any at all, at the time the physician decides which drug brand to prescribe.

Drug manufacturers are sensitive to the factors that influence the physician's prescribing decision. They know that they would not gain physician loyalty by having a low price. Instead the manufacturer may do far better by having a memorable brand name.

Many drug products have three names. One is its "chemical name," often understandable only to accomplished organic chemists. An example is the drug sedative with the chemical name 7-Chloro-2-(methylamino)-5-phenyl-3H-1,4-benzodiazepine 4-oxide monohydrochloride. A second name is the "generic" or "established" or "official" name, which is a non-proprietary name used to designate drug products with the same active chemical ingredients. In the previous example, the generic name is chlordiazepoxide hydrochloride. Finally, a "brand" or "trade" name is a designation given to a drug by the manufacturer, which, if registered, can be used exclusively by that company to distinguish its product from other products in the same generic category. In the example, chlordiazepoxide hydrochloride is the active ingredient of Librium, the brand name used by the manufacturer Hoffmann-LaRoche.[12]

Almost 90 percent of all prescriptions are written by brand name.[13] This is partly because brand names are generally shorter and easier to recall than their corresponding generic names. Dr. Solomon Garb, professor of pharmacology at the University of Missouri Medical School, observed:

> I am always amused by the fact that X, Y and Z are rather rare letters in most languages, but when you come to generic names of drugs, I would say about 75 percent of all of them have either an X, Y or Z in them and some of them have all three. Zoxazolamine has two Z's and an X.[14]

And the use of the brand name may obscure the identities of equivalent drug formulations. "Noctec," a brand name used by

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12 USAN and the USP Dictionary of Drug Names, supra note 6, at 61. See discussion of brand names and their promotion by manufacturers in Ch. II.C., infra.

13 Pharmacy Times, supra note 7, at 42.

14 Dr. Solomon Garb quoted in Cong. Research Service, "Competitive Problems in the Drug Industry: Summary and Analysis," Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, Nov. 2, 1972, at 44. ["Competitive Problems".]

E.R. Squibb & Sons, "Somonos," a brand name used by Merck Sharp & Dohme, and at least 15 other chemically identical products containing the sedative chloral hydrate (500 milligram capsules) are all made by one manufacturer--the R.P. Scherer Company -- and are sold to pharmacists at prices ranging from $1.48 to $5.00 per hundred.[15]

The total number of drug products in the market is enormous. An HEW Task Force on Prescription Drugs estimated in 1968 that there were about 4,000 different dosage forms of 1,200 single drug entities and about 6,000 combination drug products.[16] The larger drug companies normally assign an individual brand name to each product they sell. During the patent period, when the manufacturer has exclusive production rights, the drug is usually sold under its brand name. During this time, the brand name may become so closely associated with the drug in the minds of physicians that they continue to write it long after expiration of the patent (see discussion of the physician's prescribing decision in Ch. III, infra.) The association of the drug entity with the brand name is fostered by the extensive promotional campaigns of the major drug companies. The core of these campaigns is the company detailer, who makes personal visits to physicians to promote the company's new products. A 1977 FTC Bureau of Economics staff report found that in 1970 thirty of the largest prescription drug manufacturers spent $682 million on drug promotion, an amount representing 21 percent of the firms' total sales in the United States or an expenditure of over $2400 per practicing physician.[17] Faced with this proliferation of heavily-promoted brand names, physicians not surprisingly were found to demonstrate

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15 USAN and the USP Dictionary of Drug Names, supra note 6, at 61; Statement of the American Pharmaceutical Association in "Prescription Drug Labeling and Price Advertising," Hearings on H.R. 882, H.R. 884 and All Identical Bills, Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, 94th Cong., 2d Sess., at 197-198 (1977).

16 HEW Task Force on Prescription Drugs, The Drug Makers and the Drug Distributors 20 (1968). Other estimates are much higher. Dr. James Goddard, former FDA Commissioner, and Dr. Paul Stolley, for example, estimated that there were about 5,000 prescription drugs and 21,000 drug products. Stolley & Goddard, "A 'Relative Efficacy' System for New Drugs," 73 Annals Internal Med. 479-80 (1970), cited in Competitive Problems, id. at n.5.

17 R. Bond & D. Lean, "Bureau of Economics Staff Report to the Federal Trade Commission: Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets," at 1 (1977).

a strong preference for the brands that first entered the market and generally were persuaded to prescribe late-entering brands only if they offered some specific therapeutic gain. The FTC report stated:

> Physicians' preferences for a relatively small number of trademarked, brand-name drugs are probably rational responses to the proliferation of trademarked drugs in the industry as a whole. For just one dosage strength of one generic chemical, 20 mg. PETN, the physician faces a bewildering array of alternatives. In 1971, 61 firms offered PETN, 32 under a brand name. To weigh the quality and price alternatives presented by such an array of drugs would involve a notable feat of research and memory. As one pharmacologist has noted, doctors are human beings, not computers . . .[18]

Brand-name prescribing has a special significance under antisubstitution laws. If the physician writes a prescription for a drug obtainable from different sources by a brand name, neither the pharmacist nor the patient can choose from among diversely priced equivalents. And companies that succeed in familiarizing physicians with their brand-name products therefore are insulated from the competition of lower-priced generic equivalents.

Antisubstitution laws are a relatively recent development (see Ch. VII.A., infra, for a discussion of the history of antisubstitution laws). At the same time the pharmaceutical industry underwent a rapid expansion after World War II, producing sophisticated drugs marketed by brand names, a large number of "counterfeit" drugs appeared on the market.

These counterfeits, resembling the popular brand-name product in color, size, shape and sometimes packaging, but of unknown quality, content and origin, were passed off to consumers through unwitting or unscrupulous pharmacists. Against this background of brand promotion and drug counterfeiting, the National Pharmaceutical Council (an organization of large drug manufacturers) led a highly successful effort to enact antisubstitution laws specifically prohibiting pharmacists from dispensing, not only a different

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18 Id. at 76.

drug entity, but a different brand from the one prescribed.[19]

As new federal controls virtually eliminated drug counterfeiting, states began in the 1960's and 1970's to question the appropriateness of restrictive antisubstitution laws. Within the last five years or so, an ever-accelerating number of states, with major support from consumer groups and pharmacy associations, have replaced their antisubstitution laws with drug product selection laws. These laws, now enacted in 40 states and the District of Columbia (see Table of State Laws and accompanying discussion at Ch. VII.B., infra), permit the pharmacist, unless otherwise directed by the physician or the patient, to select a lower-cost generic equivalent for the brand-name prescribed. The laws recognize that the pharmacist is aware of price differences and can more efficiently select from among competing products than can physicians. The laws foster price competition by allowing the only principals who have financial incentives to make price comparisons--the pharmacist and the patient--to select drug products on the basis of price.

B. The Issues

In examining antisubstitution laws and deciding whether or not to endorse drug product selection, we considered (and discuss in this Report) several important issues. One group of issues involves drug quality -- the nature and adequacy of FDA's regulation of drug quality, the extent to which drug products with identical active ingredients also provide equivalent therapy, and the question of potential differences between the quality of brand-name and generic-name products (see Ch. VI.A. and Ch. IX.C., infra). Related to these concerns are the pharmacist's technical ability to select drug sources (Ch. IV.A., infra) and the assurance of the physician's right to specify a particular brand when medically necessary (Ch. III. and Ch. IX.B., infra).

A second group of issues involves economic concerns -- the pharmacist's incentives to select low-cost generic equivalents (Ch. II.B., infra) and the extent to which pharmacists actually do choose such products (Ch. VII.C., infra), the potential savings to consumers from drug product selection (Ch. VIII., infra) and the actual savings passed on to consumers by pharmacists (Ch. VII.C., infra). Related to these concerns are the extent to which pharmacists' anxiety about potential liability lawsuits inhibits product selection (Ch. IX.E., infra) and the potential effect of increased selection of low-cost generics on the research and development incentives of brand-name manufacturers (Ch. IX.A., infra).

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19 The role of the National Pharmaceutical Council is discussed at Ch. VII.A.1.c., infra.

Studies show that opening up the multisource prescription drug market to the forces of competition potentially can save consumers hundreds of millions of dollars a year (see discussion of potential consumer savings at Ch. VIII, infra). For example, the FTC Bureau of Economics' analyses indicate that annual wholesale-price savings from pharmacist selection of low-cost drug products could be between $400 million and $500 million.[20] Similarly, a Wayne State University study in Michigan that matched the retail prices of actual substituted prescriptions with the retail prices of comparable nonsubstituted prescriptions for the same drug estimated that potential savings in Michigan alone could range from $11 to $15 million a year.[21] If these figures are extrapolated nationwide, they indicate a potential savings of $260 to $450 million a year. And an independent research study prepared for the Pharmaceutical Manufacturers Association showed that in 1976 prescriptions written by brand name cost consumers an average of 19 percent more than prescriptions written by generic name.[22] Although this study was biased downward because it dealt with generically-written prescriptions, which may be filled with an expensive brand-name product, rather than generically-dispensed prescriptions, it still estimated an annual retail-price savings of $323 million from generic prescribing.

Yet existing state laws permitting product selection vary greatly in their effect. For example, the Wayne State University study showed an 18 to 20 percent rate of product selection in Wisconsin as compared to a 1.5 percent rate in Michigan.[23] A significant number of states are amending their drug product selection laws to make them more effective. In view of this promising activity, we think the most appropriate use of Commission resources is to assist states in their efforts to make product selection work by providing relevant information and by recommending adoption of the Model Drug Product Selection Act discussed below (for a complete discussion of the Model Act, see Ch. X.A., infra).

Working closely with staff from FDA to design the Model Act,

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20 See Ch. VIII.A.1., infra.

21 See discussion of the "Goldberg study" in Ch. VIII.B.3., infra.

22 See discussion of the IMS study in Ch. VIII.B.1., infra. The IMS results showed that the brand-generic price ratio had increased from 110.62 in 1973 to 119.08 in 1976.

23 Carolee A. DeVito, Wayne State University, "Drug Product Selection Legislation: Issues and Alternatives," Presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Seattle, Washington, Sept. 21-22, 1978, at 11. For a discussion of state laws and surveys of their effects, see Ch. VII.B. and C., infra.

we have endeavored to make it as simple and as self-enforcing as possible, and to minimize any regulatory intrusion into the pharmacist's management prerogatives. We think that laws that are cumbersome or contrary to the pharmacist's self-interest are unlikely to work well.

C. The Recommended Solution: The Model Drug Product Selection Act

The Model Act permits but does not require the pharmacist to select a lower-cost chemically equivalent drug product.[24] We think that providing pharmacists an economic incentive to select low-cost products makes a mandatory law unnecessary. And we think that mandatory laws may be unworkable because pharmacists' resistance to such government intrusion may produce low rates of product selection unless costly enforcement efforts are undertaken.[25]

The Model Act limits the pharmacist's selection to products listed on a formulary of all products determined by the Food and Drug Administration to be therapeutically equivalent.[26] The opinions of physicians and other professionals and objective measurement indicate that pharmacists are qualified to select drug sources competently and efficiently.[27] They have, in fact, been selecting drug sources for generically-written prescriptions for years. However, a relatively small percentage of chemically equivalent drug products, when administered to the same individual in the same dosage regimen, may not provide the same efficacy or toxicity (i.e. may not be "therapeutically equivalent").[28] Therefore the Model Act supplements pharmacists' decision-making by recommending use of a formulary based on an FDA list of therapeutic equivalents to ensure that products with serious unresolved equivalence problems are not selected. The Model Act makes FDA the primary source for this single formulary of equivalent products

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24 See discussion of Section 2 of the Model Act at Ch. X. A., infra.

25 See discussion of surveys supporting this contention, id.

26 See discussion of Section 5 of the Model Act, id.

27 See Ch. IV.A., infra.

28 Because therapeutic effects are difficult to measure, drug equivalence is usually determined by measuring how fast and how much of the active drug gets into the body, appears in the bloodstream or is excreted in the urine. Two or more chemically equivalent products with this same "biological availability" or "bioavailability" are said to be "bioequivalent." See Ch. VI.A.4., infra, for a discussion of bioavailability.

because FDA is the best source of drug information and scientific expertise, and already has responsibility for premarket drug approval and assurance of product quality.[29] Studies also indicate that higher rates of product selection are associated with states that establish drug formularies.[30] And the study conducted for the FTC showed that four times as many pharmacists preferred a positive formulary (listing all substitutable drugs) as preferred a negative formulary (listing non-substitutable drugs).[31]

The Model Act recognizes the absolute authority of the prescriber to insist upon a particular drug source he or she judges medically necessary.[32] The Act requires simply that the physician who wants a brand-name product for a specific medical purpose take a second or two to handwrite "medically necessary" or words of the same meaning on the prescription.[33] The Act thus ensures that the additional cost of an expensive brand-name product is not imposed on the consumer without a conscious decision by the physician. Studies conducted in states with similar provisions show that rarely (generally less than five percent of the time) do physicians find it necessary to use the "medically necessary" designation.[34]

The Model Act requires that the product selected be lower in cost than the brand name prescribed, but does not require that the pharmacist pass on all cost savings to the consumer.[35] By denying pharmacists additional profit for costs that may be

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29 See discussion of FDA regulatory authority at Ch. VI.A., infra.

30 See discussion of Section 5 of the Model Act at Ch. X.A., infra.

31 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978, at 50. See also Ch. X.A. and Ch. VII.C., infra.

32 See discussion of Section 2(b) of the Model Act, Ch. X. A., infra, and discussion of physician control of therapy at Ch. VII.B.3. and Ch. IX.B., infra.

33 This phrase is identical to that required by HEW's Maximum Allowable Cost program, discussed in Ch. VI.B., infra.

34 See discussion of extent to which physicians prohibit product selection under various state provisions at Ch. VII.B.3. and C., and Ch. X.A., infra.

35 See discussion of Section 2(c) of the Model Act., Ch. X.A., infra.

incurred in searching for, stocking and dispensing lower-cost generic equivalents, mandatory pass-on provisions may provide an economic disincentive for product selection.[36] The Model Act requires that the consumer be notified when substitution occurs, thus alerting the consumer to expect to pay a lower charge.[37] With price information now available through advertising, the marketplace should work to ensure that pharmacists pass on to consumers a large portion of the cost savings. Indeed, existing studies show significant consumer savings when drug product selection takes place.[38]

The Model Act includes an optional provision assuring pharmacists that their liability for product selection will not exceed the liability incurred when filling a generically-written prescription.[39] Various studies[40] show that pharmacists are concerned about the liability risks of product selection and that many are therefore deterred from selecting drug sources as frequently as they would otherwise. Yet our search has failed to identify a single lawsuit or insurance claim filed against a pharmacist for legally substituting a lower-cost generic for the prescribed brand name. Nor are we aware of any pharmacist ever being held liable for selecting the source used to fill a generically-written prescription. We see no reason to believe that drug product selection will create significant new liability problems (see Ch. IX.E., infra).

Because most pharmacists in states with provisions limiting or defining their liability for product selection apparently are

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36 Mandatory pass-ons are discussed in Ch. VII.B.6. and C.3., infra.

37 See discussion of Sections 2(d) and 3 of the Model Act, Ch. X.A., infra.

38 See Ch. VII.C., infra. A PMA Committee report shows that non-PMA firms, which normally have only about a five percent share of the prescription drug market, are capturing nearly two-thirds of the substitution market in California and Florida, thus indicating that most products selected were probably low-cost unbranded generics. PMA Committee on the Effects of Amendments to State Antisubstitution Laws, "Preliminary Report on the Effect of the Repeal of Antisubstitution Laws in California, Michigan, Florida and Delaware," Apr. 25, 1977.

39 See discussion of Section 6 of the Model Act, Ch. X.A., infra.

40 See Ch. VII.B.4. and C.3., infra.

unaware of those provisions,[41] we cannot judge whether such provisions are effective in encouraging pharmacists to engage in product selection. We do think that whether or not a state specifically addresses the liability issue in its law, it must provide objective information about liability to pharmacists, who otherwise may be presented only with biased statements by interested parties.

Even the best product selection law will take a period of time to become fully effective as consumers and health professionals are informed of the benefits of generic drug products.[42] Our research strongly indicates, however, that drug product selection laws that follow the principles of the Model Act will work to foster price competition and reduce drug costs without compromising the quality of health care.

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41 See Ch. VII.C.3., infra.

42 See discussion of the role of education, Ch. VII.B.4., C.3., and C.4., infra.

CHAPTER II. THE MANUFACTURER'S ROLE

A. Introduction

1. Description of the Industry

The domestic pharmaceutical industry consists of approximately 1,300 firms, of which about 750 produce prescription drugs. The prescription drug makers, in turn, generally fall into two categories: (1) large firms specializing in patented brand-name products and (2) generally smaller firms specializing in generic versions of multisource drugs. The first group is composed of the 130 members of the Pharmaceutical Manufacturers Association (PMA) who account for more than 90 percent of domestic pharmaceutical sales.[1] They have also introduced more than 90 percent of all new prescription drugs currently on the market in the United States.[2] While some of these large firms carry full product lines, many tend to specialize in several therapeutic categories.[3] The PMA firms also conduct most of the industry's research, patent, and promotional activity and are generally more profitable than the rest of the industry.[4]

The second group, the non-PMA firms, do little new drug development or promotion, but usually specialize primarily in producing unbranded (i.e., not bearing a brand name) versions of multisource drugs.[5] Most of these firms are small in terms of size and production,[6] and as a group account for a relatively small

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1 Pharmaceutical Manufacturers Association, Prescription Drug Industry Factbook '76 37 (1976).

2 Id. at i.

3 U.S. Dept. of Health, Education and Welfare, Office of the Secretary, Task Force on Prescription Drugs, The Drug Makers and The Drug Distributors 9 (1968).

4 Schifrin, "The Effect of Repeal of Retail Anti-Substitution Laws on Drug Research and Development and New Drug Innovation," Feb. 28, 1978, at 2. (Paper submitted to FTC); PMA Factbook '76, supra note 1, at i.

5 Smith, Barney & Co., "The Impact of Regulatory Patterns on the Relative Attractiveness of Drug Stocks," Oct. 16, 1975, at 9.

6 Only 17% of the firms have assets of $1 million or more.

Drug manufacturing firms by asset size, 1971:

(Footnote Continued)

percentage of total sales.[7] Many of these smaller firms perform specialized services such as bulk drug manufacture, repackaging, and dosage form fabrication for other companies. Other small firms manufacture unbranded pharmaceuticals in their finished dosage form. The former are referred to as "service" firms, while the latter are known as "generic houses."[8]

The division between large brand-name companies and small generic manufacturers is not absolute. Some large firms, for example, manufacture generic-name products, while some small companies conduct new drug research and market patented drug

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6 (Footnote Continued)

Assets	Number of firms	Value of assets (thousand of dollars)
$100 million or more	24	$10,092,733
$10 million to $99.9 million	18	562,952
$1 million to $9.9 million	47	212,292
$500 thousand to $.9 thousand	99	65,006
$100 thousand to $499 thousand	226	48,136
Less than $100 thousand	725	22,296
All firms	1,139[a]	$11,004,215

[a] Variations in number of firms among PMA, Census and IRS reports is due primarily to differences in definition of manufacturing entities.

Source: U.S. Internal Revenue Service, "Source Book of Statistics of Income," data for 1971.

Cited in PMA Factbook '76, supra note 1, at 40.

Of the 875 establishments that the Bureau of Census classified in the "pharmaceuticals preparations" industry (SIC 2834) in 1967, close to 400 of them had fewer than five employees and most were single plant companies. Jadlow, "The Effects on Research Incentives of Eliminating Drug Antisubstitution Laws." Mar. 1, 1978, at 11. (Paper submitted to F.T.C.).

7 Smith, Barney & Co., supra note 5, at 15. The top 25 firms account for approximately 83% of total sales.

8 Schifrin, supra note 4, at 2.

products.[9] Two large generic houses, Generics Corporation of America and Philips-Roxane Laboratories, Inc., for example, engage in substantial research for their own products and have between 1965 and 1975 developed six new chemical entities between them (none of which was marketed by brand name).[10] Several PMA members have in the past several years begun marketing lines of generic drugs called "branded generics", whereby the generic name is incorporated as part of the brand name (e.g., SmithKline's version of ampicillin: "SK-ampicillin"). Finally both large and small manufacturers sometimes produce pharmaceuticals for each other.

2. Manufacturing History

The industry has changed significantly since the 1930's. Prior to that time, manufacturers were primarily producers and processors of bulk chemicals supplied to pharmacists. The pharmacists would then compound the drugs for each prescription.[11] Market entry was easy, requiring only a small amount of capital investment.[12] At this time manufacturers competed in terms of the form in which pharmaceutical ingredients were packaged with emphasis on such variables as the size, taste, and price of products made from these ingredients. Production efficiency was important, but rapid product obsolescence, patent and trademark protection, and governmental regulation were not.[13] The industry in the United States did little research, mainly marketing under licensing arrangements the products discovered by foreign, mostly German, pharmaceutical firms.[14] The majority of the 600 industry firms were small and served local or regional territories, though eventually five firms (Parke Davis, Eli Lilly, Abbott Laboratories, E.R. Squibb and Upjohn) emerged as leaders distributing nationally.[15]

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9 M. Silverman & P. Lee, Pills Profits and Politics 26 (1976).

10 Drug Topics, Feb. 3, 1975, at 19.

11 P. Brooke, Resistant Prices 1 (1975).

12 P. Hirsh, The Organization of Consumption: A Comparison of Organizational Effectiveness and Product Innovation in the Pharmaceutical and Recording Industries," unpublished Ph.D. thesis, U. Mich., 1973, at 53. Eli Lilly and Co., for example, was started on an investment of $1,300 in 1876.

13 Id. at 53-54.

14 Id. at 55-56.

15 Id. at 56.

The static nature of the industry changed with the discovery of the so-called "wonder drugs," beginning with sulfanilamine in 1937. One commentator described the succession of new discoveries:

> Each new anti-infective drug not only improved on older therapies, but in fact also opened up the possibility of treatment in new areas. Sulfa drugs were followed by penicillins; the tetracyclines by the cephalosporins. Each major step produced a series of significant derivatives, such as ampicillin and erythromycin . . . The success of the industry in innovation was spectacular.[16]

Significant innovation also occurred with the introduction of tranquilizers, steroids, and contraceptives.[17]

With the advent of the antibiotic drugs, production technology was altered, and so, in turn, was the role of the pharmacist. Mass production methods facilitated the manfuacture of pharmaceuticals in their finished dosage forms.[18] This changed the role of the pharmacist from that of compounding prescriptions to dispensing products purchased from manufacturers in their final dosage form.[19]

As the production function changed, marketing strategies were vastly altered. Research and development, promotion, and political-legal activity became important.[20] Whereas firms used to compete on the basis of appearance of their products, competition now turned more on the specific contents of their medicines.[21] Some of the bulk chemical suppliers such as Chas. Pfizer and Co. entered into the pharmaceutical manufacturing industry.[22] At about the same time, political and legal constraints became more influential as manufacturers had to deal with the Food and Drug Administration, the U.S. Patent Office, and the

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16 Brooke, supra note 11, at 7.

17 Id.

18 D. Schwartzman, The Expected Return From Pharmaceutical Research 4 (1975).

19 Hirsh, supra note 12, at 54.

20 Id. at 75.

21 Id. at 54.

22 Id. at 80.

AMA in addition to individual physicians, wholesale distributors, and retail and hospital pharmacies.[23] Until 1938, there was little governmental regulation. The only regulatory influence at the time was exerted by organized medicine via the American Medical Association's Council on Drugs.[24] As governmental regulation increased in 1938 (with the passage of the Food, Drug, and Cosmetic Act) and again in 1962 (with the passage of the Kefauver-Harris amendments), the industry succeeded in taking advantage of and adapting to changes in its institutional, political, and legal environment.[25] The patenting of newly discovered drug products and their promotion through the use of trademarks or brand names became important marketing strategies.[26]

Thus two developments -- the discovery of new "wonder" drugs and the ability of manufacturers to shape their environment-- radically transformed the industry.

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23 Id.

24 Id. at 59-60.

25 Id. at 4, 109, 234.

26 Id. at 54.

II.B. Research and Development

1. The Research and Development Process

Research in the pharmaceutical industry, largely a process of trial and error,[1] usually begins with a working hypothesis, followed by the synthesis of chemicals in the laboratory, and finally by animal and human tests. Biologists and organic chemists are utilized to discover leads and then to engage in organic synthesis of new chemical compounds based on those leads.[2] New compounds are often derived from this synthesis or from the modification of existing molcular structures. In either case, after a new compound is discovered, it must be tested, first through animal screening, and later through clinical human tests.[3]

The discovery, development, and marketing of pharmaceutical products is largely affected by the regulatory policies and practices of the Federal government. Pursuant to the 1938 Food, Drug and Cosmetic Act and the 1962 Kefauver-Harris Amendment, drug firms generally are required to submit to the Food and Drug Administration documented scientific evidence on a new drug's safety and efficacy as part of a New Drug Application before a product can be marketed.[4] The steps that a drug manufacturer must undertake to receive FDA approval are:

a. Synthesis (Discovery)

b. Animal Testing

c. Submission of an Investigational New Drug Application

d. Human Testing: Phase I, Phase II, Phase III

e. New Drug Application

This process usually begins in a chemical laboratory with

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1 Wesolowski & Wesolowski, "The Economics of Research and Development in the Pharmaceutical Industry," 14 Marquette Bus. Rev. 162 (1970).

2 Id.

3 D. Schwartzman, Innovation in the Pharmaceutical Industry 58 (1976).

4 See discussion of FDA premarket approval at Ch.VI.A.1., infra.

the organic synthesis of a new chemical structure.[5] The synthesized compound is then tested by pharmacologists in experimental animals to determine its activity. These are followed by tests for toxic effects, both short and long-term. If the drug compound survives this process, the next stage entails testing with humans.[6]

If a decision is made to study a compound in humans, then the remainder of the research and development procedure comes under the scrutiny of the FDA. Prior to such testing the drug firm must file an Investigational New Drug Application (IND) with the FDA outlining its plans for human testing. Clinical testing in humans is then conducted in three overlapping stages:

> Phase I - a tiny dose is tested on a limited number of health human volunteers to establish a safe dose, to determine how the compound is metabolized and to indicate its effect or activity on body functions.
>
> Phase II - controlled studies are administered on patients who have the disease to establish safety and efficacy.
>
> Phase III - long-term safety studies are completed and the product is evaluated on a widespread clinical basis. The product is given to a large number of physicians who evaluate the product as it is used in their practice.[7]

If the research firm believes that the safety and efficacy of the compound has been established through clinical studies it may then file a New Drug Application (NDA) presenting all data from animal and clinical testing with the FDA. If all goes well for for the company, final approval for marketing is then granted.[8]

The industry engages in both basic and applied research to discover new drugs and the two types of research complement each other. In fact, the line between the two types of research is

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5 Standard & Poor's Industry Surveys, Health Care, Drugs and Cosmetics, "Drugs: Rapid changes lie ahead," July 29, 1976, at H-15.

6 Id. at H-14-15.

7 Id. at H-14-15; Clymer, "The Changing Costs of Risks of Pharmaceutical Innovation," in The Economics of Drug Innovation 111 (J.D. Cooper ed. 1970).

8 Standard & Poor's, supra note 5.

not precise. Moreover because the state of knowledge is incomplete, development of new therapies "still involves a high degree of serendipity."[9] Cephalosporins (a type of antibiotic), two of which are among the five largest selling prescription drugs in the United States, for example, "were derived rather inelegantly from a fungus originally found in a sewage outlet off the cost [sic] of Sardinia."[10] In addition, industry sources contend that

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9 Smith, Barney & Co., Inc., "The Impact of Regulatory Patterns on the Relative Attractiveness of Drug Stocks," Oct. 16, 1975, at 21.

10 Robertson, "Merck Strains to Keep the Pots Aboiling," Fortune, March 1976, at 168. The two producs referred to are Eli Lilly's cephalexin (Keflex) and cephalothin sodium (Keflin). This article also relates that "[p]enicillin was discovered accidentally by a Scottish bacteriologist after a green mold turned up in his laboratory and began destroying some bacteria he was growing."

Serendipity has played an important role in several other new drug discoveries:

1. Although iproniazide was first prepared and tested as an antituberculosis drug, it became apparent in the clinic that it was a potent psychostimulant; in fact, this action was first considered a side effect.

2. Chlorpromazine was first studied as an antihistamine and anticholinergic drug, but observations in man pointed out its remarkable tranquilizer properties.

3. Based on animal experiments, imipramine was a weak tranquilizer, but studies in man demonstrated its valuable antidepressant activity.

4. The use of the muscle relaxant, zoxazolamine, in the therapy of gout was discovered by finding enhanced urinary excretion of uric acid in the course of metabolic studies with the drug.

5. Chloroquine was used as an antimalarial for many years until its beneficial action in relieving the symptoms of Parkinson's Disease.

6. Recently the antiviral drug, amantadine, has been reported to possess unexpectedly therapeutic action in relieving the symptoms of Parkinson's

(Footnote Continued)

the less precise nature of underlying biological theory makes innovation in this area more difficult than in areas involving the physical sciences.[11]

Drug research involves specialists from many disciplines including chemistry, physiology and pharmacology. The lines between the basic and applied stages of research and between the research and development state are indistinct. Usually synthesis marks the beginning of the applied research stage, while animal toxicology testing is associated with the beginning of the developmental state.[12]

Firms usually will conduct several research projects simul-

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10 (Footnote Continued)

Disease.

Burns, "Modern Drug Research" in The Economics of Drug Innovation, supra note 7, at 58-59.

11 Those close to the drug industry maintain that innovation based upon biological sciences, as in the drug area, is more difficult than technological innovation developed from the physical sciences. They contend that new drugs are seldom designed from basic theories or principles because knowledge in this area is less precise and less complete than in the physics-related sciences. Harold Clymer, Vice President, Research & Development, Pharmaceuticals, Smith, Kline & French Laboratories, for example states:

> But the biological sciences -- as opposed to physical science, where there are unifying theories -- are still much less precise, with a great deal of empiricism in their makeup ... the transfer of animal data to humans is inherently less certain than it is in the innovative process where the invention is grounded on the physical sciences.

Clymer, supra note 7, at 120-21. See also Burns, supra note 10, at 55 and Schwartzman, supra note 3, at 45.

12 Schwartzman, "Research Activity and Size of Firm in the U.S. Pharmaceutical Industry," in Regulation, Economics and Pharmaceutical Innovation 188 (J.D. Cooper ed. 1976).

taneously to provide insurance against failure.[13] This also permits the firm to gain knowledge in several therapeutic areas and permits windfall discoveries when unintended, but beneficial side effects develop in the laboratory.

Drug industry research and development is characterized by another factor: there is a delay, which can extend to several years, between the discovery phase and marketing. This delay, the time needed to obtain FDA approval for marketing, increases the costs, financial risks, and uncertainty inherent in all research and development.[14]

2. Financing of R & D

The drug industry spends relatively more than most other industries on both basic and applied research. And unlike most other industries, it funds this research internally rather than through outside sources. According to figures provided by the Pharmaceutical Manufacturers Association, company-financed R & D expenditures for human-use pharmaceuticals have grown from $50 million in 1951 to $937.5 million in 1975. An additional $9 million was provided in 1975 by government grants and contracts.[15] The National Science Foundation estimate for R & D expenditures for "drugs and medicines" in 1975 is somewhat lower -- $804 million.[16] The NSF figures, however, exclude the pharmaceutical divisions of large chemical companies. Use of NSF estimates thus leads to understating of the actual R & D effort.[17] Under either estimate, however, it appears that the drug industry is research intensive.

The National Science Foundation estimates that producers of "drugs and medicines" spent 7.5 percent of their sales dollar on R & D in 1975 compared to 3.1 percent for industry as a whole.[18]

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13 Id. at 190.

14 Clymer, supra note 7, at 110.

15 Pharmaceutical Manufacturers Assoc., Annual Survey Report, Ethical Pharmaceutical Industry Operations 1975-1976 18 (1976).

16 National Science Foundation, Research & Development in Industry, 1975 31-32 (1976).

17 U.S. Dept. of Health, Education and Welfare, Office of the Secretary, Task Force on Prescription Drugs, The Drug Makers and The Drug Distributors 17 (1968).

18 NSF, supra note 16, at 59. Estimates of industry expenditures on R & D from other sources vary within a range of 6 to 12%

(Footnote Continued)

Moreover, the R & D sales ratio for the drug industry has increased over the past decade in contrast to the declining trend for all

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18 (Footnote Continued)

of their total drug sales. The Pharmaceutical Manufacturers Association estimates that the R & D sales ratio has ranged from 10.5 to 12.2% from 1965 to 1975, with 11.6% for 1975. This estimate is considerably higher than that compiled by NSF for the entire drug industry, but may reflect differences in measuring sales. PMA notes:

> [I]ts R & D sales ratio for U.S. pharmaceuticals is the ratio of total U.S. pharmaceuticals in the U.S. This includes export sales of U.S. plants but not the sales of overseas affiliates and subsidiaries. It covers research-performing firms only; sales of companies without R & D activities are excluded. Most importantly, it is a homogeneous ratio: nonpharmaceutical R & D and nonpharmaceutical sales are excluded. This makes it difficult to compare with other industries, surveyed by the National Science Foundation, for which R & D is given as a ratio of total corporate sales.

Pharmaceutical Manufacturers Assoc., Prescription Drug Industry Factbook '76 5 (1976). See also PMA Annual Survey Report, supra note 1, at 16.

The HEW Task Force on Prescription Drugs in 1968 estimated an R & D to sales ratio of 6.5%. But this estimate may be understated due to the fact that it includes non-pharmaceutical sales for more than half of the firms in its sample. The Task Force qualified its estimate by stating that "R & D expenditures as a percentage of pharmaceutical sales are probably higher for companies which produce largely prescription drugs" The Drug Makers, supra note 17, at 14.

Other estimates include: 9-11% (Schifrin, "The Effect of Repeal of Retail Anti-Substitution Laws on Drug Research and Development and New Drug Innovation, February 28, 1978, at 15, Paper submitted to FTC); 6% (estimate by the Social Security Administration, cited in Prescription Drug Labeling and Price Advertising, Hearing on H.R. 882 et al., before the Subcomm. on Consumer Foreign Commerce, 94th Cong., 2d Sess. 138 [1967]).

manufacturing industries conducting research and development.[19] In 1975, only aircraft and missiles (13.8%), office, computing and accounting machines (10.9%), and communication equipment (8.2%) had higher R & D to sales ratios than did the pharmaceutical industry.[20]

Drug companies finance their R & D almost entirely from their own resources.[21] PMA estimates that 99.2 percent of the industry's expenditures for R & D in 1975 came from company funds.[22] In the same year 37 percent of all industrial R & D was financed by the federal government.[23] In comparison, the federal government financed 79 percent of industrial R & D for aircraft and missiles, 45 percent electrical equipment, 14 percent for machinery, and 14 percent for motor vehicles.[24] Thus the drug industry as a whole spends a higher proportion of its own funds for R & D than any other industry,[25] and nearly four times that of all industry.[26]

The drug industry also spends proportionately more of its total R & D budget on basic research than any other industry. About 12 percent of the industry's R & D budget, according to NSF data, is spent on basic research compared to an average of 3 percent for all private industry. Manufacturers of aircraft and missiles, for example, spend less than 1 percent of their R & D budget for basic research.[27]

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19 See NSF, supra note 16, at 59.

20 Id.

21 The Drug Makers, supra note 17, at 15.

22 PMA Annual Survey Report, supra note 15, at 17.

23 NSF, supra note 16, at 28. This represents a decline in Federal support of industrial R & D from earilier years. Between 1956 and 1968, the federal share ranged from 49% to 59%.

24 Id. at 2.

25 The Drug Makers, supra note 17, at 16.

26 NSF, supra note 16, at 60. In 1975, the drug industry spent 7.5% of its own funds on R & D while all manufacturers averaged only 1.9% of their own funds. Comparable figures for other research-intensive industries include: aircraft and missiles 2.9%; communication equipment and communication 4.6%; electrical equipment and communication 3.9%

27 Id. at 66. The top five industries in terms of basic research as a percent of net sales in 1975 were: drugs and

(Footnote Continued)

Thus, on the basis of R & D expenditures as a percentage of net sales the drug industry is one of the most research intensive industries, and on the basis of both company-generated R & D funds and basic research, is the most research intensive.

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27 (Footnote Continued)

medicines (12.1%), industrial chemicals (10.8%), chemicals and allied products (10.4%), stone, clay, and glass products (6.4%), and other chemicals (5.9%).

See also Clarkson, Intangible Capital and Rates of Return, Effects of Research and Promotion on Profitability 62 (1977).

II. C. The Effect of Antisubstitution Laws on Brand-Name Promotion and Marketing

The pharmaceutical industry engages in extensive promotional activities to differentiate each manufacturer's products. Often this differentiation occurs among products with similar or even identical therapeutic characteristics.

The industry and its supporters contend that the tremendous sums the pharmaceutical industry spends facilitate the communication of useful information.[1] Critics maintain that the information doctors rely upon comes exclusively from the industry and relates only to brand-name products. They also contend that drug makers create confusion and undue brand-name loyalty among doctors by over-promoting and needlessly proliferating the number of brand names.[2] To the extent that these criticisms are valid, antisubstitution laws may be partly responsible. We will thus confine our discussion of this controversy to the effect of antisubstitution laws on incentives to engage in brand-name promotion. The first section will discuss the importance of brand names to pharmaceutical manufacturers. The second section will describe the manner in which drug manufacturers assiduously engage in brand-name promotion, and how antisubstitution laws encourage this promotion.

1. The Role of Brand Names

Most of the drug industry's promotion involves trademarks distinguishing one firm's product from that of its competitors. While each drug product already has a chemical name and an established generic name, brand-name drug manufacturers apply a third distinctive name for marketing purposes. This practice has been harshly criticized for creating confusion and undue brand loyalty among doctors. Although other factors also are involved, we will see, nevertheless, that the antisubstitution laws may have contributed to the vast number of brand names.

Many products, in fact, have three names - a chemical name, a generic name, and a trade or brand name. The chemical name describes the drug product's chemical structure, based on standard rules of chemical nomenclature. Often this nomenclature is unwieldly, and usually meaningless to all but accomplished organic chemists. An example of a chemical name is "dextro 3-methoxy-N-methylmorphinan hydrobromide." The generic name is usually

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1 See, e.g., D. Schwartzman, Innovation in the Pharmaceutical Industry 182-211 (1976).

2 See, e.g., Schwartzman, id.; See also M. Silverman & P. Lee, Pills, Profit & Politics 48-80 (1974).

a shorter, simpler version of the chemical name and is not protected by a trademark. This name, also referred to as the "official" or "established" name, is the name most commonly used in scientific literature. In the previous example, the generic name becomes "dextromethorphan hydrobromide." Finally, the brand name is assigned to the drug compound by the manufacturer to distinguish it from identical compounds produced by other firms. The drug "dextromethorphan hydrobromide" is the active agent in the product called "Romilar", manufactured by Hoffmann-LaRoche, Inc.[3] As can be perceived from the examples below, the generic name is both more complex and more difficult to remember than the brand name:

Comparison of Brand and Generic Names[4]

Generic Name	Trade Name
Dioctyl Sodium Sulfosuccinate	Colace
Dimenhydrinate	Dramamine
Potassium Penicillin G	Pentids
Diethystilbestrol	Stilbetin

The use of a separate trade or brand name in lieu of the generic name and in addition to the company name is criticized as a poor means of identifying pharmaceutical products. In most industries, the brand name identifies the manufacturer and is usually accompanied by a generic name to identify the content of the goods being sold. But this is not the practice in the pharmaceutical industry:

> Some typical brand names of food products are Heinz, Beech-Nut, Quaker . . ., and so forth. Thus, the usual name Heinz beans, tells the customer two things: what the can contains, and who made it. There are many makers of canned beans. All use their brand name in adjectival sense, and all have the common noun "beans" prominently displayed on their labels. The pharmaceutical industry does things differently. They use two sets of brand names. The one set consists of the name of the company, such as Lederle . . . In addition they add a second brand name by inventing a new name for the product

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3 R. McMurray, "The Use of Trademarks and Generic Names on Pharmaceutical Specialties," 51 Trademark Rep. 111 (1961).

4 USAN and the USP Dictionary of Drug Names (M. C. Griffiths, ed. 1976), at 95, 97, 99, 124.

> and registering it as a private trademark. Examples are Diamox, Gantirisin, and so forth. This second brand name causes confusion because it is used as the name of the product . . . To understand fully the extent of the confusion caused by this usage, let us consider what would happen if drug manufacturers took over the manufacture of baked beans. They would all stop using the word "bean," and each would give the product a new, coined name. Some might use anagrams of beans, like "Sneabs, or Nabes," and others might call them "Lo-Cals," or "Hi-Pros." Picture the confusion in the grocery store if beans were no longer named "beans," but if each maker gave a complete new name to his product. Further, try to imagine what would happen if there were 300 to 500 additional new names of this type in the grocery store every year.[5]

Those critical of brand name promotion would prefer the use of generic names accompanied by the name of the manufacturer. If this approach were utilized, one would see drug products identified as "Lilly propoxyphene hydrochloride" with Lilly the trade name, and propoxyphene hydrochloride the accompanying generic name. Instead, manufacturers usually coin a third name, in this case "Darvon," for the purposes of brand name identification. Critics contend that names such as "Darvon," while distinctive and easy to remember, do not really serve the purpose of a trade name -- to identify the maker or source of the product -- nor do they lend a clue to the generic drug they contain. This practice of applying a different name for each version of the same product abounds. For example,

> the mild tranquilizer drug, meprobamate, may be prescribed alone or in combination under any one of the following tradenames: Apascil, Atraxin, Biobamat, Calmiren, Cirpon, Cyrpon, Ecuanil, Equanil, Harmonin, Mepantin, Mepavion, Meproleaf, Meprosin, Meprospan, Meprotabs, Miltown, Nervonus, Meuramate,

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5 Cited in P. Hirsh, "The Organization of Consumption: A Comparison of Organizational Effectiveness and Product Innovation in the Pharmaceutical and Recording Industries," unpublished Ph.D. thesis, U. of Mich., 1973, at 105-06. Of course, the pharmacy industry is not entirely unique in engaging in this practice. Laundry detergents for example are not identified by company or generic names, but by "Tide," "All," "Fresh Start," "Dynamo," "era," etc.

Oasil, Pamaco, Penediol, Perequil, Perquietil, Pertranquil, Placidon, Probamyl, Quanil, Quilate, Sedabamate, Sedasil, Urbil, and Viobamate.[6]

Likewise, Senator Gaylor Nelson estimates that for 700 different drugs there exist 20,000 names.[7]

So far, we have considered instances where the same chemical entity may be marketed by different manufacturers under a number of separate and distinct brand names. This occurs during the patent period when the original manufacturer licenses other firms to manufacture and distribute the drug product or after patent expiration when numerous firms enter the market, some with their own brand-name products. Sometimes, however, even the same product produced by one manufacturer will be distributed by several companies under various tradenames. R. P. Scherer, for example, manufactures chloral hydrate 500 mg. capsules for 17 other companies, which then sell it at widely differing prices.[8] Uncertainty can also result from changes in formulation or even changes in manufacturers without corresponding changes in brand name.[9] There are even cases where the same drug product is marketed under different names by the same manufacturer.[10] Squibb, for example, changed the formula of its tetracycline hydrochloride product called Sumycin so that it became identical to another Squibb tetracycline hydrochloride product called Steclin. Thus the same company via a formula change now markets the same drug product under two different brand names.[11] Squibb, in still another instance, also markets a generic name and tradename version for the same

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6 Cong. Research Service, "Competitive Problems in the Drug Industry: Summary and Analysis," Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, Nov. 2, 1972, at 42.

7 P. Brooke, Resistant Prices 19 (1975).

8 Statement of the American Pharmaceutical Assoc., "Prescription Drug Labeling and Price Advertising: Hearings on H.R. 882, H.R. 884, et al.," Subcomm. on Consumer Protection and Finance of the House, Comm. on Interstate and Foreign Comm., 94th Cong., 2d Sess. 197 (1976).

9 Id. at 196-97.

10 Id. at 197.

11 Id. at 197; Feldmann, "The Brand Name System - An Intrusion Upon the Profession," J. Am. Pharm. Ass'n, July 1971.

drug: Penicillin G and Pentids.[12]

This proliferation of brands, it is argued, presents problems for physicians trying to distinguish between them. First, doctors respond by working with and prescribing only a few of the many available brand name drugs, thus enhancing the market position of those few drug products selected.

> Physicians' preferences for a relatively small number of trademarked, brand-name drugs probably are rational responses to the proliferation of trademarked drugs in the industry as a whole. For just one dosage strength of one generic chemical, 20 mg. PETN, the physician faces a bewildering array of alternatives. In 1971, 61 firms offered PETN, 32 under a brand name. To weigh the quality and price alternatives presented by such an array of drugs would involve a notable feat of research and memory. As one pharmacologist noted, doctors are human beings, not computers, and the proliferation of brand names means that physicians can learn and work with only a few.[13]

Second, in cases of emergency, multiplicity of identical drug products can hamper recall efforts. The drug Thalidomide, for example, was sold abroad under 50 to 100 different names and packages, making it difficult to trace and identify the product when it was recalled because of its serious, adverse side effects.[14] Finally, another problem may occur when a physician desires to change the therapy for a patient, but inadvertently ends up prescribing exactly the same drug under a different name.[15]

Others, however, contend that the proliferation of brand names is probably explained by many factors, and in itself may not demonstrate that anything is amiss. For instance, the

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12 Address by Dr. Edward G. Feldmann, Assoc. Exec. Dir. for Scientific Affairs, Am. Pharm. Assoc., Before the Georgia Pharmaceutical Association (May 2, 1972).

13 Bond & Lean, "Federal Trade Commission Staff Report on Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets" 76 (1977).

14 Garland, "Dissemination of Information on Drug to the Physician," in Drugs in Our Society, (P. Talalay ed. 1964), at 206.

15 Feldmann, supra note 9.

typical physician may find a brand name easier to use because he is primarily interested in selecting a drug entity, not in comparing competing versions of that same drug (see Ch. III. C., infra.) Physicians may prefer working with a more memorable name for a drug. As one writer put it: "Generic names are usually chemical tongue-twisters while brand names are short, simple and catchy designed to be recommended easily by physicians."[16] An official of the American Medical Association commenting on a proposal to prohibit physicians from prescribing by brand names asserted: "It would be a great irritation for doctors. We believe tradenames are easier to remember, and it would require a whole new learning process."[17]

Thus proponents of product-unique tradenames contend that while their vast number may be confusing when viewed in the abstract, they may be very serviceable to drug prescribers. Promotion of tradenames does provide a valuable incentive to firms to provide information about new drugs. Indeed, the lack of product differentiation may impede the marketing of new products. A study cited by the Council on Economic Priorities, for example, notes that utilization of innovative drugs in the Soviet Union is hampered because of the lack of information conveyed to doctors.[18]

Drug product selection laws, of course, do not prevent manufacturers from establishing brand names and doctors from prescribing by those names, but merely enable the pharmacist,

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16 Bonner, "The Last Stand of Brand-Name Drugs," Los Angeles Times, July 17, 1975.

17 Cerra, "Study Reports Antibiotics Prices Inflated by Limited Competition in Drug Sales," New York Times, Jan. 6, 1975, at 35.

18 "In a study of drug utilization in the Soviet Union, the authors found that although products were developed that had advantages over older products, physicians did not utilize those newer products." Brooke, supra note 7, at 12, citing N. Lisman and M. Field, The Soviet Pharmaceutical System Revisited (1973). See also Goldman, "Product Differentiation and Advertising: Some Lessons from Soviet Experience," 68 J. Poli. Econ. 346-357 (August 1960) for an account of "the problems created by a lack of product differentiation in a planned state." Id. at 357. In a society with little or no product differentiation and trademark coverage, "[a] consequence is that the manufacturer and retailer lack an important incentive to maintain quality." Id. at 349, Goldman found that Soviet Union was gradually recognizing the need to utilize product differentiation to enhance quality maintenance.

absent contrary direction by the doctor, to select a less expensive generic equivalent for the brand-name product prescribed. Antisubstitution laws in themselves, however, may increase the incentive to use product-unique brand names. The important effect that brand-name prescribing can have on a product's sales when its patent has expired makes it less likely that an innovative firm will designate its product by the generic name. Similarly, after the patent expires, antisubstitution laws may increase the incentive for entering drug manufacturers to market their version of the drug using a product-unique brand name. Therefore, antisubstitution laws increase the incentive for innovative and entering firms alike to proliferate the number of brand names. Moreover, as discussed below, antisubstitution laws increase the incentive of manufacturers to promote on the basis of brand names.

2. Antisubstitution Laws Increase the Incentive to Promote

The pharmaceutical industry spends a large portion of its total revenues on brand-name promotion. Athough the figures vary, most estimates run between 20 and 30 percent of the sales dollar.[19] The promotion budget is considerably larger than for research and development, and depending on the figures used, can be a multiple of two to four times as large as the budget for R & D. One large firm, Merck and Co., spent nearly $145,000,000 on R & D for all products in 1977 (based on sales of $1,724,410,000) and $438,000,000 on marketing and administration expenses ($47,000,000 for advertising alone).[20] A recent tabulation published in Advertising Age showed that the top twenty drug firms (according to promotional expenditures) spent nearly $327,000,000 on three forms of promotion (detailing, journal advertising, and direct mailing), of which nearly 70 percent ($222,485,000) was spent on manufacturers' personal representatives, called detailers, who make personal visits to physicians to inform them of their companies'

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19 FTC economists Bond and Lean estimated that in 1970 the thirty largest drug manufacturers spent $682 million on promotion, or 21% of their sales dollar and $2,400 per physician. Bond & Lean, supra note 13, at 1. Other estimates are: 25% for sales expenses including advertising and promotion (Report on Administered Prices of Drugs, Subcommittee on Antitrust and Monopoly, of Senate Comm. on the Judiciary, S. Rep. No. 448, 87th Cong., 1st Sess., 1961, Report 31, at 157); 25% for promotion (Rep. Rosenthal, Cong. Record, Mar. 19, 1973, H. 1884); 35% for marketing: 20% for direct sales, 5% for administration, 10% for advertising and promotion (Hughes, "Prospects for U.S. Health Care Companies, 1975-1977," April 1975, Arthur D. Little, Inc., at 9).

20 Merck and Co., 1977 Annual Report.

new products.[21] Advertising Age reports that a leading auditing service found that drug companies spent $604,900,000 on promotional activities in 1976, though the same article mentions that "trade estimates" put the total at $1 billion.[22]

Data compiled by economist Kenneth Clarkson also reveal that the drug industry spends relatively more on advertising than most other industries:

ADVERTISING AS PERCENTAGE OF NET SALES

1949-1971, BY INDUSTRY

Industry	Advertising of Percentage of Net Sales
Pharmaceuticals	3.7
Chemicals	3.7
Foods	2.3
Electrical machinery	1.6
Rubber products	1.5
Office machinery	1.0
Motor vehicles	0.8
Paper	0.7
Petroleum	0.5
Ferrous metals	0.3
Aerospace	0.3

Source: K.W. Clarkson, Intangible Capital and Rates of Return, Effects of Research and Promotion on Profitability (1977), at 60.

Promotion is carried on through numerous means and media. About 70 percent of the promotional budget is used for detailing.[23] Commercial information is also disseminated through journal advertising, direct mail advertisements, publication of "regular house magazines" reports on clinical studies of new drug products, various information services, medical conferences and educational materials, exhibits at medical meetings, and free samples of

21 Advertising Age, Feb. 13, 1978, at 28.

22 Id. at 68.

23 Council on Economic Priorities, "In Whose Hands?," 4 Econ. Priorities Report 28 (1973); Advertising Age, supra note 21, at 28.

drug products.[24] These activities are discusssed in greater detail in Ch. III, infra.

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24 Advertising Age, supra note 21, at 68, estimates that medical journal advertising takes up 22% of total promotional outlays followed by direct mail, 8%. See also U.S. Dept. of Health, Education, and Welfare, Office of the Secretary, Task Force on Prescription Drugs, The Drug Makers and the Drug Distributors (1968), at 27; the FTC Econ. Report on Antibiotics Manufacture, (June 1958), at 128-140; Steele, "Monopoly and Competition in the Ethical Drugs Market," 5 J. Law and Econ., 131, 141 (1962).

Greater promotional efforts are made by manufacturers when introducing a new, unknown drug. FTC Econ. Report on Antibiotics Manufacture, at 129; Contra: Vernon, "Concentration, Promotion, & Market Share Stability in the Pharmaceutical Industry," Marketing Science Institute, Cambridge, Mass., unpublished paper (September 1970), at 22, and Hornbrook, "Market Structure and Advertising in the U.S. Pharmaceutical Industry: Some Implications for Public Policy," Div. of Intramural Research, Nat'l Ctr. for Health Svcs. Research, Dept. of Health, Education and Welfare (1977), at 27. Promotion serves to inform physicians of the existence of a new product and convince them to switch brand loyalties. Hornbrook, supra, at 14. This is not an easy task, for "physicians are generally unlikely to switch to a drug [entity] that offers equal, but no better, therapy." Bond and Lean, supra note 13, at 80. Sales for many products never do match promotional costs. "The evidence which shows that some promotional campaigns are unsuccessful suggests that a drug must have valid therapeutic claims in order to become a big seller." Schwartzman, supra note 1, at 193-94. If a product does succeed, then less intensive "maintenance" advertising and promotional activities are engaged in by manufacturers to remind physicians and pharmacists about availability of their established products. FTC Econ. Report on Antibiotics Manufacture, supra at 129; Kedersha, "The Impact of Brand Name Prescription Products on the Traditional Practices of High Prescription Volume Pharmacies in Northern New Jersey," unpublished Ph.D. thesis, New York Univ., 1964, at 142. The difference in emphasis and budget allocation according to the type of drug promoted is illustrated below:

Method	Percent of promotional budget	
	New Product	Old Product
Personal selling	50	------

(Footnote Continued)

Given the significance of brand-name prescribing under antisubstitution laws, however, it is easy to see how these laws encourage huge promotional expenditures: by reinforcing doctors brand-name prescribing habits, drug companies are able to retain their dominant position and continue charging premium prices long after patents have expired.

Most authorities and studies in the area conclude that physicians are less likely than pharmacists to be aware of price differences among multisource drugs. Doctors have numerous responsibilities besides prescribing drugs and appear to be preoccupied with the drug's therapeutic effect when writing a prescription.[25] They use little of their valuable time to learn the availability and price of competing sources of the same drug. And nearly all the information they do receive pertains only to brand-name products.

Antisubstitution laws increase this incentive to promote brand-name drug products. During the patent period, an innovative firm has increased incentive to promote its product's brand name to physicians, hoping that physicians' familiarity with the brand name will lead to widespread prescribing by that name even after the patent expires.

Many analysts see antisubstitution laws operating in a synergistic manner with trademarks, patents, and promotion. During the patent period, the tradename of the drug product often becomes synonymous with the name of the drug entity, at least in the minds of prescribing physicians. Since the trademark never expires, competing firms cannot use that tradename to call attention to their products. This process may effectively extend the patent monopoly past its formal expiration, as is implied in the following passage:

> The patent-holder typically uses the patent period and the revenues it derives from monopoly pricing, to mount a massive promotional

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24 (Footnote Continued)

Journal advertising	10	15
Direct mail	15	70
Sales promotion devices	10	10
Exhibits and conventions	10	------
Other	5	5

Source: FTC Econ. Report on Antibiotics Manufacture, at 129.

25 See Ch. III.C., infra.

> campaign aimed not only at selling the drug under its brand name while the patent lasts but also at linking its name with the product permanently, so that physicians will continue to prescribe the drug by its original brand name long after the patent period has elapsed.[26]

Thus in conjunction with prior patent coverage, heavy promotion campaigns, and state antisubstitution laws, "[t]he value of a trademark may continue long after patent protection has vanished."[27] This interaction is described by the Senate Select Committee on Small Business as follows:

> By promoting and advertising drugs by trade names, manufacturers hope to build loyalty among prescribers who use these products. In States with antisubstitution laws, loyalty to trade-named products is especially important. If the prescriber designates a drug by a trade name assigned to it by a manufacturer, pharmacists must fill the prescription order with the product of the particular supplier, or obtain authority from the physician to use some other versions of the drug available to the pharmacist.[28]

Brand-name promotion, of course, deemphasizes the existence of equivalent products. Antisubstitution laws prevent pharmacists (who are aware of equivalent alternatives) from interchanging lower-cost products for prescriptions written by brand name. Therefore, to the extent that heavy promotion by manufacturers focuses on tradenames, it "reduces the degree of substitutability between products," giving the distributor of brand name products greater latitude in its promotional and pricing behavior.[29]

Moreover, we will see later that in advertising their products to doctors, generic manufacturers face several disadvantages not encountered by the brand-name firms (see Ch. II.D., infra.) Thus, antisubstitution laws may lead to over promotion by brand-name firms attempting to bar the success of lower-priced substitute

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26 Consumer Reports, January 1975, at 51.

27 The Drug Makers, supra note 24, at 41.

28 Cong. Research Service, supra note 6, at 40.

29 Hornbrook, supra note 24, at 29.

brands.[30]

This is not to say that drug promotion and the use of brand names would disappear or necessarily decline absent antisubstitution laws. What is clear, however, is that antisubstitution laws do increase the incentive to promote on the basis of brand names.

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30 Bond & Lean, supra note 13, at 79.

II.D. The Post-Patent Period

Unless a patent holder issues a license for the patent, competition for the product must wait until the patent has expired. When that occurs, firms may enter and market duplicative versions in competition with the innovator's product. This section will describe the role that generic producers play during the postpatent period by entering the market with lower-priced equivalents. It will also describe how the original manufacturers respond to this new competition. This section will also provide a brief analysis of the conditions and prospects of the emerging generic market. As will be seen, generic competition has so far affected pricing for only a relatively small number of drug products but may have a substantially greater effect as drug product selection by pharmacists increases.

1. Marketing and Pricing Behavior by the Original Manufacturer

When the patent period expires, the producer of a drug product may face competition from both generic manufacturers as well as major brand manufacturers. As competition increases, the market share of the original manufacturer may erode until it is forced to reduce its price. Usually, however, even after the patent expires, the original manufacturer maintains a dominant market share as well as a substantial price premium.[1] As will be discussed below, antisubstitution laws help the original manufacturer to maintain its dominance.

The original manufacturer enjoys many advantages over new entrants. FTC economists Bond and Lean have noted that the first pharmaceutical firms to enter a therapeutic market with a new or different drug compound enjoy a substantial advantage in controlling the market.[2] During the patent period, manufacturers use heavy promotion of the brand name to foster physician loyalty to that firm's product. After the patent has expired, a firm need only engage in "maintenance" advertising and promotion to keep the product in the minds of prescribing physicians. Antisubstitution laws also help the brand-name firm perpetuate the patent monopoly, at least to a degree. In some cases, manufacturers have also attempted to ward off competitive entry by marketing new versions of their old products and treating them as new innovations. Not surprisingly, many drug products have been able to maintain their

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1 Wertheim & Co., Inc., "Drug Industry: Current Perspective," (January, 1977) at 15 describes why entry has been difficult for imitators of Merck's Aldomet after its patent expired.

2 R. Bond & D. Lean, "FTC Staff Report on Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets," at vi (1977).

price premiums even after competitors have entered the market.[3]

As drug products come off patent, new competitors enter the market, though few are ever very successful. For some products, more than 50 producers have entered the market within a few years after patent expiration.[4] In a few cases, generic competition has had a substantial impact upon the price levels of leading brands as indicated by the following table submitted by the National Association of Pharmaceutical Manufacturers:

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3 Wertheim & Co., supra note 1, at 15:

> The financial impact of patent expiration traditionally has not been a serious negative. Competitive generic entries typically capture less than 10%-15% of market share, despite their lower prices, because the established brand is too well entrenched in terms of marketing, distribution and acceptance by physicians. Prices, therefore, do not usually decline materially. Moreover, economies of scale are much in favor of the established brand leader. New and improved formulations of old products usually carry premium prices, re-stimulate product consumption and maintain the line's profitability.

4 The following list indicates the number of companies entering the market for several drug products whose patents expired in 1966 and 1967:

New Manufacturers in 1969 of Drugs on Which the Patents Expired in 1966 or 1967

Brand Name	Generic Name	Sales of Brand(s) in 1966 ($million)	Number of New Complaints in 1969
Dramamine	Dimenhydrinate	4.8	11
Chlortrimeton	Chlorpheniramine maleate	5.8	48
Hydrocortone Cortef	Hydrocortisone	2.1	69
Meticorten Deltasone	Prednisone	2.0	63

Source: D. Schwartzman, Innovation in the Pharmaceutical Industry 255 (1976).

EFFECT OF GENERIC DRUGS IN THE MARKET PLACE ON THE PRICE OF THE BRAND NAME PRODUCTS:

1) METICORTEN TABLETS 5 mg. (SCHERING)
reduced from $17.50 per 100 to $2.25 per 100
Generic name is PREDNISONE

2) METICORTELONE TABLETS 5 mg. (SCHERING)
reduced from $17.50 per 100 to $10.80 per 100
Generic name is PREDNISOLONE

3) BRISTOL POLYCILLIN CAPSULES 500 mg.
reduced from $48.00 per 100 to $30.00 per 100
Generic name is AMPICILLIN

4) ERYTHROCIN TABLETS 250 mg. (ABBOTT)
reduced from $22.00 per 100 to $12.00 per 100
Generic name is ERYTHROMYCIN

5) ACHROMYCIN CAPSULES (LEDERLE)
reduced from $30.00 per 100 to $3.75 per 100
Generic name is TETRACYCLINE

6) THORAZINE TABLETS 100 mg. (SMITH, KLINE & FRENCH)
reduced from $9.00 per 100 to $5.40 per 100
Generic name is CHLORPROMAZINE

Source: Competitive Problems in the Drug Industry: Hearings Before the Subcomm. on Monopoly of the Senate Select Comm. on Small Business, 93d Cong., 2d Sess. 10268 (1974).

The most price competition after patent expiration has occurred in the area of antibiotics.[5] As patents expired on these products, numerous manufacturers entered with lower-priced generic versions, causing the innovators to lose market share and reduce their prices.[6]

In many cases, the most aggressive price cutters were firms with small market shares.[7] The history of Neomycin, an antibiotic originally supplied by Upjohn, illustrates how steep price reductions occurred as competition increased:

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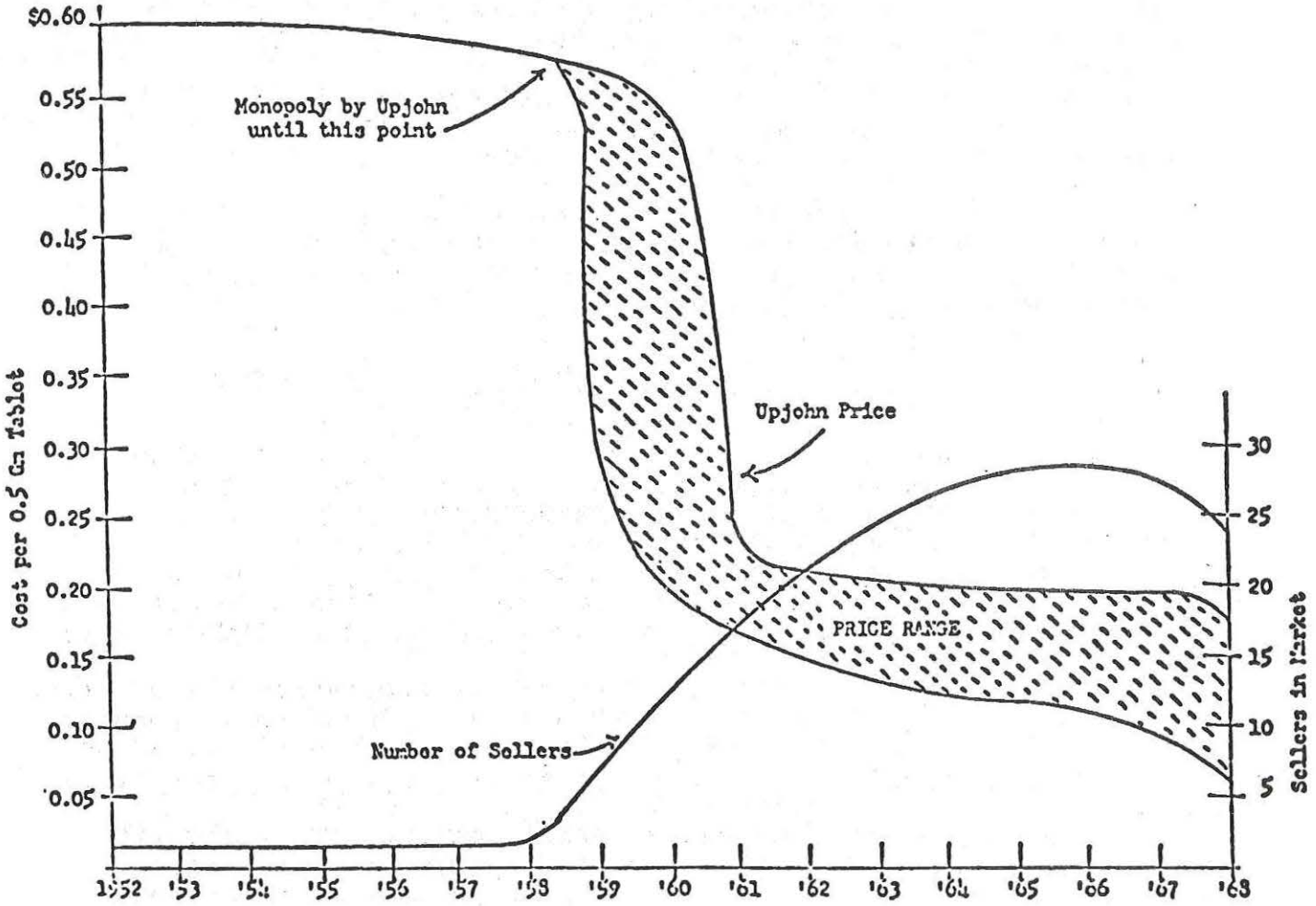
5 Schwartzman, supra note 4, at 255.

6 Id. at 251.

7 Id. at 298.

Price History of Neomycin - The Effects of the Loss of a Monopoly Position



Cited in John Robert Glennie, "Public Policy and the Pharmaceutical Industry: Potential Impact of Proposed Legislation," Unpublished Ph.D. thesis, George Wash. Univ. (February 1971), at 98. Reproduced with permission of the author.

But the vigorous price competition for multisource drugs characteristic of many antibiotics generally has not occurred in other therapeutic areas.[8] In these other areas, generic manufacturers generally failed to attract enough of a market to force the original manufactuter to lower its price significantly.[9] One reason brand-name manufacturers have been able to command a "premium" price for their products after they become generically available is because physicians continue to specify the innovator's brand when prescribing. When this occurs in a state where antisubstitution laws are in effect, the pharmacist is compelled to dispense the brand specified. Thus, as noted before, the continued use of the tradename in conjunction with such laws, enables the manufacturer to perpetuate the benefits derived from the patent monopoly.[10]

In any event, the innovator's brand-name product often continues to maintain its patent-period price, as well as to dominate the market, despite competition from numerous generic and "brand-generic" producers (to be discussed shortly). This is not to imply

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8 Two reasons why there may be more price competition in antibiotics are suggested in P. Brooke, Resistant Prices 32 (1975):

1. All antibiotics are batch certified by the FDA fostering greater physician confidence in the generic versions (this rationale assumes that doctors are aware of the batch certification process).

2. Approximately one-third of antibiotic use occurs in hospitals, many of which are cost-conscious and use a formulary.

See also Curran, Reynolds Securities, "Multi-Source Drugs: An Acceleration in the Use of Lower-Costing Substitutes," May 13, 1977, at 4.

9 Green, "Welfare Losses from Monopoly in the Drug Industry: The Oklahoma 'Antisubstitution' Law," 5 Antitrust Law & Econ. Rev. 97, 102 (1972).

10 Glennie, "Public Policy And The Pharmaceutical Industry: Potential Impact of Proposed Legislation," unpublished Ph.D. thesis, George Wash. Univ., February 1971, at 152.

that no price competition exists outside the antibiotic area, but rather that it is limited. Moreover, as Bond and Lean note, when price competition does occur it usually affects only the lower-priced products themselves and not the major brands.[11]

Thus, while price competition does occur after patent expiration for many drug products, in most instances factors such as physician brand loyalty and the existence of antisubstitution laws insulate the leading drug firms from its full effects.

2. Role of the Generic Manufacturer

a. Expanded Opportunities for Generic Drug Producers

Until recently, the opportunity for competition in the drug industry was limited. In the years following World War II, many of the popular products were still under patent. By the time their patents had ended, most of these products were obsolete and thus not suitable for imitation.[12] As late as 1966, there were generic versions available for only 15.5 percent of the top 500 prescription drugs.[13] Two contemporary trends--the increase in expiration of patents for popular drugs and the decline in the rate of introduction for new chemical entities--have changed the picture so that today over one-half of all prescriptions are written for multisource products.[14] Therefore, the opportunity for generic duplication has been greatly enhanced in just over a decade.

Moreover, this trend should continue over the forseeable future:

> The trend toward a greater availability of

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11 Bond and Lean, supra note 2, at 23. See Schwartzman, supra note 4, at 287-92 for a discussion of price competition in drugs other than antibiotics.

12 During the 1950's and 1960's the average life cycle for pharmaceutical products was only 22 months, due to the rate of innovation then. Nelson, Jr., "The Saliency of Price in the Acceptance of the Pharmacist substituting Chemically Equivalent Drugs on a Prescription," unpublished Ph.D. thesis, Univ. of Iowa, July 1973, at 14.

13 Green, supra note 9, at 110.

14 IMS America Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978, at 3. ["FTC Study".] For the 200 most prescribed drugs during 1977, 60% of new prescriptions and 54% of all prescriptions are written for multisource drugs.

> multiple source drugs is largely a consequence of the trends in new product innovation . . . In particular, with the number of new drugs being introduced annually down sharply from the early sixties, the sales of drugs coming off patent each year have significantly exceeded the sales of newly marketed drug introductions under patent protection. Hence, the number of drugs with multiple suppliers has steadily increased over time.[15]

Besides the loss of patent protection,[16] other reasons given for the trend toward selection of lower-cost generics include: (1) FDA sanctioning of generic equivalents as substitutes; (2) continued

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15 Grabowski & Vernon, "The Effect of Repealing Anti-Substitution Laws on Pharmaceutical Innovation," March 5, 1978, at 33 (paper presented to FTC).

16 Some Important Drug Products Which Will Lose Their Patent Protection Over the Period 1978-1980

Product	Company	Approx. 1976 Retail sales (millions of $)	Patent Expiration (year)
E.E.S.	Abbot	19.0	1978
Tanderail	Ciba-Geigy	8.0	1978
Ilosone	Lilly	35.0	1978
Decodron-oral	Merck	4.0	1978
Vibramycin	Pfier	30.0	1978
Ionamin	Pennwalt	20.0	1978
Tenuate	Richardson-Merrel	25.0	1978
Adactone	Searle	17.0	1978
Adactazide	Searle	45.0	1978
Darvon-new	Lilly	45.0	1979
Hygroton	U.S.V.	25.0	1979
Regroton	U.S.V.	13.0	1979
Mycolog	Squibb	25.0	1979
Kenalog	Squibb	10.0	1979
Garamycin	Schering-Plough	55.0	1980
Dyazide	Smith Kline	50.0	1980

Source: Curran, "Multi-Source Drugs: An Acceleration in the Use of Lower Costing Substitutes," Table 7, at 19-20.

Cited in Grabowski and Vernon, supra note 15, at 34.

repeal of antisubstitution laws; (3) promotion of lower-cost drugs by retail pharmacies since dollar margins are often greater than on brand-name drugs; (4) adoption of price control programs for government and third-party reimbursements of prescription costs; (5) expanding promotion of generic equivalents by major industry firms such as Smith Kline, Lederle, Parke Davis, Pfizer, Eli Lilly, and Squibb.[17]

A major impetus for generic products occurred with the inception of third party programs such as Medicaid, under which the cost of drug products to the retailer became an important factor. In addition, many hospitals using various formulary systems became cost-conscious in their choice of drug products. To take advantage of this trend, generic pharmaceutical houses began duplicating many of the widely prescribed pharmaceuticals that were no longer protected by patents.

b. The Generic Market Today

Currently, 600 to 700 drug companies either manufacture or distribute generic drug products. Most of these are small firms which do little or no research and development of new drugs. About 100 are major firms, including many large brand-name firms developing their own generic lines.[18]

In 1977, about one out of every eight (12.5%) new prescriptions was written generically, almost double the proportion in 1966 (6.4%).[19] Of course, nearly half the market is still single-source and therefore does not offer generic alternatives.[20] For the reasons mentioned previously in the discussion of price competition, more generic prescriptions are written for antibiotics than for any other therapeutic category.[21] Antibiotics account for six of the top ten generically-prescribed drugs. In fact, the leading four generically-written prescriptions are all antibiotics, and these four--ampicillin, tetracycline, pencillin VK, and erythromycin--account for a majority (50.5%) of all generically-

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17 James T. Doluisio, Dean, Univ. of Texas College of Pharmacy, "A Perspective on Bioequivalence/Bioavailability," Presented to APhA Academy of Pharmaceutical Science, Phoenix, Arizona, Nov. 14, 1977, at 5.

18 Frost and Sullivan, Inc., "The Generic Drug Market," January 1976.

19 Pharmacy Times, April 1978, at 43.

20 FTC Study, supra note 14, at 3.

21 Brooke, supra, note 8, at 32.

written prescriptions (not including refills).[22]

Thus, the impact of generic products in terms of price competition and market share has been limited mostly to antibiotics.[23] In other therapeutic areas, generic products have so

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22 Pharmacy Times, supra note 19, at 42, 48. Of the top 20 generically prescribed drugs, 7 are antibiotics. Of the top 200 drugs, 18 were prescribed generically in 1977.

23 The tables below show the degree of generic prescribing for selected antibiotic and non-antibiotic products:

PERCENTAGE SHARE OF GENERIC PRESCRIPTIONS

BY PRODUCT FOR THEIR RESPECTIVE THERAPEUTIC CATEGORIES

1974-1976

Product	Rank	1974	1975	1976
Ampicillin	1	49.3%	55.9%	61.8%
Tetracycline	2	40.4	45.2	48.7
Erythromycin	4	19.5	17.8	25.3
Prednisone	5	40.3	43.8	47.2
Penicillin VK	6	14.6	18.7	22.6
Meprobamate	9	41.6	46.4	50.5
Penicillin G	11	36.7	45.1	44.5
Hydrochlorothiazide*	13	5.9	8.4	12.3
Amoxicillin	15	8.2	13.3	20.2

* As a % of Hydrodiuril prescriptions
c IMS America, N.P.A. data

GENERIC PRESCRIPTIONS

AS A PERCENTAGE OF PRESCRIPTION MAJOR BRANDS

1974-1976

Brand Name	Manufacturer	1974	1975	1976
Pavabid	Marion Labs.	5.7	9.8	12.6
Tofrauil	Geigy	0.4	2.6	4.6
Darvon Cmpd 65	Eli-Lilly	0.5	0.7	1.8
Thorazine	Smith Kline	0.8	2.2	3.7
Darvon	Eli-Lilly	2.3	5.0	5.7
Diuril	Merck	1.1	1.0	2.9
Antivert	Pfizer	0.8	1.0	1.7

(Footnote Continued)

far not been very successful in competing with the major brands.

Moreover, the rate of generically-written prescriptions is not an accurate measure of the number of generically dispensed prescriptions since a generically-written prescription may be filled with a brand-name product.[24] Such a prescription transfers the choice of product selection from the physician to the pharmacist who may for reasons such as quality concern, inventory limitations, presence of antisubstitution laws, or type of fee system utilized (mark-up) fill the prescription with a branded product.[25]

There is limited evidence indicating a trend toward using products from the generic houses to fill generically-written prescriptions. A recent survey of pharmacists' preferences in filling generically-written prescriptions notes that while large companies continue to dominate, the products of smaller companies are showing up "more prominently."[26] Purepac, for example, is the preferred source for filling generically-written meprobamate prescriptions.[27] And a study reported by a Pharmaceutical Manufacturers Association committee on the effects of state antisubstitution laws reveals that pharmacists in California and Florida heavily favor non-PMA firms (such as Zenith, Sheraton, and Rexall) when substituting. Although non-PMA firms normally have only a five percent share of the market, products of non-PMA firms were used over 60 percent of the time when drug product selection occurred.[28]

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23 (Footnote Continued)

Source: Curran, Reynolds Securities, Inc., "Multi-Source Drugs: An Acceleration in the Use of Lower Costing Substitutes," May 13, 1977, at 4, 5.

24 Glennie, supra note 10, at 157.

25 Brooke, supra note 8, at 33.

26 Pharmacy Times, September 1978, at 56.

27 Pharmacy Times, March 1977, at 59.

28 PMA Committee on the Effects of Amendments to State Antisubstitution Laws, "Preliminary Report on the Effect of the Repeal of Antisubstitution Laws in California, Michigan, Florida and Delaware," Apr. 25, 1977. Products of non-PMA firms were utilized in 63-67% of the prescriptions subject to substitution in California during May-October, 1976, and in 61% of the substitutions occurring in Florida during October-December, 1976.

Obviously these two trends--increasing legalization of drug product selection and the selection by pharmacists of non-PMA products -- will have an impact upon the sales and profits of the major firms. The marketing response to increasing substitution will be discussed next.

c. Types of Generic Products

Most generic houses produce their versions of popular selling drugs. In addition to disclosing the firm's name, most generic houses identify their products on the basis of the generic or established name, rather than a proprietary or brand name. Such a product--one that has no proprietary name--is referred to as an "unbranded" generic product.

Recently some of the major pharmaceutical houses have begun marketing lines of generic equivalents often referred to as "branded generics" - drugs which copy existing drugs but use the generic name as part of a brand line of products (e.g., Smith Kline's "SK-AMPICILLIN").[29] Usually "branded generics" are priced at an intermediate level, below that of the originator's product, but above the prices charged for unbranded products. One of the first major firms to enter the "branded generic" field was Smith, Kline, and French, which began marketing its "SK-Line" for eight "high volume, standard pharmaceuticals" in 1971. The SK-Line is priced about 25 percent below that of the leading brand names.[30] Other major firms with "branded generic" lines are Lederle, Parke Davis, Pfizer, and Squibb.

Branded generics function as a hybrid type of drug product in terms of marketing and pricing strategy. They are cheaper than leading brand-name products because they require little R & D investment. They command a higher price than unbranded generics because of their distributor's reputation for quality and in some cases because the distributor offers pharmacists a greater variety of services.[31]

Most unbranded generic drug products are produced by the generic houses. The major brand-name manufacturers, on the other hand, dominate the market for branded generics. Ironically, however, one of the largest brand-name manufacturers, Eli Lilly, also

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29 Chain Store Age, April 1973, at 70.

30 Am. Druggist, Sept. 20, 1971, at 13.

31 Most small firms do not provide extended payment terms and often require cash on order. Curran, supra note 8, at 6.

is the largest producer of unbranded drug products.[32]

The entry of major firms into the generic market, even though on a somewhat different level, does indicate a brighter future for generics.

d. Promotion of Generic Products

Most generic manufacturers compete primarily on the basis of price.[33] Because they neither engage in original product research nor hold patents, these firms are unable to take advantage of the product differentiation opportunities exploited by brand name manufacturers. There are three major reasons that explain why generic firms engage in little promotion.

First, antisubstitution laws discourage promotion of generic products to pharmacists. For in states where such laws are in effect, there is less opportunity for source selection by the pharmacist. In these states pharmacists can engage in source selection only for generically-written prescriptions. Since the enactment of drug product selection laws, there has been a significant increase in advertising by generic houses.[34]

Second, as indicated earlier, the generic name generally is longer and more difficult to remember than the proprietary name whose rationale is its rememberability. (See Ch. II.C.1., supra). To the extent generic names are more cumbersome than their counter-

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32 Prescription Drug Labeling and Price Advertising: Hearings on H.R. 882, et al., Before the Subcomm. on Consumer Protection and Finance, House Comm. on Interstate and Foreign Commerce, 94th Cong., 2d Sess. 213 (1976):

MANUFACTURERS OF UNBRANDED GENERICS	PERCENT
Eli Lilly	11
Darby	6
Zenith Labs	6
Parke-Davis	6
Generic Corp. of America	5
Purepac	4
Interstate Drug	3
Elkin-Sinn	3
ICN	3
Rachelle Labs	3
All others	50

33 Glennie, supra note 10, at 151.

34 See Millman, "Battle lines harden in fight over generics," Advertising Age, Feb. 13, 1978, at 76.

parts, firms promoting generic drug products find themselves at a relative cost disadvantage compared to the producers of the original drugs. When coupled with the disincentive against promotion created by the ability of competitors to free ride, the complexity of generic names explains why relatively little money is being spent by manufacturers promoting generics.

Third, a generic manufacturer does not have a strong incentive to engage in promotional activities designed to persuade doctors to prescribe generically. In fact, the manufacturer may have a disincentive because its efforts would reward all generic manufacturers of the product, including its "free riding" generic competitors. Having persuaded a doctor to prescribe generically, the generic manufacturer would have no assurance that pharmacists who filled the prescription would only dispense its product, particulary if a non-advertising generic manufacturer offered lower prices.

Moreover, even in states where drug product selection laws are in effect, generic firms do not engage in individual product promotion, since the product is not unique from that of rival producers.[35] Instead, both branded-generic and unbranded-generic houses promote lines of products with an emphasis on the name and policy of the producer. Although differences in promotional efforts exist between these two types of generic producers, usually the main target of all generic advertising is the pharmacist who selects the source used to fill generic prescriptions.

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35 Although published data are not available, it appears that the marketing costs for manufacturers of low-cost generic drugs are minimal, and consists mainly of distribution and direct mail advertising expenses. Few such companies engage in substantial medical journal advertising or promotional activities, primarily because product promotion of generically labelled products is illogical. Advertising such a generic name as meprobamate, for example, may popularize the use of the product. But since generically-written prescriptions can be filled with any brand of the product, the small market share of firms selling under generic name means that benefits resulting from their own promotional outlays would probably be uneconomic.

U.S. Dept. of Health, Education and Welfare, Office of the Secretary, Task Force on Prescription Drug, The Drug Makers and the Drug Distributors 20 (1968).

3. Production of Drug Products by Different Manufacturers

Because manufacturers produce drugs for each other without disclosing who truly did the formulating, brand names can be misleading. In some instances, major branded manufacturers rely on small generic producers to provide them with bulk or finished dosage drugs. These practices not only can lead to confusion, but they can at times mislead those who seek to rely on the reputation of the actual manufacturer. Moreover, to the extent that drugs distributed by brand-name companies are actually manufactured by generic firms, this undercuts arguments that branded products are superior.

Since the Food, Drug, and Cosmetic Act does not require that drug labels contain the name of the actual manufacturer,[36] any firm that participates in the preparation of the drug product, even a repackager, can apply its brand name to a drug. In recent testimony, FDA's Commissioner Donald Kennedy observed:

> Drug marketing follows many patterns. A formulator may make a product, and sell it only under his own label; he may also have a trade name and a generic line selling it both ways. He may also sell this product to other drug firms; or have them make the product for him. So a formulator may also be a repacker, or an own-label distributor at different times under different circumstances.[37]

According to FDA, many manufacturers, for example, employ the so-called "man-in-the-plant" technique whereby a drug company rents the facilities of another firm (usually a generic house) and places a representative at the production site to oversee production.[38] On the basis of this practice, some manufacturers put their name on the label of a product which they may not have produced, but merely repackaged or distributed. In response to this practice, FDA has proposed regulations to identify the actual manufacturer of a given drug product.[39]

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36 See Ch. XI., infra.

37 Donald Kennedy, Commissioner, Food and Drug Administration, Statement Before the Subcomm. on Monopoly, Senate Select Comm. on Small Business, Nov. 14, 1977.

38 Id.

39 43 Fed. Reg. 45614 (1978).

Often, one manufacturer will provide the same drug to a large number of firms marketing under a wide variety of brand and generic names.[40] Bristol Laboratories, for example, manufactures 70 percent of the ampicillin produced in the United States, but markets only 23 percent of it under its trade name.[41] The rest is sold to Smith Kline, Parke Davis, and Upjohn, who put their own trade names on it (SK-Ampicillin, Amcill, and Pensyn) and then sell it for less than Bristol.[42] Mylan Laboratories produces erythromycin for Smith Kline, Pfizer, Parke Davis, and Squibb, who distribute it as SK-Erythromycin, Pfizer-E, Erypar, and Ethrill respectively at differing prices.[43]

Some major firms, on the other hand, manufacture products for small (or generic) companies. Hoffmann-LaRoche, the brand-name manufacturer of sulfisoxazole (gantrisin) also sells it to numerous generic houses.[44] Lederle Laboratories, on the other hand, distributes 83 drugs in their generic line, all but two of which are manufactured under contract by outside generic firms.[45]

For most drug products, the number of distributors far exceeds the number of actual manufacturers or formulators. In Congressional testimony, Commissioner Kennedy submitted a list comparing the number of firms producing each of 50 drugs with the number of firms distributing them. Ampicillin, for example, is produced by 24 formulators, but available under 224 product labels. Other products on the list include: conjugated estrogen products (219 labels, 45 producers); tetracycline (402 labels, 74 producers); propoxyphene hydrochloride (117 labels, 18 producers); potassium chloride (26 labels, 1 producer).[46]

All of this means, of course, that doctors often do not know that the brand-name product being prescribed is manufactured by

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40 Simmons, "Brand vs. Generic Drugs: It's Only a Matter of Name," FDA Consumer, March 1973, at 7.

41 Hearings on Prescription Drug Labeling and Price Advertising, supra note 33, at 22.

42 Newsletter, Council on Econ. Priorities, CEP Publication N5-1, Jan. 6, 1975.

43 Id.

44 New York State Assembly's Office Legislative Oversight and Analysis, Are Generics Safe?, 1978, at 54.

45 Id. at 167.

46 Kennedy, supra note 37, at 8, Appendix.

another firm.[47] By disguising the true source of production, and placing their own label on the product, large brand-name firms insulate their products from price competition.[48]

The extent to which manufacturers produce for each other varies. About 70 percent of Zenith Laboratories' production, for example, is for private labeling.[49] Less than 10 percent of Philips Roxanne's production, on the other hand, is for other firms.[50] Merck and Squibb claim that none of their output is marketed by other firms,[51] while Ciba-Geigy had 74 percent of its pharmaceutical production in 1976 sold by other firms in either branded or unbranded form.[52]

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47 Not every such arrangement disguises the true relationship. Philips-Roxanne Laboratories, for example, produces 18 different products for Smith, Kline and French. The labels for these products state that they were manufactured by Philips-Roxanne Laboratories and distributed by SKF. (Conversation between Gerald C. Wojta, President, Philips-Roxanne Laboraties, Inc., and Robert Zwirb, FTC, Feb. 2, 1978). Lederle also identifies the actual manufacturer on its labels. Are Generics Safe?, supra note 44, at 167.

48 Kennedy, supra note 37, at 8-9. This is true no matter who is the actual supplier. Where the product was produced by a smaller generic firm, it is important for brand name companies to have their name appear on the label in order to command a higher price. When the reverse happens, i.e., where the brand name large firms provide finished products to generic firms, "the larger firm has little interest in disclosing the fact that a competitor is marketing a product produced by a larger firm, especially when it sells at a lower price." Kennedy, id. at 9.

49 Conversation between Phillip Blick, Vice President, Marketing Zenith Laboratories, Inc., and Robert Zwirb, FTC, Feb. 3, 1978; conversation between Kevin Rooney, Vice President, Regulatory Affairs, Zenith Labs, Inc., and Robert Zwirb, FTC, Feb. 3, 1978.

50 Conversation between Gerald C. Wojta, President, Philips-Roxanne Laboratories, and Robert Zwirb, FTC, Feb. 7, 1978.

51 Letter from D.S. Brooks, Counsel, Merck, Sharp & Dohme, to Peter D. Holmes, FTC, Feb. 23, 1978; letter from Robert C. Johnson, Assistant General Counsel, E.R. Squibb, Inc., to Peter D. Holmes, FTC, Mar. 31, 1978.

52 Letter from Hugh A. D'Andrade, Vice President - Administration and Counsel, Pharmaceuticals Division, Ciba-Geigy Corp., (Footnote Continued)

Manufacturer-distributor relationships, nevertheless, at times are confusing and complex. Moreover, these relationships are not always accurately reflected on the product label. If physicians (who desire to restrict their prescriptions to particular brands) and pharmacists (who desire to select among competing products) are expected to rely on a manufacturer's reputation[53] then they ought to be able to know the identity of the actual manufacturer. Currently, this is not always possible.[54]

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52 (Footnote Continued)

to Peter D. Holmes, FTC, Apr. 6, 1978. Ciba-Geigy sales of prescription drugs sold by another firm has increased dramatically in the past seven years:

1970	15%
1971	40%
1972	64%
1973	47%
1974	64%
1975	74%
1976	74%

53 The problem is not so much one of reputation, as one of disclosure. A firm's reputation is at stake even if it did not actually manufacture a product bearing its name. The head of FDA's Bureau of Drugs Antibiotic Certification Brand remarked about the "man-in-the-plant" situation:

> When a company puts their name on the label, they are assuming responsibility for that product. God forbid someone should have an adverse reaction from the product. Somebody will get sued and it is going to be the company whose name is on the label. They are going to take responsibility for the product and they are going to put their people in there to insure that the product comes out the best way they know how to make it.

F-D-C Reports, Sept. 11, 1978, at 14.

54 See Ch. XI., infra.

CHAPTER III. THE PHYSICIAN'S ROLE

The physician is the principal participant in the prescribing decision and in states with antisubstitution laws the physician's decision has added significance. The physician diagnoses the patient's condition and determines which drug, if any, will improve it. The doctor must also decide whether to prescribe a drug by its generic name or by a particular brand name. If the physician prescribes generically the pharmacist is required to select the particular product to be dispensed. If the physician prescribes by brand name in a state with an antisubstitution law the pharmacist is required to dispense that particular brand-name product.

Antisubstitution laws are widely attacked because it is alleged that many physicians prescribe by brand name because of convenience or habit and because they place a low priority on prescription drug prices. This section will explore the extent to which these factors explain brand-name prescribing. We will examine the two most significant influences on the practicing physician's knowledge of drugs: medical school training and promotion by pharmaceutical manufacturers. We will also consider evidence of doctors' lack of knowledge of specific drug prices, the low priority they give price when selecting a drug product, the rememberability of brand names versus generic names, and other factors that explain why they usually prescribe by brand name. Our evaluation of this evidence leads us to conclude that many physicians do prescribe by brand name for reasons other than a preference for a particular brand-name product and that enactment of drug product selection laws will make it easier for those physicians who use brand names out of convenience with little regard for price to prescribe generically.

A. The Physician's Medical School Training in Drug Products and Drug Therapy

To practice medicine in the United States a doctor must successfully complete a course of studies at an accredited medical school, a one-year residency in an approved hospital and the three National Board of Medical Examiners' certification tests.[1] To varying degrees, physicians receive training in the use of drugs throughout this process. The program at an approved medical school includes a wide spectrum of theoretical and clinical education leading to the award of the M.D. degree.[2] Traditionally,

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1 The specific requirements are more detailed and vary by state.

2 Liaison Committee on Medical Education, "Accreditation (Footnote Continued)

during the second year of medical school, the student takes a course in pharmacological theory seting out the principles of drug action.[3] In the first part of the National Board certification, a two-day written multiple choice examination, one-seventh of the questions concern these general principles of pharmacology.[4] Invariably, pharmacological considerations also are considered in other courses, such as obstetrics or gynecology.

The last two years of medical school emphasize clinical experience. One commentator has maintained that some knowledge about pharmacology and medication is acquired in every clinical course.[5] But the clinical emphasis on pharmacology varies.[6] Some critics of medical education believe doctors are not properly trained to meet the changes in drug therapy that they will confront throughout their careers. They believe the greatest weakness in the medical school curriculum lies in the area of clinical pharmacology.[7] The increasing attention given clinical pharmacology at many medical schools[8] and the now widespread use of generic names in pharmacology courses[9] indicate these concerns may be

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2 (Footnote Continued)

of Schools of Medicine: Policy Documents and Guidelines," adopted Mar. 31, 1975, at 3.

3 B. Barber, Drugs and Society 40 (1967).

4 National Board of Medical Examiners, "Bull. of Information and Description of Examination," at 17 (1977).

5 Barber, supra note 3, at 41.

6 Hearings on HB 4145 Before the Michigan Senate Comm. on Agriculture & Consumer Affairs, April 1974, at 8, 23 (statement of Richard Penna).

7 Hearings on S 1831 Before Subcomm. on Health and Scientific Research of the Senate Comm. on Human Resources, 95th Cong., 1st Sess., at 1-4 (prepared testimony) (July 27, 1977) (statement of John A. Oates); Biron, "Dosage, Compliance & Bioavailability in Perspective Drug Equivalency," The Scientific Evaluation of Drugs 23 (1974); and Lasagna, "Problems of Drug Development," 145 Science 362-367 (1964).

8 Task Force on Prescription Drugs, Dept. of Health, Education, and Welfare, The Drug Prescribers 8 (1968); Barber, supra note 5, at 41-44.

9 Administered Price Hearings on S. Res. 238 before Subcomm. on Antitrust and Monopoly, Comm. on the Judiciary, U.S. Senate., 86th Cong., 2nd Sess., 1960, at 11871.

well placed. On the other hand, most physicians continue to receive clinical experience with drug products during internship and residency in an approved hospital. Regardless of the merits of this controversy, two points about physicians' pharmacological education bear emphasis:

(1) although physicians receive training in clinical application, they receive little instruction about the relative efficacy and retail cost of the different sources of off-patent drugs; and

(2) physicians' pharmacological training in medical school, no matter how rigorous, will need supplementation throughout their careers as drug therapy improves.

B. The Physician's Continuing Medical Education (CME)

Physicians supplement their pharmacological training by attending continuing medical education programs, reading medical journals and drug product advertising, visiting with pharmaceutical sales representatives or detailers, and consulting with pharmacists.

Over thirty states require continuing medical education of physicians. According to the Continuing Medical Education Fact Sheet, a 1977 publication by the American Medical Association, 15 states do or in the near future will require continued membership in state medical societies and 21 states do or will require re-registration of the license to practice medicine.[10] These requirements of medical society membership or re-registration mandate that physicians engage in specified amounts of accredited and non-accredited CME activities.[11] Because of their flexible nature, none of these required CME programs guarantees that physicians will be exposed to pharmacology and it is unclear how many practicing physicians do receive continuing education in pharmacology.

While the medical society and state continuing education programs are growing in importance, the most significant sources of drug product information to practicing physicians are the medical journals, brand-name advertisements and representatives of the pharmaceutical manufacturers. Every year drug makers spend upwards of a billion dollars on these and other promotional activities.[12]

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10 American Medical Association, "Continuing Medical Education Fact Sheet," Sept. 1, 1977.

11 Id. at 8-9.

12 See discussion of promotional expenditures Ch.II. C., supra. It should be noted, however, that the pharmaceutical manufac-
(Footnote Continued)

One of the most important sources of continuing medical education are journals and journal advertising. In 1973 there were 440 medical journals of widely different content published in the U.S.[13] Today there are about 1000 journals and this figure may continue to grow.[14] The typical doctor is said to receive between seven and 20 journals a month.[15] Many of these carry substantial amounts of drug product advertising. As a whole, the pharmaceutical industry spends between 15 and 22 percent of its promotional budget of journal advertising or in the neighborhood of 150 to 200 million dollars a year.[16]

Many critics of the industry believe that journals and their advertising lead to an undue emphasis on brand name drugs. The FDA requirements that labels and advertising contain generic names it is said, can be largely undercut by the clever use of coloring and typography to make the trade name stand out and capture the reader's attention.[17] Also, those journals which provide disinterested comparative analysis of drug efficacy are thought not to be widely disseminated.[18] Similarly, journals provide physicians only limited exposure to retail prices.[19]

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12 (Footnote Continued)

turers do fund several projects unrelated to particular product including the support of various fellowships in clinical pharmacology. See, e.g., "1976 Annual Report Pharmaceutical Manufacturers Association Foundation, Inc."

13 Garland, "Dissemination of Information on Drugs to the Physician", Drugs In Our Society 205 (1964).

14 Advertising Age, Feb. 13, 1978, at 72.

15 Compare, Caplow & Raymond, "Factors Influencing the Selection of Pharmaceutical Products." 19 J. Marketing 18,23 (1954) with Advertising Age, Feb. 13, 1978, at 74.

16 Pharmaceutical Manufacturers Association, "Questions and Answers, Prescription Drug Marketing" (May 1977); Advertising Age, Feb. 13, 1978, at 70.

17 "Drug Amendments of 1962 - Generic Name Prescribing: Drug Price Panacea?" 16 Stan. L. Rev. 649, 659 (1974).

18 Garland, supra note 13, at 209; Drug Prescribers, supra note 8, at 11; Counsel on Economic Priorities, "In Whose Hands?", 4 Econ. Priorities Report 28 (1973).

19 Drug Prescribers, supra note 8, at 11.

Another important source of drug advertising by brand-name manufacturers is direct mail. Although in recent years direct mail expenditures for all therapeutic products have declined, total annual expenditures for direct mail approach 40 million dollars and the top ten pharmaceutical companies yearly spend over 18 million dollars.[20] Competing for this business are several companies some of which specialize in direct mailing in health care.[21] These companies rely on computer-stored lists which contain such specifics as type of practice, year started practice, specialization brands used, and attitudes toward certain aspects of medical practice. Although apparently more expensive per reader than journal advertising, the direct mailing companies claim that they reach a more select audience.[22] One direct mailing company claims that 43 percent of the people who receive its mail read it.[23] A typical mailing by a pharmaceutical company, according to Advertising Age, may each cost 35 cents and some companies annually send out 12 to 20 mailings of 35,000 to 40,000 pieces.[24]

Perhaps the most important factor in disseminating drug information to doctors is the detailer system. The largest portion, almost 70 percent, of the pharmaceutical industry's promotional budget is devoted to detailers.[25] These company sales representatives provide product information to physicians, pharmacists, and other health professionals.[26] Moreover, according to audit estimates the total amount spent on detailing activities increased 36 percent in the last four years.[27] In 1976, for example, drug companies spent $51 million to detail antibiotics, $27 million for tranquilizers, $24 million for antiarthritic drugs and $20 million for non-narcotic analgesics.[28] In 1977, an estimated 24,000 detailers provided approximately 200,000 physicians with various sorts of written and verbal information about several

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20 Chew, "Medical Mailers Seek Way Out of Doldrums." Advertising Age, Feb. 13, 1978, at 73.

21 Id.

22 Id.

23 Id. at 74.

24 Id.

25 Supra note 16.

26 Id.

27 Advertising Age, Feb. 13, 1978, at 68.

28 Id. at 70.

thousand drug products.[29] Detailers come from mixed educational backgrounds and, according to Advertising Age, as a group are not highly paid.[30] Most major drug companies have internal training programs designed to equip the detailer with technical information.[31] Besides working with doctors, detailers organize seminars and exhibits for hospital and medical school personnel. They also forward doctors' complaints about drug efficacy, complications, and interactions.

The well-funded and far-flung detailer system affects most doctors' prescribing decisions. For example, the AMA survey Opinions of AMA Members 1973 found that detailers have a "moderate" or "marked" influence on the prescribing habits of 50 percent of the doctors in its sample.[32] Similarly, physicians' mail or detailers were found to be the first sources of information about a new drug for 74 percent of all physicians.[33] Neither is there any dispute that detailers recommend only brand-name products and seldom provide price information. Drug companies' promotional expenses are aimed at maximizing the use of brand-name products.[34] And an industry spokesman candidly stated:

> [W]hat the detailman does is seek to persuade the doctor that when he writes a script he should write it for the detailman's product in preference to another product. Indeed, that is his job.[35]

Undoubtedly, the large expenditures devoted to detailing and other promotion by drug manufacturers produce a system in which practicing physicians are most familiar with drugs by their brand names.

Finally, a limited albeit potentially important source of prescription drug information to physicians is the pharmacist.

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29 Id. at 67.

30 Id. at 68.

31 See, e.g., PMA, "Guidelines for Programs of Technical Education for Training for Pharmaceutical Representatives," Oct. 16, 1975.

32 "In Whose Hands?," supra note 18, at 28.

33 Advertising Age, supra note 20, at 68.

34 Willig, "The Prosubstitution Trend in Modern Pharmacy Law," 6 U. Mich. J.L. Reform 1,16 (1972).

35 Furland, Chairman PMA, Pres., Squibb Corp. "The Pharmaceutical Industry faces the Future," Address, Apr. 3, 1974, at 7.

Although some doctors find the pharmacist to be a reliable source of prescription price information, most doctors seldom consult with pharmacists.[36] In a recent survey only 5.5 percent of the physicians and 5.7 percent of the pharmacists said that doctors consult with pharmacists "very often."[37] About 35 percent of the physicians and 39 percent of the pharmacists said "occasionally," while over one half of both groups characterized the rate of consultation as "seldom" or "never."[38]

C. The Role of Brand Names and Retail Prices in the Physician's Prescribing Decision

We turn now to quantitative evidence bearing on the influence these sources of drug information have on the physician's decision to prescribe by brand-name. As we have seen, the physician's formal pharmacological training usually does not include retail price information, and his continuing education relies predominantly upon brand-name information supplied by the pharmaceutical manufacturers. These facts indicate the limited role of retail prices and the large role of more convenient brand-names in most physicians' prescribing decisions.

Estimates vary, but the prevalence of prescribing by proprietary name is undisputed. The rate of brand name prescribing has soared from ten percent in 1909 and 42 percent in 1929 to about 90 percent in 1972.[39] Much of this meteoric rise may reflect the shift, described earlier, from drugs compounded by community pharmacists to the sophisticated brand-name products of the large drug makers. Nonetheless, it is commonly thought that the brand-name promotion described above together with unawareness of drug prices by physicians explain much of this phenomenon with respect to multisource drugs.[40] We will now

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36 Am. Druggist, November 1976, at 27.

37 20 Am. Med. News 5 (1977).

38 Id.

39 Compare, Richard G. Kedersha, "The Impact of Brand Name Prescription Drugs on the Traditional Practices of High Prescription Pharmacies in Northern New Jersey", 1964 (unpublished Ph.D. thesis, New York Univ.), at 64 with Am. Druggist, Feb. 1, 1974, at 44.

40 The summary and analysis of the hearings on Competitive Problems in the Drug Industry put it this way:

> Firms which have acquired patent pro-

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consider evidence demonstrating that drug product selection will make it easier for physicians more familiar with brand-names and preoccupied with their other medical duties to delegate product selection to pharmacists.[41]

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40 (Footnote Continued)

> tection . . . are free to promote the uses of the product without concern that other manufacturers will supply the same drug while the patent is in force. During this patent period, company sales representatives meet personally with prescribers to call attention to the drug. . . . The prescriber sees the product advertised widely in his professional journals. A variety of reminder advertisements and other materials are mailed to the practitioner and the detail man may visit the prescriber again and again to call attention to the company's new product. Each time the drug is discussed, it is identified by its trade-name, rather than by a generic name which identifies the active drug ingredients contained in the company's particular formulation.
>
> Over a period of time, physicians prescribing this product become familiar with its uses and limitations first-hand. . . . In any event, the practitioner becomes accustomed to thinking of, and ordering the drug by, its trade-name each time he finds it necessary to prescribe it for one of his patients. Before Subcomm. on Monopoly, Comm. on Small Business, U.S. Senate, 90th & 91st Cong., Nov. 2, 1972, at 7.

41 There is a much broader controversy over promotion in the drug industry which is not germane to the present discussion. The drug industry and its critics vehemently disagree, for example, on whether brand name promotion (1) causes overutilization of prescription drugs and (2) creates an irrational brand loyalty among physicians that hampers competition. The drug manufacturers maintain that detailing and other promotional efforts lead to better informed prescribing and that many promotional abuses are held in check by FDA regulations, the expertise of doctors, and the importance of reputation to both the detailer and his company. See PMA, "Purpose and Activities of Pharmaceutical Company Sales Representatives (Detailmen)," May 1974, at 3-4 and "How Physicians Rate Drug Companies," Product Management, at (Footnote Continued)

First, because physicians are busy people, many prescribe a brand name out of convenience; in effect the brand name becomes a shorthand version of the generic name. For example, twenty percent of 60 physicians surveyed in a Wisconsin study explained that their decision whether to prescribe by brand or generic name was due to convenience or habit.[42] Similarly, a PMA Committee re-

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41 (Footnote Continued)

30 (April, 1974). The PMA contends that although detailers are an important source of information, they have little effect in the physician's final decision to prescribe a particular drug. Advertising Age, supra note 20, at 7; "Purpose and Activities," supra, at 4-7.

Numerous drug industry critics, on the other hand, lament that this predominant source of doctors' drug product information is not provided by more disinterested parties. "In Whose Hands," supra note 18, at 28. Pointing to evidence of high profits for the drug industry, critics believe that these large sums spent on detailing grossly distort physician's prescribing habits. They also point to attempts by detailers to circumvent FDA warnings. One often cited example involved the National Research Council's recommendation that the chloramphenicol label warn that the drug "not be used indiscriminately or for minor infections" because a potentially fatal blood disease had occasionally been found to occur with its use. Parke Davis distributed a letter telling its detailers of the new warning label while insisting that the FDA and National Research Council had officially cleared the product with no restrictions. The letter appears to directly contradict the spirit if not the letter of the NRC's recommendation. Burack, The New Handbook of Prescription Drugs 15-16 (1976).

Neither drug product overutilization nor irrational brand loyalty among doctors, however, need be addressed here because neither issue is directly relevant to the generic substitution debate. The repeal of antisubstitution laws will not affect the physician's prerogative to decide when to prescribe nor can it override the physician's judgment to require that prescriptions be filled with a specific brand. Drug product selection laws need not alter either the flow or the reliability of the information disseminated by detailers. They will make it more convenient for physicians who customarily prescribe by brand name to delegate product selection authority to pharmacists.

42 Hammond & McCormick, "Some Economic Considerations in Generic and Brand Prescribing," 5 Med. Marketing & Media 14 (1970).

port found that except for old products that have lost or never had a brand image, convenience and habit are very strong secondary reasons for prescribing brands.[43] Furthermore, individual physicians have noted the important role convenience plays. Dr. Michael Halberstam, author of several books and articles, and nationally syndicated columnist on health, admitted, "Sometimes I prescribe by brand name because I don't remember the generic name."[44] Indeed, Dr. Halberstam supported drug product selection laws in part because he believed they could "obviate the problem of physicians forgetting the generic name."[45] (For a discussion of why generic drug manufacturers do not actively promote to physicians and for examples of how cumbersome generic names can be see Chapter II. D., supra).

Second, many doctors place a low priority on price when writing prescriptions. It is well established that most doctors are not familiar with specific drug prices. Although some doctors are aware that unbranded products are lower priced,[46] when it comes to specific drug prices the vast majority acknowledge their ignorance. In a Philadelphia County survey designed to measure physicians' knowledge of drug prices, over 32 percent of the respondents from a diversity of practices replied that they had no idea of drug prices of commonly prescribed drugs.[47] Moreover, on a scale of one to five, nearly two-thirds of the remaining respondents ranked their knowledge of drug prices in the two lowest categories.[48] The same study measured physicians' objective knowledge of drug prices. Less than a third of the responding physicians correctly estimated (to within 20 percent) the price of drugs commonly prescribed in their respective specialties.[49] Furthermore, two and a half times as many incorrect answers

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43 PMA, Preliminary Report on the Effect of the Repeal of Antisubstitution Laws, Apr. 25, 1977.

44 "Generic Drugs," The MacNeil/Lehrer Report, Apr. 28, 1977, at 5.

45 Id. at 7.

46 Jerome Brown Communication Inc., "Antisubstitution Attitudes Among Physicians" (undated), at Question 1.

47 Fink & Kerringan, "Physician's Knowledge of Drug Prices," 1 Contemp. Pharm. Prac. 18, 19 (Summer 1978).

48 Id.

49 Id.

underestimated the price as overstated the price.[50] Using a similar technqiue, an earlier study of physicians in Palo Alto, California attempted to measure doctors' knowledge of prices. While a clear majority of the physicians indicated that they considered drug costs when prescribing, only a third could estimate the drug price to within 20 percent.[51] Finally, another survey found that neither physicians nor pharmacists believed that most doctors knew retail drug prices. Eighty-four percent of the pharmacists and 62 percent of the physicians said most physicians do not know the cost to the patient for drugs they commonly prescribe.[52]

This evidence that doctors lack knowledge of specific prices does not establish that they should spend more of their valuable time learning drug prices. Indeed, to do so may be an inefficient use of their time. The advantage of drug product selection is that it facilitates physician delegation to pharmacists whose primary professional endeavor is product selection. In any event, physician unawareness of drug prices (as demonstrated by the wide price disparity among equivalent versions of the same drug) is strong evidence of the low priority placed on drug prices. (For further discussion see Chapter VIII., infra). Differences are even found in the prices of drugs made exclusively by one firm but marketed by several firms under different names. The New York State Assembly's Office of Legislative Oversight and Analysis has documented cases in which generic manufacturers sell products both to a trade name house and to a wholesale distributor. For example, Barr Laboratories manufactures chlordiazepoxide hydrochloride and sells it to both Lederle Laboratories, for resale as a branded generic, and to Darby Drug Company, for resale as an unbranded generic. At wholesale, Lederle sells its product for $17.01 per bottle and Darby sells its product for $4.85 per bottle.[53] Assuming a comparable difference in retail prices, the patients of doctors prescribing the Lederle brand are paying a premium price for a product identical to Darby's.

Another indirect measure of the low priority physicians give

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50 Id.

51 Lowy, et al., "A Survey of Physicians' Knowledge of Drug Costs," 47 J. Med. Educ. 349, 350 (1972). This study compares the responses of physicians from academic and private settings. We need not concern ourselves with these distinctions.

52 Supra note 37.

53 Callahan, Fensterer, Langdon & Haddad, Report on Branded Generics, The Assembly State of New York, February 1978, at 167. For other examples, see Ch. II.D., supra.

drug prices is evidence that physicians receive most of their price information from patients rather than pharmacists. When asked to list their principal sources of drug price information, a majority of physicians polled in the Palo Alto, California study cited patients first and pharmacists second.[54] Similarly, the Philadelphia County study found that doctors received some 66 percent of their drug price information from patients. In contrast, pharmacists, possibly the most accurate source of such information, provided only 21 percent.[55]

Still other studies directly demonstrate the relatively low weight doctors place on retail prices when prescribing. A 1953 study attempted to measure the reasons doctors use a particular drug in preference to whatever drug or treatment they had been using previously.[56] The primary reason given by 56 percent of the doctors was the drug's therapeutic effect. Another 30 percent cited side effects or ease of administration and only 3 percent cited price.[57] A more recent study conducted in Sweden reached similar conclusions about the relative importance that physicians place on a drug's curing effect, side effects, and cost.[58] For the two drugs studied, the drug's curing effect was by far the most important factor.[59] Cost narrowly surpassed side effects in the case of one drug, and was a distant third in the other.[60] From his study Lilja concluded that physicians have a bias to consider the curing effect as the only decision criterion and that it would therefore be inefficient to give doctors price information.[61]

Perhaps also contributing to a lack of awareness about drug prices and their low priority among physicians is a widespread belief among physicians that prescription drugs are not overpriced. A 1974 national mail survey determined that roughly one-half of some 260 physicians believed that prescription drug prices were either a bargain or about right. Approximately

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54 Lowy, et al., supra note 51, at 349.

55 Fink, supra note 47, at 19.

56 Caplow & Raymond, supra note 15, at 18.

57 Id. at Table 5.

58 Lilja, "How Physicians Choose Their Drugs," 10 Sci. & Med. 363, 364 (1976).

59 Id.

60 Id.

61 Id. at 365.

37 percent thought they were overpriced.[62] However, since those doctors concerned about drug prices are the most likely to support generic prescribing and the repeal of antisubstitution laws,[63] it is likely that most of those doctors dissatisfied with drug prices are also those doctors who are already prescribing generically. Conversely, those doctors currently satisfied with prescription prices are most likely the ones unaware of the possible savings to be achieved by prescribing generically.

To sum up, we have found ample evidence that many physicians prescribe by brand name out of convenience and that many at the same time place a low priority on price. We believe this combination of factors explains the continued high rates of brand-name prescribing for multisource drugs in the face of wide price variation. Given the low priority physicians place on price, we conclude that enactment of drug product selection laws can dramatically increase the use of lower-priced products by making it easier for many doctors who currently find it inconvenient to use generic names in prescribing to allow pharmacists to select drug sources. (For a discussion of the incentives pharmacists have to select lower-cost products see Chapter IX.D.)

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62 Nelson & Gagnon, "Physician Acceptance of Three Proposed Programs Designed to Reduce Prescription Prices," 1 Drugs In Health Care 27, 32 (1974).

63 Id. at 32, 33.

CHAPTER IV. THE PHARMACIST'S ROLE

A. Pharmacists' Competence to Select Drug Products

The enactment of drug product selection laws will not change the nature of a pharmacist's duties. With or without antisubstitution laws doctors can and often do prescribe generically and thereby require pharmacists to select from among various products when the drug is multisource. Currently about 11 percent of all prescriptions give pharmacists such authority.[1] Indeed, it has been estimated that between 1963 and 1973, doctors prescribed generically over one billion times.[2] In the remaining cases, of course, pharmacists were obligated to dispense a specified brand. The successful implementation of drug product selection laws will increase pharmacists' opportunities to select from different sources of the same product. When the physician so indicates, however, pharmacists will remain obligated to fill prescriptions as written.

This section will examine whether pharmacists' training and experience warrants widening their authority to select products for multisource drugs. It will review doctor and pharmacist opinions and other evidence bearing on whether pharmacists are competent to select drug products. We will see not only that pharmacists can competently select products but that their profession is well suited to exercise this responsibility to benefit consumers.

1. Pharmacists' Formal Education

Although the formal training of pharmacists is far from uniform, widespread agreement exists that they receive ample training--much more than the typical physician--in those subjects relevant to the prudent selection of multisource drugs. We sent a questionnaire to the deans of all 72 accredited schools of pharmacy and received 24 responses. The near unanimous opinion of those responding was that pharmacists, particularly recent graduates, are qualified to select drug products.[3] Even the American Medical Association which is actively opposing product selection, acknowledged in an editorial in Journal of the American Medical Association:

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1 Statement of APhA to Subcomm. on Consumer Protection and Finance, Comm. on Interstate & Foreign Commerce, U.S. House of Rep., 94th Cong., 2d. Sess., July 28, 1976, at 12.

2 Gumbhir, "Drug Quality: Practising Pharmacists' Viewpoints" Med. Marketing & Media, September 1973, at 24.

3 See responses of pharmacy school deans to staff inquiry.

> There is no question that the technical training of the pharmacist is great and that his knowledge of drugs is considerable since the study of drugs is his primary professional endeavor.[4]

Almost all of today's graduating pharmacists have spent a minimum of five years in pharmacy school.[5] While a variety of subjects are presented during this time period, the typical school of pharmacy thoroughly trains its students in the science of biopharmaceutics -- the study of the influence of pharmaceutical formulation on a drug's therapeutic activity within the human body.[6] They also learn various methods of evaluating drug product information.[7] This training ensures that a pharmacy student is able competently to assess the value of different sources of drug products.[8]

In contrast, some pharmacy school deans asserted that medical students received less training in this area. Two pharmacy deans cited specific figures. University of Nebraska's medical students receive only 80 hours in pharmacology whereas their pharmacy students, according to the pharmacy school dean, received 180 hours in various pharmacology courses.[9] Similarly, the dean of the pharmacy school at the University of Missouri in Kansas City believed that pharmacists' training for product selection was far superior to physicians'. He noted that a medical student attends one to three lectures on pharmacokinetics and bioavailability, whereas the average pharmacy student will attend 30-60 such lectures.[10]

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4 "Drug Substitution - How to Turn Order Into Chaos," 217 J.A.M.A. 817, 818 (1971).

5 Feldmann, "Drug Product Selection -- Freedom with Responsibility," Statement before the Georgia Pharmaceutical Ass'n., Calloway, Ga., May 2, 1972, at 15-16.

6 Id.

7 Letter from Dean Varro E. Tyler, Purdue U., to Claudia Farrell, FTC, Oct. 25, 1977, at 1.

8 Compare Letters of Deans of Auburn U., Nov. 10, 1977, U. of Nebraska, Nov. 4, 1977, U. of Oklahoma, Oct. 27, 1977, and U. of Utah, Nov. 8, 1977; see also Letter from Robert Greenberg, American Society of Hospital Pharmacists, to Peter Holmes, FTC, Jan. 24, 1978, at 1-2.

9 Letter from Dean A. R. Haskell, Ph.D., U. of Nebraska, to Claudia Farrell, FTC, Nov. 4, 1977.

10 Letter from Dean Donald L. Sorby, U. of Missouri - Kansas City, (Footnote Continued)

Regardless of the relative competence of the two professions in this area, it does seem clear that pharmacists are adequately trained to select drug sources.

2. Pharmacists' Continuing Education

After completing their academic training, serving an internship and passing state board examinations,[11] pharmacists have numerous and increasing opportunities to continue their pharmacological education. In addition to journals and manufacturers' advertising and other promotional materials, pharmacists may elect and often are required to participate in continuing education programs. Approximately 15 states currently require for relicensure[12] that pharmacists attend continuing education courses. The state of Oklahoma, for example, requires 15 hours of continuing education a year for relicensure.[13] Even when not mandated, continuing education participation by pharmacists is substantial: in Wisconsin, a state with no mandatory requirements, an estimated 60

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10 (Footnote Continued)

to Claudia Farrell, FTC, Oct. 17, 1977. "Pharmacokinetics" and "bioavailability" concern the effects of drugs in the body. Because therapeutic effects are difficult to measure, drug equivalence is usually determined by measuring how fast and how much of the active drug gets into the body, appears in the bloodstream or is excreted in the urine. Two or more chemically equivalent products with the same "biological availability" or "bioavailability" are said to be "bioequivalent." See Ch. VI. A.4., infra, for a discussion of bioavailability.

Pharmacokinetics is the study of rates of absorption, distribution, metabolism and excretion of drugs. Office of Technology Assessment, Drug Bioequivalence Study Panel, Drug Bioequivalance 77 (1974).

11 Feldmann, supra note 5, at 15. See also Letter from of Dean Joseph P. Buckley, Ph.D., U. of Houston, to Claudia Farrell, FTC, Nov. 7, 1977.

12 See Letter from Dean A. C. Glasser, U. of Cincinnati, Oct. 13, 1977; Letter from Dean A. R. Haskell, Ph.D., U. of Nebraska, Nov. 4, 1977; Letter from Dean Tom S. Miya, Ph.D., U. of North Carolina, Oct. 13, 1977; and Letter from Dean Harold H. Wolf, Ph.D., U. of Utah, Nov. 8, 1977.

13 Letter from Dean R. D. Ice, Ph.D., U. of Oklahoma, to Claudia Farrell, FTC, Oct. 27, 1977, at 2.

percent of pharmacists participate in some way.[14] Any pharmacy school deans responding to our inquiry placed the overall participation rate of pharmacists in continuing education at about 50 percent.[15] Finally, the fastest growing area of continuing education involves courses in drug product selection. Because biopharmaceutics is a relatively new discipline, schools of pharmacy together with local or national pharmaceutical associations have sponsored continuing education programs designed to reach past graduates of pharmacy schools.[16] As one pharmacy dean noted:

> Since continuing education is obviously responsive to the expressed needs of practitioners, any significant increase in the involvement of pharmacists in drug product selection would assure that a large portion of continuing education programs would speak to the competencies needed to accomplish this task. Certainly, the expertise necessary to conduct such continuing education programs can be found among the faculty in the vast majority of our colleges of pharmacy.[17]

Some pharmacists, however, believe that currently there is insufficient uniform and competent bioavailability data to permit them to use their professional skills.[18] These fears are significant because many pharmacy school deans conditioned their endorsement of pharmacists' competence to select an alternative source to those pharmacists provided with meaningful bioavailability data.[19] The implication is that if acceptable bioavailability

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14 Letter from Dean George Zografi, U. of Wisconsin - Madison, to Claudia Farrell, FTC, Oct. 14, 1977.

15 See, e.g., Sorby, supra note 10.

16 Tyler, supra note 7.

17 Wolf, supra note 12.

18 See DeSalvo & Hem, "Community Pharmacists and Drug Product Source Selection" NARD J., August 1974, at 39; Cawthorne & Eckel, "The Pharmacists' Dilemna Drug Product Selection Using Bioavailability Data," 7 Drug Intelligence and Clinical Pharm. 447 (1973).

19 See, e.g., Sorby, supra note 10:

> "I must qualify this with the statement that they must have available to them appropriate data concerning the biopharmaceutic performance

(Footnote Continued)

data is not available, pharmacists will not be able competently to select alternative sources for certain drugs. However, many state laws and the Model Act we recommend (see Chapter X. A. Section 5, infra) allow pharmacists to select products already proven bioequivalent. Furthermore, pharmacists in states with no formulary (a list of substitutable or non-substitutable drugs) can rely on the information disseminated by the FDA and on the formularies of other states. Finally, this perceived scarcity of bioavailability data is subject to question. For example, 48 percent of pharmacists polled in the FTC study believed that the quality of information disseminated to them by the pharmaceutical industry had improved since enactment of their state's product selection law.[20] Moreover, 72 percent of the pharmacists said that they had sufficient information about drug products to exercise their authority to substitute.[21]

In general, dissemination of meaningful drug information from various sources appears to have increased. The American Druggist Blue Book, which provides drug price and source information, recently was changed to cross-reference over a thousand generic names to branded products.[22] Similarly, the American Pharmaceu-

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19 (Footnote Continued)

> of the drug products which will allow them to make accurate decisions concerning quality. The present 'state of the art' is such that data is frequently lacking or is sufficiently limited in its scope to prevent comparison of all products available on the market. Given such information, however, our students are able to select an appropriate product."

20 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978, at 14. ["FTC Study"].

21 Id. In contrast, only 19 percent of pharmacists replying to the question of biological equivalency felt that sufficient standards and data exist to determine such equivalency. DeSalvo, supra note 18, at 39. However, many of these pharmacists may have view equivalence in absolute terms. If so the significance of the statistic is questionable. At least one pharmacists has said, "Absolute equivalence has and I suspect never will be demonstrated." Sullivan, "A Pharmacist's Perception of Quality," 16 J. Am. Pharm. Ass'n 609 (1977).

22 Am. Druggist, Mar. 22, 1972, at 26.

tical Association provides pharmacists with a monthly series of bioavailability monographs, developed by academic and industry scientists, which evaluate bioavailability literature and data submitted by pharmaceutical manufacturers.[23] Moreover, journal advertising directed to pharmacists has increased substantially as they expand their professional role.[24] The president of a medical advertising agency states that brand-name manufacturers are stressing the quality standards developed for their products.[25] At the same time, generic manufacturers, having increased assurance that their promotion will lead to sales,[26] are trying to familiarize pharmacists with their products.[27]

Pharmacists, then, not only are adequately trained, but also have opportunities at schools of pharmacy and through journal articles and drug formularies to keep informed about the appropriate selection of drug products.

3. Other Evidence of Pharmacists' Competence

Thus far we have reviewed pharmacists' formal training and their continuing education opportunities. We turn now to other evidence establishing that pharmacists are competent (or at a minimum are as capable as doctors) to select drug products for multisource drugs. In considering this question we will examine the consensus of opinion among pharmacists and physicians, and analyze studies attempting to measure pharmacists' and physicians' knowledge concerning multisource drugs. Lastly, we will consider how pharmacists are used in hospitals. Although no one factor is decisive, taken as a whole the evidence is unambiguous: pharmacists are qualified to select drug products and increasing their opportunity to select drug products will benefit consumers.

a. The Opinions of Doctors and Pharmacists

Most doctors believe pharmacists are competent to select drug products. A survey of representative samples of practicing pharmacists and physicians in Wisconsin found that almost two-thirds of the physicians agreed with the statement that "more than 60 percent of practicing physicians believe pharmacists have the

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23 Tyler, supra note 7.

24 Am. Druggist, November 1976, at 27.

25 Millman, "Battle lines harden in fight over generics" Advertising Age, Feb. 13, 1978, at 76.

26 See Ch. II.D., supra.

27 Millman, supra note 25.

technical knowledge to substitute safely one drug product for another;" only 26.8 percent of the physicians disagreed.[28] A similar survey of Minnesota physicians found that 87 percent of those polled believed that pharmacists are adequately prepared to exercise brand selection.[29] And a nationwide opinion poll of 1000 physicians and 1000 pharmacists found that 94 percent of the responding physicians described pharmacists' pharmacological competence as excellent (39.4%) or good (55.1%).[30]

Most pharmacists also believe they are competent to select drug products and support the repeal of antisubstitution laws.[31] The same nationwide poll described above found that pharmacists overwhelmingly favored the substitution of a lower-cost generic

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28 W. McCormick, "Attitudes of Pharmacists, Physicians, and Consumers Toward the Repeal of Antisubsitution Laws," at 148-150 (1972). (unpublished Ph.D. thesis, University of Wisconsin).

29 pharmaSYST reports, March 1977.

30 20 Am. Med.News 5 (1977). Only 5.2 percent of doctors described pharmacists' pharmacological competence as fair and less than 1 percent described it as poor. Notwithstanding physicians' high opinion of pharmacists' knowledge, they closely split on whether they favored (46) or opposed (48.5) the substitution of a cheaper drug for a brand name. Id.

31 APhA's view on pharmacists' competence is well known. The American Society of Hospital Pharmacists also strongly agree that pharmacists are competent. In its response to our inquiry a spokesman stated:

> We see no problem in the ability or competency of pharmacists to select the source of multi-source drugs. Pharmacists receive five to eight years of professional training which focuses primarily on drugs; they are more expert than any other health professional in this area and are eminently qualified to select one of several brands of a multi-source drug.

Greenberg, supra note 8. Similarly, a nationwide survey of pharmacy leaders revealed broad support of product selection laws and implicitly of pharmacists competence. Of those responding, 79 percent supported laws permitting pharmacists to select generally equivalent drugs. pharmaSYST reports, July 1976.

drug product for a brand name, 69 to 28 percent.[32] The Wisconsin survey, described above, also found that over 60 percent of pharmacists believed they had the technical knowledge necessary to safely substitute one drug product for another.[33] Lastly, "the Goldberg Study," an extensive prescription drug audit conducted at Wayne State University, determined that a majority of both physicians and pharmacists in Michigan believe that pharmacists have the technical knowledge to substitute drug products safely.[34]

Further evidence of pharmacists' confidence in their professional abilities is their overwhelming support for the repeal of antisubstitution laws. According to APhA, pharmacists' support for repeal steadily increased from 25 percent in 1970 to 90 percent in 1977.[35] Corroborating this view is a 1976 questionnaire survey of approximately 200 pharmacists attending continuing education classes at the University of Minnesota. Of the 166 responding

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32 20 Am. Med. News, supra note 30, at 5. Also, the FTC Survey of pharmacists in seven states with product selection laws only 17.4 percent perferred antisubstitution laws. FTC Study, supra note 20, at 55.

33 McCormick, supra note 28, at 144 (at a 95% confidence level).

34 Goldberg, et al., "Evaluation of Report of Drug Substitution Legislation," 16 J. Am. Pharm. Ass'n 64, 68 (1976).

Physicians' and Pharmacists' Attitudes Regarding Technical Knowledge of Pharmacists to Safely Substitute Drug Products

	Physicians	Pharmacists
Strongly agree	94 (14.6%)	198 (37.1%)
Moderately agree	308 (47.7%)	242 (45.4%)
Moderately disagree	139 (21.5%)	48 (9.0%)
Strongly disagree	82 (12.7%)	37 (6.9%)
Missing data	23 (3.6%)	8 (1.5%)
Total	646 (100.0%)	533 (100.0%)

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35 Statement of APhA Before the Subcomm. on Monopoly Select Comm. on Small Business, U.S. Senate, 95th Cong., 1st Sess., Nov. 15, 1977.

pharmacists, 148 or 90 percent supported laws permitting pharmacists to select generically equivalent drugs.[36] A similar survey of the leadership of pharmacy associations found that 78 percent favored drug production selection.[37]

Finally, the Goldberg study surveyed the attitudes of physicians and pharmacists in Michigan toward generic products. Goldberg found that a majority of both physicians and pharmacists believe these products are therapeutically equivalent and could be substituted for brand drugs in all or most cases.[38]

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36 pharmaSYST reports, August 1976.

37 Id.

38 Goldberg, supra note 34, at 67. The following tables summarize these Goldberg findings.

Physicians' and Pharmacists' Attitudes Regarding Generic and Therapeutic Equivalency:

	Physicians	Pharmacists
No difference in effect	18.0%	6.8%
Some substantial difference only for a few products.	50.8%	48.6%
Some substantial difference for many products	23.7%	35.1%
Substantial differences for most products	2.9%	6.8%
Missing	4.6%	2.8%

Physicians' and Pharmacists' Attitudes Regarding Substitution of Generically Equivalent Drugs:

	Physicians	Pharmacists
No significant difference	22.4%	9%
Significant difference but only for a few drugs	47.1%	48.6%
Significant difference for many drug products	21.8%	35.1%

(Footnote Continued)

b. Four Studies of Pharmacists' Abilities to Select Drug Products

Not only do most opinion surveys of pharmacists and doctors demonstrate their confidence in pharmacists' pharmacological competence, there exist other more quantitative measures of pharmacists' ability to select drug products prudently. We will consider four studies of this question by university scholars: those of (1) Cronk, Williams and Moore, (2) Vinson and Schumacher, (3) Moore, Goldberg, Aldridge, Vidis, DeVito, and Dickson, and (4) Horovitz, Morgan, and Fleckenstein. The first two studies attempted to determine whether pharmacists are able to correctly interpret bioavailability data. The third and fourth studies considered doctors and pharmacists' knowledge of multisource drugs.

In the first study, Cronk distributed 44 pretested questionnaires to pharmacists in Detroit, Michigan. The questionnaires tested the participants' ability to use bioavailability data in evaluating four brands of an antibiotic.[39] Analyzing the 19 completed questionnaires, the researchers concluded that these pharmacists could use dissolution data to measure physiological availability, and could interpret blood levels. On the other hand, the study found that the responding pharmacists lacked an awareness of the use of toxicity and urinary excretion data, and an understanding of the relative importance of correlating the various types of bioavailability data.[40] Despite mixed test results, the study concluded that with increased emphasis in continuing education in a few areas, pharmacists could adequately use bioavailability data in drug product selection.[41]

A similar study in southwestern Michigan by Vinson and Schumacher found that pharmacists did significantly better than doctors in evaluating bioavailability.[42] Eighteen physicians

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38 (Footnote Continued)

Significant difference for most drug products	3.4%	3.6%
Missing	5.3%	3.8%

39 Cronk, Williams, & Moore, "The Pharmacist's Ability to Use Bioavailability Data," 3 Am. J. Hosp. Pharm. 46 (1975)

40 Id. at 48.

41 Id.

42 Vinson & Schumacher, "Biopharmaceutics and Pharmokinetics," 33 Am. J. Hosp. Pharm. 1164-66 (1976).

(five general practitioners and 13 specialists), 34 community pharmacists (nine chain and 25 independent pharmacists), and 34 hospital pharmacists completed the questionnaire.[43] The results were compared with the answers given by a panel of experts. Table 1 presents the mean scores and range of the participants.[44]

Table 1

GROUP MEAN SCORE (% correct answers)		RANGE
Panelists	83	50-100
Pharmacists	52	10-100
Physicians	35	10-60
Hospital Pharmacists	61	30-100
Community Pharmacists	42	10-80

All of the differences are statistically significant.[45]

The same questionnaire also asked whether there was a "great" need to acquire bioavailibility data for any of 13 commonly used drugs.[46] A majority of the panelists and the pharmacists agreed on the same five drugs,[47] but the physicians cited only two of these five.[48] Although they believed this study could be refined in several ways, the authors thought it provided some insight into

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43 Id. at 1165.

44 Id.

45 Researchers qualify the results in Table 1, however, noting the pharmacists on average were more recent graduates. Id. at 1166. Although this difference in age may be significant, it is worth noting that the study by Cronk, et al. found no correlation between the number of correct answers by pharmacists and the length of time since graduation. Cronk, supra note 39, at 47.

46 The drugs listed were ampicillin, chlorpromazine, codeine, digoxin, ferrous sulfate, hydrochlorothlazide meprobamate, phenytoin, prednisone, procainamide, sufisoxazole, tetracycline, and warfarin.

47 They cited digoxin, phenytoin, prednisone, procainamide, and warfarin.

48 They cited only prednisone and procainamide.

the ability of practitioners to evaluate promotional bioavailability data.[49]

A third study, part of a larger evaluation of the impact of Michigan's drug product selection laws, also concluded that pharmacists are generally more familiar than doctors with information about product sources.[50] During the winter of 1974-75, prior to the implementation of the Michigan drug product selection law, Moore asked physicians and pharmacists, among other things, whether seven specific prescription drug products and supposed "substitutes" were in fact equivalent and therefore interchangeable.[51] Six of the seven products were among the top 100 drug products dispensed in 1975-76.[52] Selecting a non-equivalent as equivalent was labeled a Type A error; not selecting a product which was generically equivalent was labeled a Type B error.[53] Focusing on the more serious Type A errors, the study determined how many of the participants "passed" by answering correctly at least 70 percent of the time. Pharmacists did significantly better than physicians: only 10 percent of the physicians passed as compared to 56 percent of the pharmacists.[54]

Finally, Horvitz asked a sample of about 50 doctors and 30 pharmacists whether each of 22 major drug brands was a multisource or single source product. The pharmacists correctly identified an average of 18.5 out of 22 drugs whereas physicians correctly identified an average of 14.1 drugs.[55]

Separately, these studies may not be conclusive, but their consistent findings indicate that although pharmacists' knowledge

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49 Vinson & Schumacher, supra note 42, at 1166.

50 Moore, Goldberg, Aldridge, Vidis, DeVito, & Dickson, "Evaluation of the Impact of Drug Substitution Legislation: III Implication for Continuing Education for Michigan Pharmacists," Presented at 124th Annual Meeting of APhA, New York, N.Y., May 17, 1977.

51 Id. at 3.

52 Id. at 4.

53 Id. at 3-4.

54 Id. at 4. The results for Type B errors showed a similar pattern of inaccuracy. Id.

55 Horvitz, Morgan, & Fleckenstein, "Savings from Generic Prescriptions -- A Study of 33 Pharmacies in Rochester, N.Y.," 82 Annals of Internal Med. 602, 605, 607 (1975).

is not perfect, they are more competent than doctors in drug product selection.

c. Hospitals' Use of Pharmacists to Select Drug Products

The vast majority of hospitals give their pharmacists authority to select generic drug products even when the physician prescribes by brand name. Since hospital pharmacies combine aspects of both the prescribing function of the physician and the dispensing function of the pharmacist, hospitals tend to be both more informed and more concerned about drug costs than most physicians. Consequently, their widespread delegation of drug product selection to pharmacists speaks persuasively of hospitals' confidence in pharmacists' abilities.

Most hospitals authorize their pharmacists to select drug products for all prescriptions. According to the American Society of Hospital Pharmacists, 67 percent of the nation's 4,700 hospitals use a formulary in which prescribers consent to use of a formulary drug of the same generic composition in place of the brand name prescribed.[56] This view is substantiated by a 1976 national mail survey of hospitals which found that 67 percent of pharmacists have authority to select the brand or supplier on all drug orders and prescriptions unless the prescriber makes a specific notation to the contrary.[57] Another source indicates that 94 percent of all hospitals usually allow pharmacists to select products.[58]

Moreover, the evidence shows that hospital pharmacists are given meaningful responsibility. A 1972 study by the American Society of Hospital Pharmacists found:

> In 85 percent of the hospitals responding, pharmacists have the authority to dispense a brand of drug other than the prescribed when a brand name appears on the prescription or medication order.[59]

Pharmacists' competence to select drug source is well recognized by most hospitals and their pharmacy and therapeutics committees:

> Hospital pharmacists will verify that the

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56 Greenberg, supra note 8.

57 Stolar, "National Survey of Selected Hospital Pharmacy Practices," 33 Am. J. Hosp. Pharm. 225, 229 (1976).

58 Statement of APhA, supra note 1.

59 Id.

> authority given to them by the Pharmacy and Therapeutics (P & T) Committee is a truly delegated authority in that the pharmacist is not required to submit recommendations back to the P & T Committee for verification prior to acting. The fact of the matter is that the physicians serving on P & T Committees recognize the expertise of pharmacists in choosing quality drug products and delegate to them the necessary authority to carry out this function.[60]

Hospitals appear to give this responsibility to their pharmacists for two reasons: pharmacists are competent to select drug source and can save them money by doing so. By delegating selection authority to pharmacists hospitals can save substantial amounts. One study calculated the savings for 50 multisource drugs in a 1,000 bed hospital whose new system placed no restrictions on physicians' prescribing practices or pharmacists inventory practices.[61] Under the new system, the hospital stocked only one product for each multisource drug and obtained competitive price quotations. As a result, the hospital saved $35,141.38 or 40.4 percent of its 1974 costs for the 50 multisource drugs.[62]

Because pharmacists can competently select drug products, hospital reliance on pharmacists frees doctors from deciding which drug products the hospital should stock. Furthermore, pharmacists' time is less expensive than doctors' time. As a rough measure, the average net income for physicians appears to be nearly triple that of pharmacists. In 1974, for example, the average net income for

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60 Id.

61 Swift & Ryan, "Potential economic effects of a brand standardization policy in a 1,000 bed hospital," 32 Am. J. Hosp. Pharm. 1242, 1244 (1975).

62 Id. at 1247. That brand name products still garner a price premium in the hospital market, as the Swift study suggests, notwithstanding the possible downward pressure on brand name prices because of the promotional effect could mean two things. Either the hospital market does not have competitive prices or some quality differences (including services) between brand and generic drug products exists. At this juncture, we lack evidence to tell whether either or both factors are at work. However, it is worth nothing that any such quality-based price difference could be only a fraction of the present price disparity between brand and generic products.

all physicians was $51,997.[63] In contrast, the average salary for pharmacists in the same year was $18,992.[64] To the extent pharmacists can competently deal with drug product selection and to the extent hospitals can thereby remove this burden from doctors, hospitals can save money. Moreover, assuming that the average pharmacy deals with more prescriptions than the average physician, it could spread any added cost resulting from selecting drug products over more transactions. That is, pharmacists could select drug products more efficiently than physicians.

These reasons for hospital reliance on formularies and pharmacists' expertise also support the wisdom of increasing community pharmacists' authority to select drug products. Some have questioned the relevance of hospital experience to that of community pharmacists.[65] Undoubtedly, hospitals can supervise drug use closely; however, this argument cuts both ways. As APhA contends, the clinical experience of hospitals contains few instances of chemically equivalent products being therapeutically inequivalent.[66] Moreover, the development of new standards to assure bioequivalence should further reduce the likelihood of any problems. A second challenge to the hospital analogy is that hospitals supervise the products while a physician in a clinic cannot.[67] The premise that hospitals rigidly control their pharmacists is subject to question. As described above, hospitals use formularies and do not limit their pharmacists to only one substitute product.[68] (This system is similar to those state product selection laws using formularies). Indeed, pharmacists often develop the formulary.[69] Moreover, the merits of this argument rest heavily on the existence of a significant number of community pharmacists who, relying on formularies, FDA regulation, and other sources of information, are unable to select appropriate

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63 Center for Health Services Research and Development, Profile of Medical Practice 184 (1977).

64 This figure represents the yearly compensation for a pharmacist working a 46 hour week in a chain of between two to five stores. See 1974 Pharmacy Manpower Study, National Association of Chain Drug Stores, Inc., at 2.

65 Am. Druggist, Dec. 14, 1970, at 23.

66 APhA, "A White Paper on the Pharmacists' Role in Product Selection," March 1971, at 11.

67 Supra note 65.

68 Statement of APhA, supra note 1.

69 Id.

products. At this time, this possibility does not loom large. For these reasons the comparison of hospital pharmacies to community pharmacies is apt and the widespread use of pharmacists by hospitals is significant.

Thus, pharmacists are found by doctors, hospitals, researchers, and themselves to be qualified by their formal and continuing education to select drug sources competently and more efficiently than physicians. The establishment of drug formularies and the increased dissemination of other drug product information add to the assurances that pharmacist source selection can save consumers money without sacrificing quality in health care.

IV. B. Role as Retailer

Antisubstitution laws have had a profound impact upon retail pharmaceutical operations especially on the level of inventories. These laws have led many pharmacists to stock multiple versions of chemically identical drug products on their shelves. Laws that permit drug product selection on the other hand, enable pharmacists to reduce their inventories and thus obtain some savings in their capital investment.

How pharmacists operate their business also influences the level of drug product selection engaged in. The type of fee chosen by pharmacists, for example, can directly affect their profit margin, and, therefore, indirectly affect the incentive to choose a lower-priced drug product. To the extent pharmacists tend to price their drug products by using a professional fee (in contrast to a percentage markup) the incentive for choosing a high cost version of a drug is reduced. Thus the sale of lower-priced unbranded drug products which traditionally permit higher profit margins to the retail pharmacist is influenced primarily by the state policy regarding drug product selection, and secondarily by the operations of the pharmacy itself.

This section will discuss how antisubstitution laws influence the inventory practices of pharmacists. It will also describe the various fee systems utilized by pharmacists and the way they affect profit margins and the incentive to engage in drug product selection.

1. The Retail Pharmacy

There are many different types of pharmacies in the United States. The most common and well-known is the independent community pharmacy. In addition, there are chain store pharmacies, hospitals pharmacies, government-operated pharmacies, and mail-order pharmacies. Pharmacies also may be located in discount stores, department stores, and supermarkets.

We will discuss the practices of retail pharmacies (both independent and chain). We will not address the practices of hospital pharmacies, most of which dispense pharmaceuticals under a formulary system. About 74.5 percent of all prescription drug products are distributed by retail pharmacies compared to 14.4 percent by hospitals and 11.1 percent by government agencies.[1] In 1976, total retail sales by drugstores amounted to $19.23 billion, of which 40 percent were due to sales of prescription

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1 Schwartzman, Innovation in the Pharmaceutical Industry 24-25 (1976).

drug products.[2] These sales were divided among 50,000 pharmacies, of which 33,000 were single-unit independent operations.[3] Chain store pharmacies (two or more outlets) accounted for a majority of total (both pharmaceutical and nonpharmaceutical) drugstore sales, but independents accounted for 60 percent of prescription drug sales.[4] Independents, according to one estimate, earn more of their revenue from prescription drug products than do chains.[5] About one in every four prescriptions dispensed by retail pharmacies is paid for by a third party.[6]

The fastest growing segment of this industry appears to be small four-to-ten store chains. In addition, non-drug retailers such as supermarkets have entered the pharmacy field.[7]

2. Drug Inventories

The typical pharmacy maintains an average inventory of 33.4 products to fill prescriptions for the ten drugs most often prescribed generically.[8] Partly due to antisubstitution laws, most pharmacists are "brand conscious," and tend to stock mainly branded products in their inventory. The inclination to stock generic drugs is directly related to the number of generically-written prescriptions. It is also influenced by the price differential between generics and the leading brand. As the price

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2 Toffey, "'76 Drugstore Retailing Roundup: Sales Rise, Rxs Slip," Drug Topics, Mar. 15, 1977, at 47.

3 Id. at 48.

4 Id.

5 Lilly Digest, 1977, at 7; NACDS-Lilly Digest, 1977, at 4. Independents earn 50% of their total revenue from prescription sales, while chains earn 18%. In 1976, the average independent pharmacy unit filled 24,505 new prescriptions and 12,561 refills. This compares with 34,781 new prescriptions and 16,960 refills for chains. Toffey, supra note 2, at 48.

6 Am. Druggist, May 1978, at 10,17. Third parties paid for 25.9% of all prescriptions filled by independent and 20.5% by chains.

7 Am. Druggist, June 1977, at 27.

8 The LEA Mendota Research Group, "An Inventory Study." A Store Audit for Pharmaceutical Manufacturers' Association, March 1973, at 1-2.

differential increases so does the tendency to stock generic drugs. Conversely as the differential decreases, pharmacists may "trade-up" and stock only intermediate priced drugs such as branded generics.[9]

Antisubstitution laws force pharmacists to stock in their inventory many brands of a particular prescription drug. At the very minimum, the pharmacist is required to stock all of the popular brands of common multisource drugs in case he receives a prescription specifying a particular brand-name product. It is commonly asserted that failure to maintain such an inventory forces the pharmacist to send patients elsewhere and thus lose business.[10]

An editorial of the Journal of the American Medical Association contends that the problem of maintaining a large inventory "is not as serious as we would be led to believe." JAMA states that most drugstores especially in the larger metropolitan areas have ready access to multiple daily delivery from drug wholesalers, and can obtain temporary loans from their competitors.[11] This statement is confirmed by a study in which two-thirds of the pharmacists surveyed stated that they could obtain a rush order from their wholesaler within the same day.[12] That same study found that most pharmacists (75 percent) said that in such a case, they either asked the physician for permission to substitute a different brand, or borrowed the product from a nearby pharmacist. Less than ten percent indicated that in actual practice they called their wholesaler.[13]

The important point, however, is whether or not pharmacy

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9 Richard George Kedersha, "The Impact of Brand Name Prescription Products on the Traditional Practices of High Prescription Volume Pharmacies in Northern New Jersey," unpublished Ph.D. thesis, New York Univ. (1964), at 105.

10 "A White Paper on the Pharmacist's Role in Product Selection," Am. Pharm. Assoc., March 1971, at 14, and California Pharmacist, February 1973, at 36. Substitution laws create a conflict with the pharmacist's normal business operations. On the one hand, pharmacists desire to stock only fast-moving brands. On the other hand, they are required to carry a complete line of medications including slower-moving duplicates. Kedersha, supra note 9, at 51-52.

11 "Drug Substitution - How to Turn Order Into Chaos", 217 J. Am. Med. Ass'n, Aug. 9, 1971, at 818.

12 The LEA Mendota Research Group, supra note 8, at 30.

13 Id. at 20.

inventories are at their optimum level. There is evidence that in states where antisubstitution laws exist, pharmacists maintain inventories that are larger than optimal, the added costs of which are passed on the the consumer. One pharmacist, for example, commented:

> Presently I stock five brands of Penicillin in a multiplicity of dosage forms. Recently one of the major pharmaceutical manufacturers introduced his "me-too" version of this drug. Since one of my local prescribers has an affinity for the local representative of this manufacturers I now have in stock five new dosages forms or sizes of a duplicate product on which the manufacturer did no research or investigational work but merely marketed a duplicate of an already oversupplied product. This increased inventory must necessarily be taken into consideration when I evaluate the operational costs of my prescription department in order to arrive at the professional fee I charge my customers for their prescriptions.[14]

Without antisubstitution laws, many pharmacists will be able to reduce inventory costs since they will no longer need to stock as many brands. Pharmacists will be able to reduce both their inventory operating costs (transaction costs, labor, etc.) because they will be stocking fewer lines of pharmaceuticals, as well as the cost of the inventory itself because they will be ordering less expensive products. One example may illustrate this point. In 1970, James Hawkins, the Assistant Executive Director of the American Pharmaceutical Association, estimated the cost of carrying a full line of one brand of ampicillin to be $700. He went on to say:

> Now if you multiply this by some half-dozen brands or more, you end up with a sizeable figure. If you do this for a number of different products, you get some idea of the enormity of capital that the pharmacist is obligated to put forward.[15]

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14 Letter from Aaron M. Lauter, past President, Delaware Pharmaceutical Society, Inc., to Dr. Hugh H. Hussey, Editor, J. Am. Med. Ass'n (August 22, 1971).

15 James D. Hawkins, "APhA's Position on State Antisubstitution Law Repeal," Texas Pharmacy, February 1971, at 16.

The potential savings would not amount to the entire $700 per line. Under drug product selection, the potential savings would reflect, however, the decrease in capital outlay due to the stocking of both fewer and less expensive brands.

This "excess capital" invested in duplicate products constitutes an additional cost to the pharmacy to the extent that capital could be used better elsewhere ("opportunity cost"). One pharmacist in Michigan who kept careful records of his inventory estimated that the inventory cost savings for one year resulting from stocking fewer and less expensive sources for 90 drugs was $14,880.[16] Another study projected the nation-wide cost of capital invested in excessive inventories of "patent-licensed products" in 1969 by retail pharmacies as $6.2 million. This figure was understated since it did not include an estimate for inventories of duplicate trademark products not protected by patents.[17] Antisubstitution laws also prevent pharmacists from taking advantage of economies in purchasing greater quantities of fewer brands and being able to participate in competitive bidding for drug products.[18] Pharmacists do seem to be aware of the potential savings resulting from substitution. In one survey, over 70 percent of the pharmacists questioned expected inventories

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16 Michigan Pharmacist, June 1976. Richard Coward, a community pharmacist purchased 90 drugs with an actual inventory value of $922 which he estimates equal to $3,402 "had the medications been purchased as different brands to these drugs." Subtracting: $3,402-$922 equals $2,480 saved in inventory overhead costs. Coward estimates that this $922 inventory is turned over six times a year, so his annual savings from reduction in inventory to fill the same number of prescriptions is $14,880.

17 Arthur Alexander Nelson, Jr., "The Saliency of Price in the Acceptance of the Substituting Chemically Equivalent Drugs on a Prescription," unpublished Ph.D. thesis, Univ. of Iowa, July 1973, at 22. Nelson takes an estimate of $28 million as the investment by pharmacies in duplicate inventories for patent-licensed duplicate trade-marked products from Wertheimer & Evanson, "Patent Licensing of Pharmaceuticals," 7 Inquiry 71 (Nov. 3, 1969). He then applies the reported rate of return on investment for the average pharmacy in 1969 (22.2%) to get $6.2 million.

18 Taubman & Gosselin, "The Massachusetts Drug Formulary Act", 16 J. Am. Pharm. Ass'n 71-72 (1976); Hawkins, supra, note 15, at 16.

and inventory costs to decrease under drug product selection.[19]

In practice, however, the expected reduction in inventory costs resulting from repeal of antisubstitution laws has been reported only by some pharmacists. Most pharmacists (53.9%) surveyed in the FTC study reported that their inventory costs had increased due to substitution in their state, whereas 22.2 percent reported a decrease and 23.9 percent reported no change.[20] Other surveys also show that 10 to 20 percent of pharmacists either increase or expect to increase inventories of multisource drugs in states where product selection is permitted.[21] Other surveys find a split in pharmacist opinion on this point. A survey of pharmacists in California, for example, found that about a third reported inventory reductions due to drug product selection, while another third reported no change and the final third reporting an increase in inventory.[22] Finally, a recent survey of pharmacists in 18 states conducted by American Druggist found that 9 percent were able to reduce inventories "substantially," 28 percent "somewhat," and 61.5 percent "very little or not at all."[23]

While these findings may seem "absurd," as PMA itself describes them,[24] the reported increase in inventories may emanate mainly from small pharmacies where generic equivalents are being stocked for the first time with as yet no significant reductions in the number of brand-name products yet. In some cases, pharmacists

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19 National Pharmacist Attitude Survey, Appendix, Tables 34, 35. (Prepared by Q.E.D. Research, Inc. for Roche Laboratories, Inc, undated).

20 IMS America Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report submitted to the Federal Trade Commission, July 28, 1973, at 41 ["FTC Study"].

21 See Submission of Roche Laboratories, Inc., Appendix, Michigan study (initial results of a study to assess the effects of changes in Michigan's antisubstitution law, 1975), at viii; see also Medical Marketing Conference, "Florida Pharmacist Substitution Study," November 1976, at iii.

22 California Pharmacist, September 1977, at 6.

23 Am. Druggist, October 1978, at 17, 18.

24 Pharmaceutical Manufacturers Assoc., Memorandum, re: The Michigan Study, from Mr. Russo to Mr. Brennan, Feb. 17,

1976.
already stocked only a few large-selling brands,[25] and thus had little excess inventory to reduce. For example, in Florida, three-fourths of all pharmacies carry no more than two equivalent brands of reserpine.[26] For some of these pharmacies, drug product selection entails the need to stock an additional line of reserpine. To the extent that inventories have decreased, they have been concentrated mainly among brands, while increases have occurred mainly among generics.[27]

Significant inventory savings will occur under drug product selection in situations where the number of lines or brands of a drug product can be reduced. Theoretically, as more pharmacies gain addditional experience with drug product selection, we can expect to find futher adjustments in their inventory policies. Pharmacies currently stocking an array of duplicate products will be able to stock fewer and thus take advantage of the resultant cost savings.

3. Fee Systems and Profit Margins

The fee system used by pharmacists can affect their incentive to substitute. Originally, pharmaceutical pricing was based on raw ingredient costs plus compensation for the professional labor time involved in preparing (compounding) the dosage form. Then as manufacturers began distributing products that already were compounded, pharmacies began utilizing a pricing system employed for other products in the drugstore -- the percentage markup method.[28]

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25 P. Brooke, Resistant Prices 13 (1975). See Green, "Welfare Losses From Monopoly in the Drug Industry: The Oklahoma 'Antisubstitution' Law," 5 Antitrust Law & Econ. Rev. 97,116 (1972), which reports that only 38% of the pharmacists surveyed in Oklahoma usually stock generic equivalents, while 61% seldom or never stock them.

26 Florida Pharmacist Substitution Study, supra note 21, at 24. William E. Woods, Executive Vice President of the National Association of Retail Druggists states that New York's drug substitution law will increase the inventory of pharmacists since they will have to carry less expensive equivalents for every drug that is subject to substitution. "Such massive inventory requirements are likely to increase patient costs." Drug Topics, Apr. 25, 1978, at 13.

27 Submission of Roche Laboratories, Inc., supra note 21, at viii.

28 Kedersha, supra note 9, at 96.

The "markup" is one of three methods used by pharmacists to price prescription drugs. Under this method the price paid by the consumer is calculated by applying a markup percentage (usually 50%) to the acquisition (or invoice) cost of the drug product. Pharmacists originally favored this method to avoid the necessity of allocating overhead costs to each particular drug product.[29] The markup system is based on the concept that pharmaceuticals are commodities. A sufficient percentage markup is added to the cost to arrive at a selling price which provides the pharmacist a profit.[30]

A second method, called the "professional fee," adds to the invoice cost a single fixed fee, regardless of the cost of ingredients. The professional fee is advocated by those who view the pharmacist's role as one rendering a specialized professional service. The value of these services are reflected in the professional fee,[31] and, unlike the markup, does not vary according to the wholesale cost of the drug product dispensed.

Rigidly applied, the two systems can produce considerably different prices for the same pharmaceutical product. To illustrate, consider a drug product with an invoice cost to the pharmacist of $6.00 for 100 tablets. With a typical markup of 50 percent the price to the consumer would be $9.00 ($6.00 plus $3.00 markup). Applying a two dollar professional fee the price to the consumer would be $8.00 ($6.00 plus $2.00 professional fee). If the consumer only needed 20 tablets, however, the price under the professional fee method would be considerably more expensive -- $3.20 ($1.20 plus $2.00 professional fee) than under the markup system -- $1.80 ($1.20 plus 50%.)[32]

The professional fee system has been criticized for being too inflexible and for imposing a greater burden than the markup in those cases where only a small quantity of drugs are being

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29 Gagnon & Rodowskas, "Reimbursement Methods for Pharmaceutical Service," 14 J. Am. Pharm. Ass'n 675-76 (1974).

30 Ashok Kumar Gumbhir, "The Determination and Evaluation of the Economic Significance of the Consumer Price Differentiation Between Generic & Brand Name Prescriptions," unpublished Ph.D. thesis, Ohio St. Univ., at 45 (1971).

31 Id. at 42.

32 This illustration is taken from Gumbhir, supra note 30,

at 38.
purchased or where the ingredient cost of the drugs is low.[33]

To avoid these disparities, many pharmacists employ a third selling price system which combines characteristics of the first two systems. Often called a "sliding fee," this system imposes a higher percentage markup on low-cost prescriptions and a lower percentage markup on high-cost prescriptions.[34] Of course, this is what occurs under a professional fee system. But in many cases, pharmacists either decrease their percentage markups as ingredient costs increase, or use a combination of a professional fee and a percentage markup system. One study found that in practice, pharmacies used a minimum charge when the ingredient costs were low and a lower than average markup when ingredient costs were high.[35]

Reasons given by pharmacists for this combination sliding-fee system are "to bring prices of lower-priced versions more into line with prices of higher-priced versions",[36] and to ease the burden on patients with high-cost medication.[37] Lower markups are also used for drug products with higher rates of turnover (usually the higher selling brands).[38]

In a survey of 300 prescriptions from each of 29 pharmacies sampled in a six-county metropolitan area, one study found that the average percentage markup was 50.5 percent. The study also found "that none of the pharmacies utilized a true fixed percentage markup pricing system or a true professional fee."[39] These

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33 Id. at 44.

34 Id. at 46; James Richard Green, "The Welfare Effects of an Antisubstitution Law in Pharmacy on the State of Oklahoma," unpublished Ph.D. thesis, Okla. St. Univ., at 86-88 (1972).

35 Gagnon & Rodowskas, supra note 29, at 678.

36 Green, supra note 34, at 88. Green surveyed 271 pharmacists and found 140 using the conventional percentage markup system, 19 using a flat professional fee, and 112 using a combination of the two. Id., at 86.

37 Gagnon & Rodowskas, supra note 29, at 678.

38 Id. at 676.

39 Id. at 678.

Pharmacists usually calculate ingredients cost first before determining the markup

flexible combination pricing methods tend to narrow the retail price range (and sometimes margins) between high and low-cost prescription drug products.

The different fee systems also have implications for substitution. Using the same markup, the pharmacist obtains a higher dollar profit on high-cost products than he or she does on low-cost products. Accordingly, the profit motive here provides a disincentive for substitution. Under the flat professional fee system, the pharmacist receives the same dollar profit whether a high or low-cost product is used. If the pharmacist makes the same dollar profit (though not the same percentage profit margin) regardless of the product's cost, he should not be disinclined to choose a low-cost product. Thus the type of fee system chosen can affect the incentive to engage in drug product selection, with the professional fee providing the greater incentive.[40] For example,

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39 (Footnote Continued)

> percentage that will be applied to calculate price. Prescriptions with high ingredient costs occur less frequently and thus will have lower markup percentages. This is a departure from the past when pharmacists used a prescription's ingredient cost with a set markup percentage to determine a prescription's price.
>
> . . . it has been hinted that in actual practice pharmacists who claim to utilize a (fixed) markup system of charging for prescription medication usually do not adhere rigidly to it. A minimum charge is likely to be used at the lower end of the pricing scale, while a reduced markup may be used at the higher end. Id. at 676.

40 See Kedersha, supra note 9, at 98. See also 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 Hous. L. Rev. 666, 725 (1969):

> Under imperfectly competitive circumstances, however, there are advantages in having a "professional fee" added to drug cost, rather than having the cost subject to a flat rate markup as this induces the substitution of brand name equivalents for the specified generic drug, since the profit margin in

(Footnote Continued)
a survey of 397 pharmacists prepared for Roche Laboratories, Inc., found that 32.7 percent of the pharmacists responding used a mark-up system, 16.9 percent used a fee system, and 47.1 percent used both systems. Of those who used the fee system, roughly two-thirds had an overall opinion favorable towards substitution. Over 60% of those who used both systems were likewise favorable, but only half of those utilizing the traditional markup method were in favor of substitution.[41]

Because acquisition costs for most generic equivalents are lower than those for leading brand name drug products, drug product selection presents promising profit opportunities for some pharmacies. And no matter which fee system is chosen, there should be greater flexibility for pharmacies to obtain higher percentage profit margins on generic drug products, as some pharmacists assert. The Chairman of the Rite Aid drugstore chain, for example, states that "[t]raditionally, the profit margins [i.e., percentage markups] on generic drugs have been much higher than the profit margins on brands." He maintained that the percentage markup on generic equivalents by chain drug-stores is traditionally almost twice as high as the markup on brand names.[42]

Even though pharmacists will be offering lower-cost drugs to the patient, they should be able to earn greater percentage profit margins, and in many cases, greater dollar profits. Because whole-sale costs for generic products generally are lower, pharmacists can offer them to consumers at lower retail prices and still increase their own percentage profit margins. Moreover, these less expensive products should generate increased sales volume.

In the FTC study, 27 percent of the pharmacists surveyed reported that their stores's net profit margins increased after drug product selection had resulted in an increase in net profit margins. Most, however, reported that their margins remained the

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40 (Footnote Continued)

> applying the same markup to the higher cost good is greater. But if a "professional fee" is added to each order, regardless of the cost of the drug to the retailer, this bias disappears.

41 Nat'l Pharmacist Attitude Survey, supra note 19, Table 98.

42 F-D-C Reports, June 13, 1977, at 9.

same (61%), whereas 11.6 percent said they had declined.[43] In a Michigan study, three-quarters of the pharmacies surveyed indicated that their profits were unaffected by the state's new law permitting drug product selection.[44] It may be too early to tell whether these results will persist. According to one study, increasing profits reflect wider margins on sales of generic drugs as well as savings incurred from reduced inventories. Stable profits reflect the necessity in some cases to carry larger inventories as well as the cost pressure of third-party reimbursements.[45] To the extent that pharmacies are able to refine their inventory practices, drug product selection may enhance their profit margins.

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43 FTC Study, supra note 20, at 42.

44 Submission of Roche Laboratories, Inc., supra note 21, at viii, ix. 15% reported an increase in profits; 9% reported a decrease.

45 Id.

CHAPTER V. THE PATIENT'S ROLE

The physician prescribes, the pharmacist dispenses, and the patient pays. Except for choosing not to fill a prescription or to patronize a different pharmacy the patient's traditional role has been passive and limited. This is so even when the pharmacist selects the particular drug product used to fill a generically-written prescription. Consequently, this section will focus on the significance of drug costs to consumers and on consumers' attitudes toward product selection laws as a means of lowering these costs. Special emphasis will be given to the plight of the elderly. We also will review consumers' attitudes toward the use of generic drug products, and the modification of state antisubstitution laws to allow pharmacists to select drug sources. Finally, we briefly will discuss how product selection may give consumers a more active role in the prescribing decision.

A. Consumer Drug Costs

Drug costs are a significant part of the American public's health bill and total cost of living. In 1976, 53 percent of the population incurred some prescription drug expense and the average yearly expense for this group was $52.[1]

Like almost everything else, the cost of prescription drugs has gone up in recent years. In 1976, the average prescription cost $5.60,[2] an increase of $1.58 over 1970.[3] For new products introduced in 1976 the average new prescription price was $9.24.[4]

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1 Wertheimer, Proceedings of the International Conference on Drug and Pharmaceutical Services Reimbursement, Washington, D.C., Nov. 2-5, 1976, at 2.

2 Am. Druggist, January 1978, at 62.

3 Id.

4 Id. The prescription drug component of the Consumer Price Index (CPI) for prescription drugs has gone up more slowly than other areas of medical care. Table 1 using 1967 as the base year shows the relative change in prescription prices to 1972.

TABLE 1

Period	CPI for Prescriptions
1967	100.0
1968	98.3
1969	99.6

(Footnote Continued)

Prescription drugs represent approximately 10 to 15 percent of per capita health expenditures.[5] These figures are particularly significant to consumers because a large proportion are direct payments or out-of-pocket costs. In 1976, personal health care per capita expenditures were $552; $179 of these were in direct payments. Of this latter amount, $43 went for drugs and drug sundries.[6] The extent to which drug expenses are paid out-of-pocket is also demonstrated by comparing the proportion of hospital, physician and drug costs covered by third party

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4 (Footnote Continued)

1970	101.2
1971	101.3
1972	100.9

Social Security, Table M-32, Medical Care component of the consumer price index, 1940-73, at 76.

According to CPI estimates prescription prices did equally well against the cost of living in general. In 1976, the CPI for prescriptions was 115.2 and the CPI for all items was 170.5. PMA, "Questions and Answers, II Prescription Drug Prices", May 1977, at 3.

The relevance of the CPI figures can be challenged because they reflect price changes for only 14 prescription drugs and do not necessarily comprise the ideal "market basket." Indeed, because the vast majority of the 14 CPI list drugs are multisource, they might overestimate the extent of price competition in prescription drugs. Task Force on Prescription Drugs, Dept. of Health, Education and Welfare, The Drug Users 16 (December 1968). In fact, three other indices, the Lilly Digest Index, the National Prescription Audit and the American Druggist Index, demonstrate that over the last decade the average prescription price has been increasing at an annual rate of 2 percent. Id. Using varying methodologies, these indices cover more drugs and appear to give a more accurate picture of the charge in relative cost of prescription drugs. Id. at 16-19. In any event, low CPI drug figures do not undercut the conclusion of this report that prescription drug prices would be lower if the multisource market were made more competitive by enactment of drug product selection.

5 Wertheimer, supra note 1, at 5.

6 Social Security, supra note 4, at 8.

payments in 1976: 91, 61, and 16 percent respectively.[7] During 1972, only 53.7 percent of the civilian population was insured in any way for prescription drugs.[8] Moreover, much of this third party coverage contained high deductible requirements.[9] As we will see later these drug expenditures are higher than need be because pharmacists have not been allowed to select drug sources (see Chapter VIII., infra).

In the future the demand for prescription drugs is expected to increase dramatically. From 1964 to 1973, drug expenditures have nearly doubled from $4.6 billion to $8.7 billion.[10] This trend is expected to continue,[11] with prescription drug consumption increasing 27.6 percent by 1980.[12]

B. The Special Problems of the Elderly

If the prospects of lower drug prices are important to the American public as a whole, they are doubly significant to Americans over 65 years of age. This group uses a disproportionately high amount of prescription drugs and has a disproportionately low income.

The elderly's share of drug expenditures is large. While the elderly comprise only 11 percent of the U.S. population, they buy 25 percent of all drugs and drug sundries.[13] Per capita estimates vary from source to source and by year, but it is undisputed that the elderly spend more on drugs than other age groups. In 1971 persons over 65 spent 1.2 billion dollars on drugs; their per capita expenditures were $52, nearly triple

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7 Id.

8 M.S. Mueller, "Private Health Insurance in 1972: Health Care Services Enrollment & Finance," Soc. Security Bull., March 1974, at 32.

9 Id.

10 Memorandum to file by Jill Deal, FTC, at 11 (undated).

11 Fouch, "Supply and Demand of Prescription Drugs, 1970-80," 11 J. Am. Pharm. Ass'n 534 (1976).

12 Id.

13 Drug Topics, Sept. 1, 1977, at 14. In 1976 women made up roughly 57 percent of those over 65 and population trends indicate this disproportion is increasing. Drug Users, supra note 4, at 2. This fact is worth noting because women use significantly more drugs than men. Id.

the $18 figure for persons under 65.[14] In fiscal 1976, this age group's annual drug expenditures were $121 per person, more than double the $51 average for all ages.[15]

The elderly's problem of high drug costs is exacerbated by the fact that this group as a whole has a relatively low, often fixed, income. According to the HEW Task Force on Prescription Drugs in 1966 the elderly had an income roughly half as large as the average for all ages.[16] In light of these higher drug expenditures and lower income levels, the elderly not surprisingly spend more of their income on medication than other age groups. For those suffering from chronic maladies the burden can be

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14 HEW, Off. of Research and Statistics, "Soc. Sec. Adm. Prescription Drug Data Summary 1972," at 6-7. A government survey of Medicare enrollees found an average personal drug expenditure in 1971 of $74. See "Summary Findings of High Drug Cost Survey of NRTA and AARP Members," Washington, D.C., 1974, at 1. ["NRTA-AARP."]

15 Drug Topics, supra note 13. Their high drug expenditures can be explained by the elderly's higher incidence of disease. The HEW task force stated that 80 percent of the elderly, or twice that of those people under 65 suffer from one or more chronic diseases. See Drug Users, supra note 4, at 12.

16 Statement by Fred Wegner, Legislative Representative for Pharmaceuticals of the Amer. Association of Retired Persons and National Retired Teachers Association Before the Subcomm. on Monopoly, Small Business Comm., U.S. Senate, 95th Cong., 1st Sess., Nov. 15, 1977, at 2. On the other hand, the aged are greater recipients of government assistance. In contrast with those under 65, the health care for the elderly--since the implementation of Medicare and Medicaid in the mid 1960's--is mostly publicly funded. As a result in 1973 an aged person directly paid an average of $311 out of his total $1052 bill.

In 1966, half of the families headed by an individual aged 65 or more had incomes less than $3,645; in comparison, the median income figure in 1966 for all American families was $7436. Cooper & Piro, "Age Differences in Medicaid Care Spending, Fiscal Year 1973," Soc. Security Bull., May 1974, at 5-6. Between 64 and 59 percent is publicly funded. In 1972 the ratio remained the same with median income for families with household heads aged 65 or over half the national median of $11,116. "Income and Poverty in 1972, Advance Report, Administration on Aging," HEW, Publ. No. OHD-20008, July 1973, at 1.

extraordinary. According to a 1974 National Retired Teachers Association - American Association of Retired Persons survey of 2000 of their members, all of whom were heavy drug users, at least 10 percent of their income was spent on medication.[17] In dollar terms, the annual drug expenditures of those responding ranged from $200 to $1000.[18] This astonishing figure results from the insignicant role of private third-party drug payment plans[19] and the inability of many of those living on poor and near-poor incomes to gain Medicaid eligibility.[20] Consequently, the elderly in 1966, according to the HEW Task Force, had to pay 80 percent of their prescription drug costs out-of-pocket.[21] (It should also be noted that high costs may mean that some of the elderly go without medication to buy other necessities. To the extent product selection lowers prices it could also reduce undermedication. For further discussion see Chapter VIII., infra).

These figures on drug costs and income levels illustrate the importance of prescription drug prices to the elderly, but more graphic testimony is provided by their personal accounts.[22] The following excerpts are taken from two letters written in response to the FTC's proposed prescription drug rule dealing

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17 NRTA-AARP, supra note 14, at 1-2.

18 Id. at 2.

19 Id. at 1.

20 See Drug Users, supra note 4, at 27. See also Statement by Evan Pritchard, Chairman of the New York State Joint Legislative Committee of the National Retired Teachers & the American Association of Retired Persons at Hearings on H.R. 882 Before the U.S. House of Rep. Subcomm. on Consumer Protection and Finance, Aug. 2, 1976 at 1-11. Medicare pays for drugs used by elderly persons only when they are institutionalized. Id.

21 Drug Users, supra note 4, at 27.

22 We know that as age increases consumers are more likely to express negative opinions about prescription prices. Braucher, Jowdy and Thorp, "Consumer Attitudes and Drug Prices," Pharm. Marketing & Media 2, 15 (November 1968).

Seary, "Consumer Attitudes Toward Prescription Prices: An Investigation and Analysis of Consumer Attitudes Toward Prescription Prices by Selected Consumer Characteristics," (Master's Thesis, Oregon State Univ.), August 1968, at 58.

with price disclosure:

> I am 90 years old, disabled, and use a cane. Nethertheless, I sometimes travel by bus to Hudson Drug Co. at 421 Lexington Avenue, New York, N.Y., to have a prescription filled, because of their lower prices. For instances, at a local drug store (Bigelow Pharmacy, 414 Sixth Avenue, New York, N.Y.) a prescription for 90 Seconal was priced on January 31, 1975, at $4.50. At Hudson Drug Co. I paid on April 1, 1975, $2.75 and on June 5, 1975, $3.50.[23]
>
> * * * *
>
> Something needs to be done to help us average citizens, and in addition to being average income citizens we are senior citizens, and our incomes are not as adequate in proportion as they were in our working years.
>
> The physicians do not volunteer the generic name. Once I got a pharmacist to contact my physician to okay the generic equivalent. It is just keeping us consumers in the dark while our savings and income are siphoned right out of our pockets for drugs we need.
>
> Please do all you can for us. We know you have a headache of a job, but you are capable and we are not. Thanks for your consideration.[24]

C. Consumer Attitudes Toward Drug Product Selection

Numerous groups such as the National Retired Teachers Association (NRTA) - American Association of Retired Persons (AARP),[25]

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23 Letter from May L. Carter to FTC on Prescription Drug Prices, Aug. 8, 1975.

24 Letter from Mr. and Mrs. Rozer A. Lachtenberg to FTC on Prescription Drug Prices, Aug. 1, 1975.

25 See, e.g., John B. Martin, Legislative Consultant, NRTA and AARP, in "Prescription Drug Labeling and Price Advertising," Hearings on H.R. 882, H.R. 884 and All Identical Bills, Before the Subcomm. on Consumer Protection and Finance, Comm. on Interstate and Foreign Commerce, U.S. House of Rep., 94th Cong., 2nd Sess., 1976, at 164 ["Hearing on H.R. 882"].

Consumers Union,[26] the Consumer Federation of America,[27] and state Public Interest Research Groups (PIRG's)[28] have advocated the enactment of drug product selection laws. To a large extent, their efforts explain the accelerating repeal of state antisubstitution laws. The Legislative Representative for the NRTA and AARP, for example, observed:

> NRTA and AARP five years ago embarked upon a legislative action plan to enact state generic drug substitution laws in an effort to stimulate price competition and lower drug prices. The result is one of the remarkable success stories of the consumer movement. Today 39 states, the District of Columbia and Puerto Rico have enacted substitution laws and we have efforts underway in nearly all the remaining 11 states.[29]

A few opinion surveys have attempted to determine the attitudes of individual consumers towards drug product selection. These determinations are difficult to make because many consumers are unfamiliar with the concept of drug product selection. Furthermore, the concept involves such complicated and technical issues as chemical, biological and therapeutic equivalence, state drug formularies, and the various formats allowing physicians and consumers to prohibit or refuse substitution. Thus, the consumer surveys we examined, which presented different information and posed different questions, not surprisingly received different responses.

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26 See, e.g., Raymond T. Bonner, Director of the West Coast Regional Office of Conumers Union, Testimony Before Hearings on S.B. 384, California State Senate Comm. on Business and Professions, May 7, 1975.

27 See, e.g., Letter from Carol Tucker Foreman, Executive Director, and Kathleen F. O'Reilly, Legislative Director, Consumer Federation of America, in Hearings on H.R. 882, supra note 25, at 169.

28 See, e.g., Susan Sayler, Project Coordinator, Calpirg, in Hearings on H.R. 882, supra note 25, at 47; "How to Win at R_x Monopoly." A MaryPIRG Report, July 1976. See generally Hearings on H.R. 882, supra note 25.

29 Fred Wegner, Legislative Representative, NRTA-AARP, "Testimony on Federal Drug Substitution Legislation and H.R. 1963," Presented to the Subcomm. on Consumer Protection and Finance, U.S. House of Rep., 95th Cong., 2nd Sess., June 23, 1978, at 1-2.

The leading independent consumer surveys addressing this issue were conducted by William McCormick and by Arthur Nelson. McCormick, in his 1977 study, used telephone interviews, to ask 100 consumers their views of repealing Wisconsin's antisubstitution law:

> Do you favor or disfavor changing the law so pharmacists can choose which manufacturer's product to dispense without first obtaining the physician's consent.[30]

The respondents split almost evenly with 50 percent opposing and 46 percent favoring removal of the prohibition.[31] McCormick's results may reflect increased awareness of the advantages of generic drugs by consumers in 1977. At the same time McCormick's survey illustrates the difficulty of just looking at that simple breakdown. Many of those respondents disfavoring removal of the prohibition on brand substitution may not have understood the effect of the modification of the antisubstitution law. For example, 62 percent opposed substitution because they had "more confidence in the physician judgment," and therefore may not have realized that the doctor can prohibit substitution and insist on a particular brand.[32] Accordingly, consumer response may have been different if the operation of the product selection law were better understood.

Another McCormick study first defined "chemical equivalents" as products containing the same active ingredients in the same amounts, but made by different companies and sometimes sold under different brand names.[33] The study then asked 510 Florida consumers to indicate on a scale of 1 (strongly disagree) to 5 (strongly agree) whether they disagreed or agreed with a series of statements about chemically equivalent drug products.[34] The

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30 McCormick, "Attitudes of Pharmacists, Physicians, and Consumers Toward Repeal of Antisubstitution Laws," 1972, (unpublished Ph.D thesis, University of Wisconsin) at 220.

31 Id.

32 Id.

33 McCormick, Doering, Lambert, & Goldstein, "Prescriptions of the Elderly Regarding Pharmacies, Drugs, and Pharmacists," Presented to the Economics and Administrative Science Section at the 23rd National Meeting of the APhA Academy of Pharmaceutical Sciences, Phoenix, Arizona, Nov. 13-17, 1977.

34 Id.

respondents strongly agreed with the following statement:[35]

> If the prescription drugs are chemically equivalent, a low price band will be just as effective in relieving an illness as a high priced brand. [Mean response was 4.80 for consumers under age 65 and 4.37 for those over 65].
>
> If the prescription drugs are chemically equivalent, a low priced brand will be just as safe for a person like myself to take as a high priced brand. [Mean response was 4.87 for consumers under age 65 and 4.48 for those over 65.]

Arthur Nelson in his 1973 survey canvassed 999 consumers on a nationwide basis. Nelson first explained the concept of generic equivalence and then asked:

> As you know, a prescription drug is one which requires a doctor's order before you can obtain it. Some states have a law that says when there is a cheaper "chemically equivalent drug" available, the patient may ask the pharmacist to fill his prescription with that less expensive equivalent drug. . . . Do you think that this law is a good idea.[36]

Nelson found that 58.8 percent of consumers favor repeal of antisubstitution laws while only 15.8 percent opposed it.[37] Nelson also found that the respondents were generally disposed to accept generic products irrespective of the cost of the brand-name drug.[38] He determined that a majority were willing to "probably" or "definitely" accept pharmacists selecting the

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35 Id. at Table 9. Respondents also strongly agreed that a low priced chemical equivalent would have no more side effects than a high priced brand, and strongly disagreed with statements that the high priced brand would be fresher or more powerful than the low price brand.

36 Nelson, "The Saliency of Price in the Acceptance of the Pharmacist Substituting Chemically Equivalent Drugs on a Prescription," July 1973, (unpublished Ph.D. thesis, University of Iowa), at 222.

37 Id. at 81, 91.

38 Id. at 91.

drug product at savings levels of one or two dollars.[39] In one respect, Nelson's question may represent an improvement because it makes clear that pharmacists must notify the consumer of substitution and the customer can refuse substitution.[40] On the other hand, by omitting a discussion of the physician's role and by emphasizing the patient's choice, his question may be biased in favor of selection laws. Further, because Nelson's results are now five years old they may not accurately indicate current consumer attitudes on this subject.[41]

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39 Id. at 86, 87, 91.

40 See discussion of state laws at Ch. VII.B., infra.

41 Nelson's questionnaire also highlights the effect tacit physician approval may have on consumers willingness to accept product selection by pharmacists.

TABLE A

Attitude Toward Pharmacist Substitution	Number	Percent
Prefer substitution on all prescriptions	78	7.9
On most prescriptions except the ones the physician specifically said not to substitute	572	57.9
Only on the ones the consumer desires a substitute	87	8.8
Don't know	57	5.7
Perfer the pharmacist not substitute	199	20.0

Two points about Table A bear emphasis. First, adding the percentage for the first three categories--those respondents favoring substitution--gives an overwhelming approval figure of 74.3 percent. Second, although preservation of the doctors' veto is important, the fact that they do not use it is sufficient reason for a majority of the respondents to let the pharmacist select a drug product.

Another independent survey, conducted by pharmaSYST reports, reported findings similar to Nelson's. 180 consumers from the Minneapolis - St. Paul area were asked: "Would you be in favor of a drug product selection law?" The vast majority said "yes" (63.7%) while 16 percent said "no" and 20.4 percent were "undecided."[42]

Some manufacturer-sponsored surveys reach very different results. These surveys, however, appear to imply mistakenly that drug product selection laws eliminate the physician's ability to specify a particular brand. For example, a 1974 study, sponsored by PMA and prepared by G. D. Searle and Decision Making Information, gave adults 18 years of age and over a brief description of generic and brand-name products and asked a series of questions on the price, quality, safety, and profitability of the two types of products.[43] Then the following question was posed and responses were given:[44]

> Some people feel that doctors should be free to choose both the drug and the drug manufacturer for all prescriptions they write. Others feel that doctors should be restricted to selecting only the drug. How important do you think it is for a doctor to be able to choose both the drug and the drug manufacturer when he prescribes for his patients? (PLEASE READ OPTIONS)
>
> | | |
> |---|---|
> | EXTREMELY IMPORTANT.....1 | (42%) |
> | SOMEWHAT IMPORTANT.....2 | (29%) |
> | NOT TOO IMPORTANT.....3 | (24%) |
> | (NO OPINION).....4 | (4%) |

This question implies that pharmacists could select drug products even over the express wishes of the physician. In fact, however, for the pharmacist legally to select alternative brands the physician must at least tacitly approve under any system in effect or proposed.

Each of two other manufacturer surveys asked consumers the following question:

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42 pharmaSYST reports, September 1977.

43 G.D. Searle & Decision Making Information, "Executive Overview: Public Opinion on Maximum Allowable Cost and Substitution," Dec. 3, 1974, at 6-7.

44 Id. at 7.

> For most types of prescription medication, there are several drug products available which are made by different manufacturers. Who do you feel should determine which drug product is used for your prescription--the pharmacist or physician? [Emphasis added.][45]

Here, the problem of mischaracterization is raised again. The phrase "type of prescription medication" might mistakenly imply that pharmacists can substitute entirely different drugs as opposed to different brands of the same drug, and the second sentence implies that physicians are unable to prohibit this substitution. Consequently, it is not surprising that most of those responding preferred that the physician determine the "type of medication" used.

These problems in phraseology are not confined to the manufacturer-sponsored studies. For example, a 1966 study conducted by Braucher surveyed a non-random sample of 1000 consumers in the South and Midwest. After testing the participant's knowledge of generic drugs, the questionnaire asked the participant to select one of the following choices:

> (a) Would you prefer that the pharmacist dispense a generic drug product solely because it has the lower price, or ...
>
> (b) Would you prefer that the pharmacist dispense a brand-name drug at a slightly higher price, knowing that the drug was developed as a result of research and study by a well-known manufacturer.[46]

This formulation and the resulting responses have been challenged by Nelson as biased in favor of answer "b".[47]

Finally, there is some behavorial evidence that indicates in practice consumers are accepting the selection of lower-cost drug products. The FTC study of pharmacists provides some behavorial evidence supporting this view. The FTC study polled pharmacists

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45 Field Research Corp., "California Public's Attitude on Issues Concerning the Selection and Control of Drug Products Used in Prescription Medication", April 1974, at 3; Walker Research, Inc., "State of Wisconsin Prescription Drug Products Attitude Survey," January 1975.

46 Nelson, supra note 36, at 40.

47 Id. at 41.

from seven states with modified antisubsitiution laws. They responded overwhelmingly (71.1%) that less than 5 percent of their patients refuse a lower priced product when the pharmacist offers to substitute.[48] Likewise, 96 percent of the pharmacists in a California study reported that the patients "always" or "usually" concurred with their selection.[49] Furthermore, although many consumers do not yet understand product selection, the FTC study found that pharmacists may be filling that need. Of the pharmacists polled, 54 percent believe that as a result of product selection, pharmacists do spend more time with customers.[50] Similarly, 53 percent of the pharmacists polled believed that drug product selection has had a positive effect on patient-pharmacist relations.[51] States also might play a role in increasing consumer awareness of drug product selection and its advantages. (For further discussion of the need for consumer education see Chapter X.A. Section 5(d) of the Model Act, infra.)

Drug product selection should decrease the cost of a common and often uninsured health care expense. As we have seen the benefits will be doubly significant to the elderly who on average make more prescription drug purchases with less income. Finally, despite the difficulties involved in objectively determining consumer opinion toward drug product selection, in practice consumers appear to be accepting drug product selection.

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48 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978, at Table 16 ["FTC Study".]

49 "Perceptions on Product Selection," California Pharmacist, September 1977, at 7.

50 FTC Study, supra note 48, at 13.

51 FTC Study, supra note 48, at 34.

CHAPTER VI. FEDERAL REGULATION OF PRESCRIPTION DRUGS

A. FDA Regulation of General Product Quality and Bioavailability

The Food and Drug Administration (FDA) annually spends $62 million and employs 1,000 people in its Bureau of Drugs[1] to carry out its responsibilities, which include premarket approval of new drugs, enforcement of compendial standards, issuance of bio-equivalence regulations, and enforcement of Good Manufacturing Practices. This section will describe how FDA applies these regulations both to the original brand-name products and to their generic equivalents to assure the quality of all prescription drug products (for our discussion of how well this goal is met, see Ch.IX.C., infra).

1. Premarket Drug Approval

FDA imposes two types of legal requirements on prescription drug products: compendial specifications and premarket approval requirements. The compendial requirements (to be discussed later) are standards of strength, quality and purity that apply equally to all manufacturers: originators and generic manufacturers.

FDA premarket approval requirements vary for the three general categories of prescription drugs: (1) drugs first introduced before 1938 ("pre-1938 drugs"), (2) drugs first introduced between 1938 and 1962 ("1938-1962 drugs"), and (3) drugs first introduced after 1962 ("post-1962 drugs").

Pre-1938 drugs, whether manufactured under brand or generic names, are exempt from premarket approval by FDA so long as they continue to be marketed under their pre-1938 labeling. Manufacturers of pre-1938 drugs do, however, have to comply with applicable compendial standards.

Most drug products marketed today are versions of drugs first marketed between 1938 and 1962. The original manufacturer of a drug first marketed between 1938 and 1962 had to obtain premarket FDA approval of a full new drug application (NDA) that proved the drug's safety (a 1962 amendment to the law added the requirement that drugs be proven effective as well as safe). Manufacturers were required to submit proof of safety (and effectiveness) based upon the results of clinical tests in humans, as well as evidence of compliance with standards of strength, quality and purity. Since 1970, FDA has allowed manufacturers

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1 Donald Kennedy, Statement before the Subcommittee on Monopoly, Select Committee on Small Business, U. S. Senate, Nov. 14, 1977, at 5.

of generic versions of most 1938-1962 drugs to apply for premarket approval with an abbreviated new drug application (ANDA). Because the clinical tests performed by the original manufacturer already establish the safety and efficacy of the active drug ingredient, the ANDA generally does not require duplicate clinical testing, but does require evidence of compliance with standards of strength, quality and purity. Often "ANDA" requirements incorporate technological advances and thus impose more stringent quality controls on the manufacturers of the generic versions than were imposed on the original manufacturers.

Finally, all drugs (brand-name and generic) first marketed after 1962 require premarket FDA approval of full NDA's proving the drug's safety and efficacy.

a. Federal Food, Drug and Cosmetic Act

Until 1938, federal law did not authorize premarketing approval for pharmaceuticals sold in interstate commerce. In 1937, 107 people were killed by a sulfanilamide product called "Elixir Sulfanilamide."[2] The product, which had been tested for flavor, appearance and fragrance, but not for safety, used diethylene glycol, a toxic compound, as a solvent. The federal government was able to remove the product from the market only because it also happened to be misbranded.

This incident provided the impetus for passage of the Federal Food, Drug, and Cosmetic Act in 1938. The Act required that "new drugs" be proven safe prior to marketing. A new drug was defined as any drug not generally recognized as safe for its intended use.[3] In 1962, another tragic incident in which thousands of deformed babies were born to mothers who had taken the sedative thalidomide[4] prompted Congress to amend the Food, Drug, and Cosmetic Act to require that new drug applications contain substantial evidence of the drug's effectiveness as well as its safety.[5] Both the 1938 Act and the 1962 amendment exempted from the preclearance requirement those drugs which were on the market prior to 1938.[6]

b. Pre-1938 Drugs

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2 M. Silverman & P. Lee, Pills, Profits & Politics 86 (1974).

3 40 Fed. Reg. 26142 (1975).

4 Silverman & Lee, supra note 2, at 94-96.

5 21 U.S.C. §§321 (p), 355 (1970).

6 40 Fed. Reg., supra note 3, at 26145.

There are still being sold a small number of products based on drug entities that were introduced prior to 1938 and that subsequently were neither reformulated nor relabeled. An approved new drug application has never been required for these "pre-1938" or "old drugs." Unless FDA determined that they were no longer "generally recognized as safe and effective" and reclassified them as "new drugs," the agency could not require premarket clearance for these drugs. Pre-1938 drugs, however, are subject to FDA's bioequivalence requirements (see discussion infra), and manufacturers of such drugs can be required to complete and submit the results of adequate bioavailability studies. They also are subject to the adulteration and misbranding provisions of the Food, Drug, and Cosmetic Act.[7]

c. 1938-1962 Drugs

As noted above, the 1938 Food, Drug, and Cosmetic Act required that manufacturers of new drugs provide evidence of safety prior to marketing. When a particular active ingredient came off patent between 1938 and 1962, additional firms often sought approval of products containing the same active ingredient. FDA then had to determine whether subsequent marketers would have to duplicate previously performed safety studies involving clinical tests in humans to obtain approval for marketing. Because FDA usually did not require additional studies, firms sometimes began marketing such drugs without making any submission to the agency.[8]

The 1962 amendments required that new drugs be proven effective as well as safe and that products approved between 1938 and 1962 be reevaluated for efficacy.[9] In 1967, FDA contracted with the National Academy of Sciences - National Research Council (NAS-NRC) to establish a Drug Efficacy Study to review the effectiveness of these products. Thirty panels of experts reviewed approximately 4,000 drug formulations.[10] New drug applications previously approved for safety only were termed "deemed approved"

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7 Id.; 21 U.S.C. §§351, 352 (1970).

8 Gene Knapp, Associate Director for Drug Monographs, FDA Bureau of Drugs, "The Effect of FDA's Bioavailability and Bioequivalence Regulations on Currently Marketed and Future Drug Products," Speech presented at the 23rd National Meeting APhA Academy of Pharmaceutical Sciences, Phoenix, Arizona, Nov. 1977, at 5.

9 21 U.S.C. §355 (1970).

10 40 Fed. Reg., supra note 3, at 26143-44.

applications.[11]

Few firms had carried out efficacy studies of the type required for post-1962 products, and many products were legitimately on the market without approved NDA's because of FDA's pre-1962 approach of not requiring duplicative safety studies. As a result of its Drug Efficacy Study Implementation (DESI), FDA published announcements on those products ultimately determined by NAS-NRC and FDA to be effective or ineffective; these announcements usually required supplemental information for previously approved applications and specified conditions of approval for existing or future marketers not then holding approved applications.[12] At the time these notices were being prepared, drug bioinequivalence was beginning to emerge as a concern; consequently, demonstration of "biological availability" was usually included as a condition of approval in DESI statements, although in practice the requirement often was waived because the methodology to perform the necessary studies had not yet been developed.[13]

To eliminate unnecessary human experimentation, reduce the burden on manufacturers attempting to market duplicates of established drugs, and allow greater use of FDA resources for review of new active ingredients and dosage forms, FDA established in 1970 an abbreviated new drug application (ANDA) system for products identical, similar or related to previously approved DESI drugs.[14] Thus, firms seeking premarket approval of products based on drugs initially introduced between 1938 and 1962 have to submit either a full or abbreviated new drug

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11 Knapp, supra note 8, at 8.

12 By order of Judge William B. Bryant of the U.S. District Court for the District of Columbia on Oct. 11, 1972, a limited number of drugs for which there was a compelling medical need were allowed to remain on the market pending completion of scientific studies to determine effectiveness. In general, these were drugs for which the methodology to determine effectiveness had not yet been developed. Because this exemption was created in Paragraph XIV of Judge Bryant's order, these drugs are known as "Paragraph XIV" exempt drugs. See 37 Fed. Reg. 26623 (1972).

13 Knapp, supra note 8, at 9-13.

14 The ANDA application must include such items as a description of the methods, facilities and controls used in manufacturing, processing and packing; assurances that the drug formulation will comply with compendial specifications; and bioavailability data where necessary. 21 C.F.R. Part 314 (1977).

application.[15] The ANDA may be used only for those drugs containing well-established ingredients generally recognized as safe and effective when properly labeled and manufactured. The ANDA must demonstrate "the quality of drug products and their proper labeling and manufacture, not . . . the basic safety and effectiveness of the generic chemical entity involved."[16] This ANDA exemption from duplicative clinical testing was the same policy that had regularly been applied to drug reformulations.[17]

Frequently, ANDA requirements are misconceived to be less demanding than those imposed by full NDA's. But because most NDA drugs were introduced before 1962, whereas the ANDA mechanism was not established until 1970, ANDA requirements for marketing often reflect technological changes and therefore are more stringent and up-to-date. FDA Commissioner Donald Kennedy has commented on the technological advances incorporated in ANDA requirements:

> ANDA requirements not found in the earlier NDA may include improved analytical instrumentation and dissolution tests as final measures of drug quality and quality control. Finally, it should be noted that it was not necessary to obtain current good manufacturing practices (GMP) approval as a condition for marketing until 1963. Drug products approved before that time were therefore never faced with such a requirement.[18]

Furthermore, because the methodology to determine biological availability has improved, ANDA submissions also have at times included data demonstrating that the product for which approval is sought performs better than the previously approved (NDA) product. In such cases, FDA has usually attempted to improve the performance

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15 In 1975, Judge June L. Green held that FDA could not permit any new drugs to be marketed without an approved new drug application. Hoffmann-LaRoche, Inc. v. Weinberger, 425 F. Supp. 890 (D.D.C. 1975).

16 40 Fed. Reg., supra note 3, at 26147.

17 "FDA Analysis of Statement of C. Joseph Stetler, President, Pharmaceutical Manufacturers Association," Presented Before the Subcommittee on Monopoly and Anticompetitive Activities, Select Committee on Small Business, U.S. Senate, Nov. 16, 1977, at 2.

18 Kennedy, supra note 1, at 3.

of the original product.[19] FDA's Generic Drug Monograph Division Director, Marvin Seife, has commented on instances in which the agency has found the generic product to be superior to the original:

> Now when a pharmaceutical firm says 'we came out with propylthiouracil in 1942, therefore, we make it better than Purepac, or Barr, or Zenith in 1978,' this is not so. . . . [W]e find time and time again that under the technology of today the generic products are far superior. The large firms have not updated their formulations, their excipients are out of range, they just have not changed anything.[20]

d. Post-1962 Drugs

As mentioned earlier, all post-1962 drugs require full NDA's to prove safety and efficacy. Even as patents expire on these drugs, a manufacturer of an equivalent product cannot use an ANDA to obtain premarket approval. FDA is, however, considering ways to extend the ANDA mechanism to new drugs approved since 1962.[21]

Although post-1962 drugs approved during the 1960's were reviewed for both safety and efficacy, most of these products, like 1938-1962 drugs, were not the subject of bioavailability or pharmacokinetic studies. FDA bioavailability regulations (to be discussed later) require that manufacturers of such approved products perform bioavailability studies only if a potential problem is identified with the dosage form concerned. FDA has required bioavailability and pharmacokinetic studies on new drug products entering the market after the early 1970's. As a result of these requirements such products should present few, if any, biopharmaceutical problems in the future.[22]

2. Compendial Standards

Compendial standards are specifications of potency, purity and other measures of drug quality. Since the passage of the Pure Food and Drug Act of 1906, the United States Pharmacopeia

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19 Knapp, supra note 8, at 13-14.

20 F-D-C Reports, June 26, 1978, at 29.

21 Kennedy, supra note 1, at 2.

22 Knapp, supra note 8, at 19-20.

(U.S.P.) and the National Formulary (N.F.) have been recognized by the federal government as the official pharmacological compendia for the nation (in 1975 the two compendia were consolidated by the sale of the N.F. to the U.S. Pharmacopeial Convention, publisher of the U.S.P.; we therefore will make reference only to the U.S.P.). Medications differing in strength, quality or purity from the standards set forth in the U.S.P. are considered adulterated drugs.[23] Manufacturers may depart from these standards only if they plainly state their own standards on the drug label. Similarly, medications not packaged or labeled in accordance with U.S.P. standards are considered to be misbranded.[24] The Secretary of Health, Education and Welfare may prescribe tests and standards for drugs if none have been provided or if those described are judged inadequate. The Secretary must first allow the revisors of the U.S.P. a reasonable time to prescribe the necessary standards themselves.[25]

The U.S.P., first published in 1820, is supported by an independent nonprofit organization deriving its financial support from sales of the Pharmacopeia and from fees for the U.S.P. Reference Standards. Using a delegate system to elect the scientists who serve as unpaid volunteers on the U.S.P. Committee of Revision, the organization is composed of medical and pharmacy practitioners and educators. The U.S.P. is revised every five years, with interim supplements published as needed.[26]

The U.S.P. admits a drug solely on the basis of an evaluation of its therapeutic merits. Once the drug is accepted into the U.S.P., the manufacturer is invited to cooperate in the development of a proposed drug monograph. The typical monograph includes tests determining the chemical identity and quantity of the active ingredient among individual tablets or capsules, impurities, and physical attributes such as the time of disinte-

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23 21 U.S.C. §351(b) (1970). Not all marketed drugs are listed in the U.S.P. or N.F. Those drugs are adulterated if their strength, purity or quality differs from that which they are represented to possess. 21 U.S.C. §351(c) (1970).

24 21 U.S.C. §352(g) (1970).

25 21 U.S.C. §§351(b), 352(h) (1970).

26 The United States Pharmacopeia XIX (United States Pharmacopeial Convention 1975), at xii, xix-xx; Heller, "Drug Equivalency," in The Scientific Evaluation of Drug Equivalency 39-40 (A. Brest ed. 1974).

gration or dissolution.[27] Excipients (inert ingredients such as fillers) generally are not specified, although their effects may be evident in such physical attributes as dissolution behavior. These standards and specifications are based largely on in vitro tests ("test tube type" procedures performed outside the body) that have evolved from the results of in vivo testing (tests performed within the body) and clinical evaluations conducted by the product originator to obtain market approval from FDA.[28] Dissolution tests, which often are closely related to drug bioavailability (see discussion infra), are particularly important in furthering the U.S.P.'s goal of ensuring the bioequivalence of all sources of a given dosage form. Therefore, in 1976 the U.S.P. adopted as a goal the development of dissolution tests for all oral solids.[29]

Drugs admitted into the U.S.P. are listed by generic name only; the specified tests for strength, quality and purity must be met by all sources of that drug, whether they are marketed under its generic name alone or under brand names.

3. Batch Certification

To ensure potency, purity and sterility, FDA subjects certain drugs -- antibiotics, insulin and digoxin -- to more stringent batch certification.[30] This certification began in 1941 for insulin, shortly after its patent expired. The program was begun because any variation in batch quality for this life-saving drug is potentially serious. For the same reasons batch certification was applied to penicillin in 1945, and by subsequent amendments, to all antibiotics.[31] These amendments also placed all responsibility for

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27 As an illustration, the content uniformity test is met if the content of nine out of 10 capsules assayed is within the limits of 85% and 115% of the average specified in the potency definition in the monograph, and if the content of none of the 10 capsules falls outside the limits of 75% and 125% of that average. The United States Pharmacopeia XIX, supra note 26, at 648.

28 Bergen, "NF Role in Scientific Evaluation of Drug Equivalency," in The Scientific Evaluation of Drug Equivalency 2-3 (A. Brest ed. 1974).

29 Am. Druggist, Apr. 1978, at 82.

30 21 U.S.C. §§356, 357 (1970); 39 Fed. Reg. 2471 (1974).

31 Task Force on Prescription Drugs, U.S. Dept. of Health, Education, and Welfare, The Drug Prescribers 35 (1968).

drug standards for antibiotics on FDA.[32] Digoxin was added to the certification program in 1974 upon discovery of clinically significant differences in bioavailability among certain digoxin products.

The certification procedure requires manufacturers to submit samples of each batch to FDA and to withhold distribution of the batch until notified of FDA approval. Certification may be waived if the manufacturer establishes a satisfactory performance record over a period of time. FDA thus far has found a high degree of satisfactory performance: the overall rejection rate is less than one percent for the 20,000 batches of antibiotics and 600 batches of insulin certified each year.[33]

The batch certification program will be expanded considerably as FDA imposes requirements for batch testing as part of its bioequivalence regulations (see discussion below).[34]

4. Bioavailability/Bioequivalence Regulations

a. Terminology

The study of drug bioavailability has been a new development in part because the analytical techniques to measure drug levels in the body have been devised only recently. To understand the complex issues involved, one first must understand the following types of equivalence.

"Chemical equivalents" are drug products that contain identical amounts of the identical active drug ingredient in identical dosage forms (but not necessarily containing the same inactive ingredients). Thus, two tablets labeled as containing 400 milligrams of meprobamate would be chemically equivalent if they actually do contain that quantity of the drug.

"Biological availability" or "bioavailability" measures how fast and how much of the drug gets into the body, appears in the blood, or is excreted in the urine after the dose has been administered.[35] Two or more chemically equivalent products

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32 21 U.S.C. §357(b) (1970).

33 40 Fed. Reg., supra note 3, at 26147.

34 42 Fed. Reg. 1624, 1636 (1977).

35 In somewhat more precise terms, "bioavailability" is the rate and extent to which the active drug ingredient is absorbed from a drug product and becomes available at the site of therapeutic action. Id. at 1648.

of approximately equal bioavailability are said to be "bioequivalent."

"Therapeutic equivalents" are two or more chemically equivalent products that are equally effective in treating a particular disease state.

b. Bioavailability and Related Tests

To assure the therapeutic equivalency of all batches of a particular product ideally would require measuring the clinical effect of each batch. This practice is not possible because it is extremely expensive, it requires large numbers of patients suffering from the same disease, and because objective measurement techniques often are nonexistent. The next best approach-measuring drug blood levels for each batch--also suffers from prohibitive cost and the need for large numbers of healthy test subjects. A more practical alternative is to develop in vitro tests (tests performed outside the body) which have been based on (or correlated with) in vivo bioavailability tests (tests performed within the body). The in vitro tests then may be used as indicators of bioavailability, or as an assurance that subsequent batches will perform comparably to the batch in which clinical or blood level testing was originally conducted. For example, dissolution testing, which measures the rate at which the drug dissolves in a specified medium under specified conditions, is an in vitro method often used as an indicator of bioavailability or as one means of assuring batch-to-batch uniformity.[36]

c. The Blood Level Curve

The extent of bioavailability generally is determined by taking blood samples after administering the drug and constructing a blood level curve.[37] By plotting on the verticle axis the concentration of the drug in the blood (or serum or plasma) against time on the horizontal axis, one can derive an ordinary blood level curve (Figure 1). If the drug is administered at time zero, the drug concentration then should be zero. As the drug product passes into the stomach or intestine, it disintegrates, and the drug dissolves and is absorbed. Increasing concentrations are found as sampling continues until the maximum concentration in the blood is achieved. This point of maximum concentration is called the "peak" of the blood level curve. Past the peak

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36 American Pharmaceutical Association, The Bioavailability of Drug Products 5-6 (L. Dittert & A. DiSanto coordinators 1975).

37 Another common measure is the cumulative amount of drug excreted in the urine.

(to the right), the rate of elimination exceeds the rate of absorption and the blood concentration decreases.[38]

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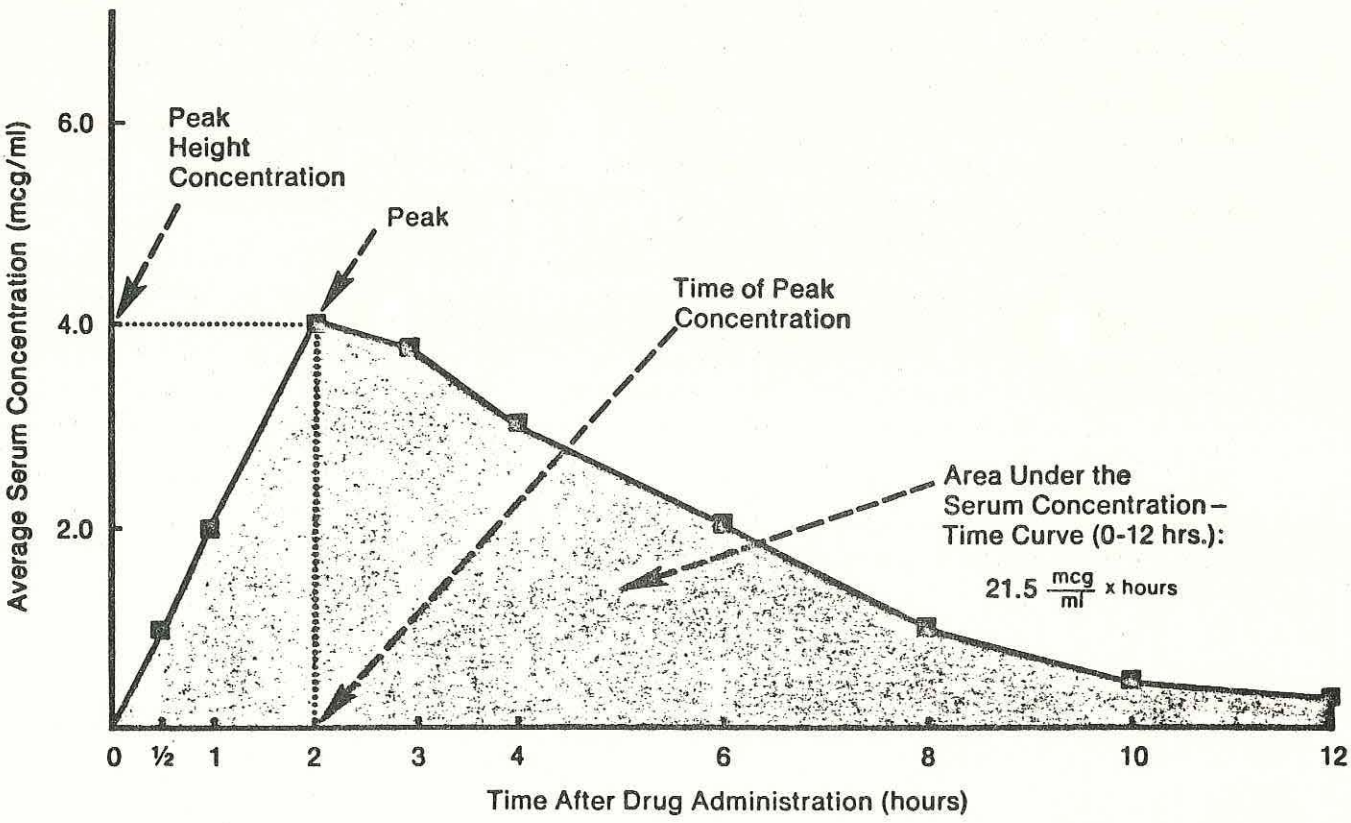
38 D. Chodos & A. DiSanto, Basics of Bioavailability 16-17 (1974).

Figure 1



Source: D. Chodos & A. DiSanto, Basics of Bioavailability (1974). (Reproduced by permission of the authors).

The three most important parameters describing the curve are a) the peak height, b) the time of the peak, and c) the area under the curve. The peak height represents the highest blood concentration achieved after oral administration of the drug. The peak height is important because it can show whether the blood level is sufficiently high to achieve or exceed the minimum effective concentration, or alternatively whether it is so high that it reaches the minimum toxic concentration (it should be recognized that actual values for effective and toxic levels have not been determined for most drugs, and that those levels would vary considerably for different individuals).[39] The time of the peak blood concentration measures how long it takes to achieve the maximum concentration of the drug. This parameter is used as a simple measure of the rate of drug absorption from a particular formulation. The area under the blood level curve measures the total amount of drug absorbed following administration of a single dose.

Figure 2 shows the blood level curves for three different formulations of the same drug. Although formulations A and B demonstrate similar peak heights and times, the area under the curve (total amount of drug absorbed) is 33 percent greater for A than B. This difference in absorption may or may not mean that A and B are inequivalent in pharmacological effect. Formulation C clearly differs from A and B in all three parameters and is not bioequivalent to either formulation. Whether this bioinequivalence is thereapeuically significant is another question.[40]

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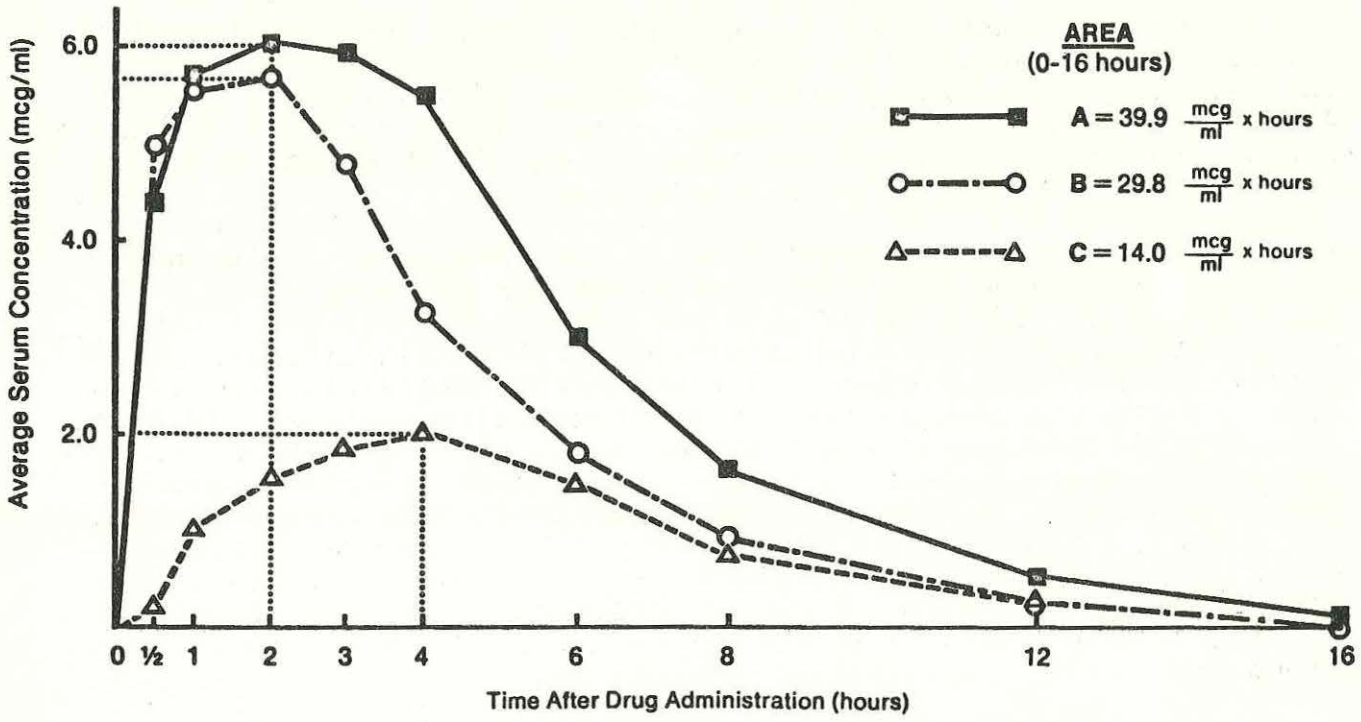
39 Id. at 18.

40 Id. at 20.

Figure 2



Source: D. Chodos & A. DiSanto, Basics of Bioavailability (1974). (Reproduced by permission of the authors).

Among the physiochemical factors believed to predispose a drug to bioequivalence problems are low water solubility, slow dissolution rate, variation in particle size or surface area, and presence of specific inactive ingredients that may promote or retard absorption.[41] Bioavailability also can be affected by non-physiochemical factors such as interaction with food or other drugs in the gastrointestinal tract, or characteristics of individual patients.

d. Digoxin - An Illustration of Bioinequivalence

Digoxin probably provides the best know example of clinically significant bioinequivalence. Digoxin, a derivative of digitalis, is a critical drug widely used by heart disease patients. Precise dosage regulation is particularly essential with digoxin because of the narrow margins separating ineffective, effective and toxic doses. In 1970, FDA recalled a large number of digoxin tablets due to the failure of several brands to maintain consistent potency from tablet-to-tablet. Subsequently, FDA initiated a voluntary batch certification program to ensure uniformity of potency.[42]

In 1971, investigators at a New York City municipal hospital[43] reported marked differences (as high as 700%) in blood levels achieved with digoxin tablets produced by different manufacturers and among different batches prepared by a single manufacturer. FDA noted certain deficiencies in the report, particularly the fact that some of the tablets failed to meet the U.S.P. specifications for potency and thus were subject to recall. Subsequent studies, however, demonstrated that problems were not solely attributable to low potency rather than poor bioavailability; bioinequivalence was found among products which did meet the compendial specifications for content uniformity.[44]

A significant correlation has been shown between digoxin bioavailability and the dissolution rate of digoxin tablets.

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41 Leslie Benet, University of California School of Pharmacy, "Bioavailability/Bioequivalence - Science or Seance," Speech presented to APhA Academy of Pharmaceutical Sciences, Phoenix, Nov. 14, 1977.

42 39 Fed. Reg., supra note 30, at 2471.

43 Lindenbaum, et al., "Variation in Biologic Availability of Digoxin from Four Preparations," 285 N. Engl. J. Med. 1344 (1971).

44 39 Fed. Reg., supra note 42, at 2471.

FDA therefore took measures in 1974 to eliminate bioinequivalence problems among different brands of digoxin tablets by requiring batch certification on the basis of specified dissolution tests (these tests specify both minimum and maximum dissolution rates). FDA also reclassified all digoxin products for oral use as new drugs for which an ANDA is required. Any company marketing digoxin must show adequate evidence of bioavailability by submitting results of in vivo studies.[45]

The digoxin incident also illustrates the susceptibility of both brand-name and unbranded products to bioavailability problems. In this country, the innovator product, Lanoxin by Burroughs Wellcome & Co., produced consistent blood levels of digoxin and was never involved in any recalls.[46] A change in the manufacturing process of Burroughs Wellcome digoxin in England, however, doubled the bioavailability of its Lanoxin tablets, thus causing the company to circulate a warning letter to British doctors in 1972.[47] Such incidents led the Director of the APhA Bioavailability Pilot Project to recommend:

> A pharmacist should not blindly rely on using any brand of digoxin (no matter what the size or reputation of the manufacturer); rather, he should continually seek to request and evaluate data on digoxin tablets from his sources.[48]

e. FDA Bioavailability/Bioequivalence Regulations

In January 1977, FDA promulgated regulations designed to assure the bioequivalence of marketed drug products.[49] The regulations consist of two major parts: the first part establishes criteria to identify products with bioequivalence problems,

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45 Id. at 2475-76.

46 Colaizzi, "The Bioavailability of Drug Products: Digoxin," in The Bioavailability of Drug Products 19 (1975); Madden & McCormick, "Digoxin: Producers and Products," January 1976 at 7 (OPE Report J, FDA).

47 2 Lancet 311 (1972).

48 Colaizzi, "Commentary on Digoxin Bioavailability," APhA Newsletter, June 23, 1973, at 4. An FDA report on digoxin confirms that bioavailability problems involved both brand-name and generic manufacturers. Madden & McCormick, supra note 46, app. B, at B1-B6.

49 42 Fed. Reg., supra note 34, at 1624.

and further establishes procedures to assure that such products perform in a predictable and reliable manner; the second part requires that all new drug applications be accompanied by evidence of the product's bioavailability.

The criteria used by FDA in establishing a bioequivalence requirement include: documented therapeutic failure; documented bioequivalence; exhibition of a narrow therapeutic ratio (i.e, drug products with narrow differences between effective and toxic doses); competent medical determination that bioinequivalence would have a serious clinical effect; physicochemical evidence such as low solubility in water or slow dissolution rate; and pharmacokinetic evidence such as poor drug absorption.[50] Drug products meeting any one of the first three criteria ordinarily will require in vivo testing in humans to satisfy the bioequivalence requirement.[51] Any person may petition FDA to establish a bioequivalence requirement.[52]

Bioequivalence requirements will have to be met by a firm with an approved NDA even if its product has been shown to be safe and effective in clinical trials. FDA has found bioequivalence problems involving products manufactured by holders of approved NDA's as well as those manufactured by firms that do not hold an approved NDA. Moreover, the clinical trials used to prove safety and effectiveness are not as sensitive, accurate or reproducible as other bioequivalence methods.[53]

The bioequivalence requirement for most products will consist of an in vitro test in which the product is compared to a reference material. Where possible, the in vitro test will be one that has been correlated with human in vivo data.[54] The use of in vitro dissolution tests is based on FDA's experience that poor bioavailability is associated with poor dissolution. FDA has stated that it is unaware of any instance in which noncontrolled release products with high dissolution rates were shown not to be bioavailable when tested in vivo.[55]

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50 Id. at 1635.

51 Id. at 1636.

52 Id.

53 Id. at 1632.

54 Id. at 1627.

55 Id. at 1628.

Another key provision requires batch testing by each manufacturer of all products for which bioequivalence requirements are established and, as necessary, batch certification by FDA (similar to the digoxin program) to assure that each lot meets the appropriate *in vitro* specification. Ordinarily, FDA will terminate the requirement that samples of each batch be certified prior to marketing upon finding that the manufacturer has satisfactorily met the *in vitro* standard on four consecutive batches.[56]

FDA estimates that about 30 bioequivalence requirements will be necessary for the drugs and drug classes presenting bioequivalence problems.[57] The first rulemaking proposals for such requirements have been made for certain anticonvulsants,[58] tricyclic antidepressants,[59] and procainamide hydrochloride.[60] The proposals would require that each manufacturer conduct an *in vivo* bioavailability study in humans and would further require *in vitro* dissolution testing on product batches.

The bioavailability regulation demands that all new drug applications (NDA's and ANDA's) and certain supplemental applications submitted after July 7, 1977, include (1) evidence demonstrating *in vivo* bioavailability or (2) information to permit FDA to waive demonstration of *in vivo* bioavailability.[61] Waiver of *in vivo* testing is permitted for certain specified conditions; a common element is the requirement that *in vitro* data be provided by the manufacturer as a basis of drug approval.[62] FDA believes this approach makes efficient use of the limited resources available for *in vivo* testing and recognizes the guiding principle that no unnecessary human research should be performed.[63] Waiver of *in vivo* testing cannot be granted for DESI effective drugs

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56 *Id.* at 1636.

57 Knapp, *supra* note 8, at 16.

58 42 Fed. Reg. 39675 (1977).

59 43 Fed. Reg. 6965 (1978).

60 43 Fed. Reg. 35056 (1978).

61 42 Fed. Reg., *supra* note 34, at 1648-49.

62 *In vitro* testing is permitted only if the *in vitro* test has been correlated with *in vivo* data, the test product is compared to a reference material shown to be bioavailable, or the test product is compared to an identical product that is the subject of an approved NDA. *Id.* at 1641.

63 42 Fed. Reg., *supra* note 49, at 1641.

which use special protective (enteric) coatings or controlled release dosage forms (both of which present unique bioavailability problems) or which are identical, related or similar to any of the approximately 110 drugs listed by FDA as having actual or potential bioequivalence problems.[64]

Because the FDA list has been so misinterpreted, it is important to emphasize that it includes (1) all products for which there has ever been any evidence of bioinequivalence, and (2) all products that have any potential for bioequivalence based on the criteria discussed earlier. Drug products are liberally included on the list if there is any question about their potential for bioinequivalence. Only 20 to 25 drug entities of the approximately 110 listed have had documented bioequivalence problems.[65]

To aid purchasers of these listed drugs, FDA in 1976 published a compilation of "Holders of Approved New Drug Applications for Drugs Presenting Actual or Potential Bioequivalence Problems", commonly known as the "Blue Book".[66] FDA has advised that most of the drug companies holding approved NDA's or ANDA's for drugs listed in the Blue Book have already submitted bioavailability data on their products; and FDA therefore recommends that until bioequivalence requirements are established purchases of these drugs be made from listed manufacturers or their distributors.[67] Of the approximately 193 drugs listed in the "Blue Book,"[68] 85 are marketed by a single approved manufacturer and only 54 are produced by as many as three firms.[69] FDA has further clarified the list by identifying those drugs for which all firms listed have demonstrated bioequivalence (e.g, chlordiazepoxide hydrochloride capsules), no firms (e.g., reserpine tablets), or only some firms

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64 Id. at 1649.

65 41 Fed. Reg. 5339 (1976).

66 HEW Publication No. (FDA) 76-3009, initial publication Jan. 1976, revised June 1976.

67 41 Fed. Reg., supra note 65, at 5339.

68 The number of drugs (193) in the Blue Book and in the proposed FDA bioavailability regulation differs from the 110 drugs listed in the final regulation because the final list excluded drugs found by the DESI study to be less than effective.

69 Bernard Cabana, Director, Division of Biopharmaceutics, FDA Bureau of Drugs, "Bioavailability/Bioequivalence Issues Concerning Drug Interchangeability," speech presented at the Food and Drug Law Institute Conference, Washington, D.C., June 8, 1977, at 29.

(e.g., tolbutamide tablets).[70]

FDA Commissioner Kennedy has recently announced[71] that a comprehensive replacement of the Blue Book is being prepared for use by all states with drug product selection laws. This list of therapeutically equivalent drug products will include all holders of approved new drug applications, as well as information about therapeutic equivalence. Indicating past and current bioequivalence problems for each product, the list is intended to provide the states with much needed information about the current state of bioequivalence problems, and thus complement the bioavailability/bioequivalence regulations, designed to remedy those problems.

5. Good Manufacturing Practices

FDA's Current Good Manufacturing Practice regulations (GMP's)[72] cover every aspect of the drug manufacturing process and apply equally to all pharmaceutical producers. The regulations are intended to assure that all products consistently meet the same standards for safety, strength, purity and effectiveness. They enable FDA to disqualify a drug product for marketing not only when the agency has discovered a faulty batch, but also when it can show that defective batches are likely because of poor production controls.[73]

The GMP's require, for example, that manufacturers prevent mixups by maintaining space between equipment used to process different drugs. To discover mixups that already may have occurred, the output of each drug must be checked against the expected output.

Contamination by foreign matter must be minimized by proper cleaning and storage of containers. Containers holding the drug at any stage must not react with the drug or permit outside material to enter. Special precautions must be taken to prevent

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70 FDA, "Multiple Source Drugs with Documented or Potential Bioequivalence Issues" (undated).

71 Donald Kennedy, "FDA List of Therapeutically Equivalent Drugs," May 31, 1978.

72 21 C.F.R. §§210, 211 (1977). A revision of the GMP regulations, updating them in light of current technology and adopting more specific requirements, becomes effective March 28, 1979. 43 Fed. Reg. 45014 (1978).

73 A drug is adulterated if not produced in conformity with current GMP's. 21 U.S.C. §351(a)(2)(B) (1970).

penicillin contamination of nonpenicillin products and to exclude microorganisms from "sterile" products.

Equipment must meet standards of accuracy to ensure consistency batch-to-batch. Product stability must be assured, and products subject to deterioration must include expiration dates on their labels.

Each significant stage of production must be performed and double-checked by qualified personnel. Employee accountability is emphasized by requiring written records to identify those persons responsible for each stage of production. Written records, including records of complaints, must be retained for at least two years.

FDA must inspect every pharmaceutical production plant at least once every two years to monitor compliance with the GMP regulations.[74] In fiscal 1977 (a fifteen-month period) the agency conducted 6,813 in-plant inspections, some extending as long as several weeks.[75]

6. FDA Monitoring and Enforcement Programs

a. Removing Defective Products from the Market

FDA has three basic methods of removing defective drug products from the market: seizures of drugs, court injunctions and recalls. The first two methods are expressly authorized by the Food, Drug and Cosmetic Act,[76] but the drug recall is the method most often used.

Recalls or removals of drug products are voluntary procedures initiated either by the manufacturer or by FDA. The manufacturer may discover a problem with a drug shipment and remove it from the market on its own initiative. If FDA first discovers the defect, it will request a recall by the manufacturer. The manufacturer may then use letters, telephone calls or telegrams to purchasers of the product requesting its return or destruction. Depending on the seriousness of the health hazard presented, the drug may be recalled from all consumers, from all retail distributors (including hospitals and physicians), or only from wholesale distributors.[77] In fiscal year 1974, for example,

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74 21 U.S.C. §360(h) (1970).

75 Kennedy, supra note 1, at 5.

76 21 U.S.C. §§332, 334 (1970).

77 Council on Economic Priorities. "In Whose Hands?", 4 Economic Priorities Report 11-12 (1973).

130 drug recalls involved an actual or potential health hazard.[78]

Seizures of drugs result when the manufacturer refuses to carry out a recall voluntarily. The action must be initiated in a civil court proceeding and carried out by a U.S. Marshal. If various concerns deter the FDA from initiating a seizure, it may request a cooperative effort through the PMA, pharmacies and physicians.[79]

FDA also can seek a court injunction to prevent a manufacturer from distributing adulterated or mislabeled goods. This might occur if GMP inspections disclosed serious production problems not being corrected by the manufacturer.[80]

b. Drug Product Surveillance Program

FDA conducts a surveillance program of marketed products to determine their compliance with compendial and other standards. The analytical work is performed at the agency's National Center for Drug Analysis in St. Louis and its field laboratories.[81] During fiscal year 1975, FDA analyzed over 20,000 drug samples requiring approximately 250,000 individual assays. According to the agency only a small percentage required regulatory action due to non-compliance with official standards.[82]

When monitoring activities reveal problems with an entire class of drug, specific intensive programs are established. These programs have studied such drug classes as diuretics, antiarrythymics, anticonvulsants, antibacterials, tranquilizers, oral hypoglycemics, bronchodilators, anti-inflammatories, antihistamines, coronary vasodilators and sedatives, but have not produced evidence of widespread industry problems in meeting appropriate standards of identity, purity or potency.[83]

c. Drug Product Problem Reporting Program

FDA funds a Drug Product Problem Reporting Program, which is operated by contract with the U.S.P. The program is cosponsored

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78 40 Fed. Reg., supra note 3, at 26147.

79 Council on Economic Priorities, supra note 77, at 12.

80 Id.

81 40 Fed. Reg., supra note 3, at 26147.

82 Id.

83 Id.

by 46 state and local pharmacy associations, is endorsed by APhA and the National Association of Retail Druggists, and is used in numerous pharmacy college teaching programs.[84] The program relies on practicing hospital nurses and hospital and community pharmacists to report such defects as broken tablets, leaky vials and cloudy solutions to the U.S.P., where the report is reviewed for signs of possible health hazards. Since its inception in 1970, the program has received over 25,000 reports;[85] in 1977, it was responsible for over 30 recalls.[86] According to FDA's analysis of reports received between September 1975 and September 1977, the number of reported problems per company roughly parallels each firm's volume of production.[87]

d. Government-wide Quality Assurance Program

In 1975 FDA assumed responsibility for quality assurance for all drugs and other medical items purchased by federal agencies.[88] FDA's responsibilities include performing all inspections necessary to evaluate the ability of drug manufacturers to meet purchase specifications, testing product compliance with compendial and other standards, and investigating complaints of poor product quality. FDA has agreed in a pilot program to provide the same type of services to at least one state -- New York.

A basic principle of the program is to apply the same standard of drug quality to federal procurement as is applied to commercial distribution to the public:[89]

> If a manufacturer is found by FDA to be unacceptable to supply drugs to a Federal

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84 Pharmacy Times, Mar. 1978, at 39.

85 Kennedy, supra note 1, at 5.

86 Pharmacy Times, supra note 84, at 40.

87 Kennedy, supra note 1, at 5. An earlier FDA analysis determined that approximately 75 percent of these reports concerned the products of "well-known" manufacturers. Caspar W. Weinberger, Secretary of HEW, Statement Before the Subcommittee on Monopoly, Selected Committee on Business, U.S. Senate, Mar. 19, 1975, at 13.

88 Sherwin Gardner, Deputy Commissioner, FDA, Statement Before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, Nov. 16, 1977, at 1-2.

89 Although in certain instances agency requirements may justify more stringent specifications.

> purchasing agency because of quality deficiencies, we will take appropriate regulatory action to prevent distribution of that product and of any other of that firm's products that are similarly deficient in quality to the general public.[90]

As a result of this program, FDA has eliminated unnecessary inspection by relying on a single inspection to determine a firm's ability to produce quality products for federal procurement and for commercial distribution. Similarly, FDA has eliminated redundant testing. Furthermore, FDA has ended the Department of Defense's "procurement bias against generic drugs, which required testing of all lots of generics . . . with virtually no testing of brand name drugs."[91]

FDA will test a pilot program with the State of New York to provide similar quality assurance evaluations of firms bidding for state procurement contracts.[92] The evaluation will assure that the firm is in full compliance with current GMP's, and that its products meet applicable quality and labeling standards. FDA will provide training in drug analysis to state chemists and give

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90 Gardner, supra note 88, at 3.

91 Id. at 4. Mr. Gardner did not identify the Department of Defense but instead referred to "one government agency." That the agency referred to was the Department of Defense is documented extensively in Part 24, Hearings Before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, 93rd Cong., 2d Sess. (1974). Defense Department statements were misused in the early and mid-1970's to suggest that inferior quality products were widespread. The Council of Medical Staffs, for example, claimed that the Department inspected the plants of low-bidding manufactuerers, "disqualifying 45% of them." Council of Medical Staffs, "The Physician's Views on Prescription Drugs," May 1974, at 63. In fact, the Department inspected only ten percent of prospective contractors and disqualified 45% of this ten percent; thus, they judged 95.5 percent of all prospective contractors as capable of providing quality products. Moreover, most of the criteria used by the Department were found by FDA, APhA, the U.S.P., and the National Formulary to be unrelated to quality and biased in favor of brand-name products. The Department itself repudiated statements by one of its officials that had been used to disparage generic manufacturers.

92 Gardner, supra note 88, at 7; Memorandum of Understanding Between the State of New York Office of General Services and the Food and Drug Administration (June 7, 1978).

guidance in development of state quality specifications. If the pilot is successful, the program may be extended to other state volume purchase plans.

VI.B. Maximum Allowable Cost Program

The Maximum Allowable Cost (MAC) program of the Department of Health, Education and Welfare is designed to assure that the government pays out no more in reimbursement for drugs under Medicaid than is truly necessary. Because it encourages the use of lower-cost generic equivalents, the MAC program raises some of the same issues, such as the adequacy of FDA regulation of product quality and bioequivalence, as are raised by drug product selection laws. Upon considering those issues, a federal court concluded that FDA could assure the quality of the vast majority of drugs on the market and that bioinequivalence was not a major or insurmountable problem. And by encouraging the selection of lower-cost chemically equivalent drug products and thus increasing price competition, the effects of the MAC program may spill over into the private pay prescription market and thereby benefit consumers in both groups -- Medicaid and self-pay.

1. The Specifics of the MAC Program

The MAC program[1] establishes a mechanism to limit federal third-party reimbursement, primarily under Medicaid,[2] for prescription drugs purchased on an outpatient basis. The MAC regulations limit reimbursement to the lowest price at which a particular multisource drug is generally available. As an adjunct to the MAC program, HEW will provide physicians and pharmacists with a guide to comparative drug prices.[3]

To establish a MAC limit,[4] HEW's Pharmaceutical Reimbursement Board first identifies those multisource drugs for which there are significant federal expenditures and significant price differences. FDA then reviews potential MAC drugs for any bioinequivalence or other quality problems.[5] If FDA does not advise delaying or

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1 40 Fed. Reg. 32284 (1975); 45 C.F.R. Part 19 (1977).

2 MAC primarily involves Medicaid payments because Medicare reimbursements cover only drugs for hospital inpatients.

3 This guide is supported in principle by the Pharmaceutical Manufacturers Association. Wrenn and Huebner, "Ethical Drug Industry: Final Federal Reimbursement Regulations (MAC Program)," Merrill, Lynch, Pierce, Fenner & Smith, Inc., September 1975, at 3.

4 45 C.F.R. § 19.5 (1977).

5 See discussion of bioinequivalence and quality problems, Ch.VI.A., supra.

withholding the establishment of a MAC, the Board recommends a MAC limit equal to the lowest price at which the drug is widely and consistently available to pharmacists from any source.

The Board then invites written comments on the proposed MAC and conducts a public hearing. After considering the written comments, the presentations made at the public hearing, and any other such evidence (including the advice of any outside consultant to the Board) the Board uses rulemaking procedures to make a final determination on the MAC limit.[6]

Once a MAC is established for a particular drug, federal reimbursement, with one exception, may not exceed the MAC price plus a reasonable dispensing fee.[7] Because the regulation does not authorize pharmacists to select lower-cost products in violation of state antisubstitution laws,[8] if the prescribed brand exceeds the MAC price, the pharmacist may either (1) fill the prescription as written and lose the difference between the cost of the brand product and the MAC limit, (2) refuse to fill the prescription, (3) request that the physician prescribe another product below the MAC limit, or (4) request that the physician certify the brand's medical necessity.[9]

Only in this last instance when "the prescriber has certified in his own handwriting [that a particular brand] is medically necessary for that patient"[10] does the MAC established for the drug not apply. The purpose of the certification requirement is to assure that physicians recognize that particular brands of multisource drugs may be priced above applicable MAC limits and that physicians "prescribe a particular brand of a multiple-source drug only when that brand of drug is better suited [in

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6 Reimbursement is limited to the lowest of (1) the MAC price plus a reasonable dispensing fee, (2) the estimated acquisition cost plus a reasonable dispensing fee, or (3) the pharmacist's usual and customary retail price. 45 C.F.R. § 19.3 (1977).

7 43 Fed. Reg. 35310 (1978).

8 40 Fed. Reg., supra note 1, at 32287.

9 The difficult situation in which antisubstitution laws place the pharmacist receiving a brand prescription for a MAC drug has been instrumental in the recent endorsement of drug product selection laws by the National Association of Chain Drug Stores. Letter from Robert J. Bolger, President, National Association of Chain Drug Stores, to Peter D. Holmes, FTC, Mar. 29, 1978, at 2.

10 45 C.F.R. § 19.3 (1977).

the physician's medical judgment] than the same drug from other sources to meet a patient's medical needs."[11] A procedure for checking off a box next to a preprinted statement does not constitute an acceptable certification.[12]

2. Status and Impact of the MAC Program

The MAC procedure thus far has established price maximums for only five drugs of various strengths and dosage forms: ampicillin, penicillin VK, tetracycline, propoxyphene and chlordiazepoxide.[13] New procedures instituted by HEW are expected to reduce from 180 days to 60 or 75 days the time it now takes to put a MAC into effect.[14] HEW hopes to have 50 MAC's, covering 20-25 drugs, by the end of 1978.[15]

HEW thus far has successfully defended suits by Eli Lilly[16] and Hoffmann-LaRoche[17] challenging MAC limits established for two of their popular brand-name drugs, and a suit by the American Medical Association and the PMA challenging the legality and constitutionality of the entire MAC program.[18]

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11 40 Fed. Reg., supra note 1, at 32295.

12 HEW Information Memorandum HCFA-IM-77-39 (MMB), July 18,1977; HEW Information Memorandum IM-77-25 (MSA), May 26, 1977.

13 42 Fed. Reg. 27306 (1977); 42 Fed. Reg. 48393 (1977); 43 Fed. Reg. 7714 (1978). HEW recently proposed lowering the MAC level for ampicillin capsules. F-D-C Reports, Sept. 11, 1978, at A-1. Eventually HEW will consider removing drugs from MAC when it believes the market is fully competitive. F-D-C Reports, June 26, 1978, at 11.

14 Drug Topics, June 20, 1978, at 40; 43 Fed. Reg., supra note 7, at 35311.

15 F-D-C Reports, June 26, 1978, at 10.

16 F-D-C Reports, Apr. 24, 1978, at 3. Lilly argued, inter alia, that the MAC Board had insufficient evidence of the quality of generic forms of propoxyphene.

17 F-D-C Reports, May 15, 1978, at 18; F-D-C Reports, June 12, 1978, at T&G 1. Roche claimed, inter alia, that chlordiazepoxide was not widely and consistently available at the MAC price.

18 American Medical Ass'n v. Mathews, No. 75-C-2512 (N.D. Ill. Mar. 7, 1977).

The AMA suit is relevant to the issue of drug product selection because one of its major contentions was the inadequacy of FDA's regulatory activities and monitoring programs to assure the therapeutic equivalence of all MAC-listed products. The court found that HEW could reasonably conclude that:

> (1) FDA programs, despite some inadequacies, are functioning well enough to assure drug quality, and (2) that bioinequivalence is neither a major problem nor an insurmountable obstacle to the MAC program.[19]

The court cited statements by medical experts on the Office of Technology Assessment's Drug Bioequivalence Study Panel that bioinequivalence presented potential problems for only about 15 percent of marketed drugs, and that the remainder could be put on an interchangeable list without any serious health problem.[20] The court stated that PMA's arguments failed to undermine HEW's conclusion that "the vast majority of drugs marketed in this country are of an acceptable quality for patient care."[21]

HEW estimates that the MAC program will produce considerable savings on Medicaid prescriptions, which constitute about 15 percent of all prescriptions.[22] For example, acquisition costs

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19 Id. at 53.

20 Id. at 55. See discussion of the OTA Panel's report, infra at Ch.IX.C.1.a.

21 Id. at 59.

22 Am. Druggist, May 1978, at 10. Other third-party prescriptions account for about 10% of total prescriptions, and just as MAC lowers the government's drug bill, so too can drug product selection lower prescription drug costs for private third party payors. Because insured consumers lack the incentive to reduce costs, private third party payors may have to develop special mechanisms to reap the full cost savings.

Consumers appear to act differently when their prescription drug costs are covered by insurance. One study found that price comparisons occurred more often among respondents who paid for their own prescriptions than among those whose prescriptions were paid by third parties. Wills, "The Incidence of Price Comparison Activity in Prescription Purchasing," Presented to the American Pharmaceutical Ass'n, Nov. 13, 1973, at 7. One commentator expressed the concern that purchasers covered by insurance "may well demand 'the best money can buy' in spite of the fact that increased costs of health care are reflected in the premium charged

(Footnote Continued)

for different generic versions of 100 capsules (250 milligram strength) of ampicillin trihydrate range from $18.74 to $6.00.

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22 (Footnote Continued)

for health insurance." See, e.g., "Improving Michigan's Generic Drug Law," 9 U. Mich. J. L. Reform, 394, 409 (1976). Another noted:

> Many third-party patients do not want a generic equivalent and refuse it outright if it is offered. Bob Shapiro indicates that without the economic incentive to save out of their own pockets, few third-party patients are inclined to have any interest in an unknown drug.

Gorman, "Why Substitution Fizzled in Michigan," Drug Topics, Apr. 15, 1977, at 43. The limited systematic evidence confirms these concerns. The Goldberg study in Michigan found that in the second year after the law had been changed, the rate of drug product selection for patients covered by insurance was only half that for self-paying patients (.69% v. 1.1%). Goldberg, et al, "Evaluation of Economic Effects of Drug Product Selection Legislation," Presented to the 105th Annual Meeting of the American Public Health Ass'n, Wash., D.C., Oct. 31, 1977, at 18.

Not surprisingly, private insurers of prescription drug costs have begun to develop mechanisms to provide incentives for pharmacists to select lower-cost products. The Blue Cross and Blue Shield of Michigan (BCBSM), for example, has developed an incentive program using bonus payments for prescriptions dispensed to subscribers of its third-party programs. Am. Druggist, April 1978, at 79. According to BCBSM, the plan enables pharmacists who reduce ingredient costs, either through drug product selection or prudent purchasing by source or quantity, to share in savings realized by the third party. Under its bonus plan, BCBSM calculates each participating pharmacy's acquisition costs for a sample of about 100 single and multisource drug products. Those pharmacies whose average acquisition cost for these products is 90 percent of the state average receive a bonus of 20 cents for each multisource and single-source prescription dispensed to a BCBSM subscriber. Similarly, those billing at 91 and 92 percent will receive 19 and 18 cents per prescription, and so on. BCBSM maintains that this novel program will allow the pharmacy and the third party to work together to reduce health care costs. Of course, by lowering their costs third party insurers

(Footnote Continued)

By setting a MAC limit of $7.25, HEW estimates annual savings of $354,000 on this one dosage form alone.[23] The MAC program is similar to Ontario's Drug Benefit Program, which has produced an estimated savings of $2.5 to $10.5 million a year.[24]

But MAC should promote competition in such a way that both Medicaid and self-pay consumers will benefit. Manufacturers who charge a price above the MAC level will have to lower the price if they are to retain a share of the Medicaid market. Because manufacturers charge pharmacists the same price whether the final buyer is a Medicaid consumer or not, the wholesale cost of drugs dispensed to non-Medicaid consumers would go down also.

Futhermore, if a pharmacist chooses to stock a MAC-level product for Medicaid patients, he or she is more likely to use this low-cost product in filling generically-written prescriptions and in selecting generic products for brand-name prescriptions. This would dramatically change the past situation, in which pharmacists, perhaps unsure of sufficient demand for non-branded products, stocked primarily brand-name products.

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22 (Footnote Continued)

can keep their premiums attractive to their clients--primarily unions and company trust fund administrators. At least one investment consultant believes these groups will become increasingly interested in the use of low-cost generic products and will exert pressure on third party insurers when they find, for example, that the government was paying a price of only 7 cents for ampicillin, while they were being charged as much as 20 cents. Curran, "Multi-Source Drugs: An Acceleration in the Use of Lower-Costing Substitutes?", Reynolds Securities Information Report, May 13, 1977, at 15.

In sum, although consumers benefiting from private third party plans appear to be less concerned about getting lower priced prescription drugs, recent developments suggest that private third-party insurers also may save substantial sums from drug product selection.

23 See discussion of MAC savings, Ch.VIII., infra.

24 Allan E. Dyer, Ontario Ministry of Health, "Implementation and Implications of Applying Drug Product Selection to Selected Populations", Presented to Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13, 1978, at 11.

Thus, both the MAC program and drug product selection laws attempt to remedy a lack of price competition in the multisource prescription drug market and thereby benefit consumers. Drug product selection laws, however, foster consumer savings by removing market impediments to price competition without incurring the problems inherent in establishing a price-setting mechanism.

CHAPTER VII. STATE REGULATION OF PRESCRIPTION DRUGS

A. Antisubstitution Laws

1. Historical Background

Modern antisubstitution laws were enacted primarily through the efforts of manufacturers seeking to protect sales of their brand-name products from "counterfeit" drugs and other substitutes. These events occurred as the growth of the pharmaceutical industry after World War II caused dramatic changes in the professional role of the pharmacist.

a. Background Prior to World War II

In the 1800's, a number of physicians and apothecaries flooded the market with patent medicines of questionable value. The failure of these "secret nostrums" to perform as advertised led a small group of reformers within pharmacy to produce "ethical specialties," dependable medicines providing full directions for use and a statement of strength and ingredients.[1] Although these products were intended to replace the "secret nostrums" used for over-the-counter sale to patients by pharmacists, they also were prescribed by physicians. According to a long-established pharmaceutical manufacturer, substitution of duplicate or similar products was a problem to innovators nearly at the inception of "ethical specialties." The manufacturer describes the following condition in 1858:

> The partnership's advertisements to the retail trade, appearing in the Druggist's Circular, featured a large variety of specialties, including "Compound Syrup of Phosphates or Chemical Food" which became so popular among prescribing physicians that Blair and Wyeth felt obliged to denounce imitations as a "reprehensible appropriation."[2]

One of the aims of the Proprietary Association, founded in 1881, was "the extermination of imitation goods." The association argued that the real evil was the pharmacist's practice of

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1 R. Kedersha, "The Impact of Brand Name Prescription Products on the Traditional Practices of High Prescription Volume Pharmacies in Northern New Jersey," unpublished Ph.D. dissertation, New York University, 1964, at 25-26.

2 VanItallie, "100 Years of Drug Progress," Pulse of Pharmacy, Wyeth Laboratories, Philadelphia, Vol. 24, No. 2, at 4, quoted in Kedersha, id. at 27.

selling his or her own formula in place of the patent medicine made by others; this evil was labeled "substitution."[3] According to the Pharmaceutical Manufacturers Association, an April 1897 editorial in the American Journal of Pharmacy noted the practice of substitution and argued that the pharmacist "has no right . . . to substitute his own or anybody else's preparation for the one specified, even if he is sure the substitute is as good, or, as he may think, better."[4]

In 1903, M. I. Wilbert, a distinguished pharmacist, expressed pharmacists' resentment of increased product duplication and use of tradenames by manufacturers:

> The nuisance arising from this self-evident right (to trademarks) is that we, particularly in connection with the medical and pharmaceutical professions, are being overwhelmed with a multitude of meaningless and in many cases misleading names. Many of these names are dangerously similar, and are likely to lead to serious misunderstanding and possible fatal mistakes. The injustice to the public, as well as the pharmacist, is evidenced by the unnecessary duplication of names and titles for substances or mixtures that are not themselves covered by patents.[5]

The aversion by physicians and pharmacists to the use of trade names and patented products was so great that The Pharmacopeia of the United States - Seventh Decennial Revision of 1890, the officially recognized pharmacopeia of the time, refused to list any "substance which cannot be produced otherwise than under a patented process, or which is protected by proprietary rights." This policy remained unchanged until the Tenth Decennial Revision

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3 "A White Paper on the Pharmacist's Role in Product Selection," A Background and Position Paper Issued by the Board of Trustees, American Pharmaceutical Association, March 1971, at 6, reprinted in 11 J. Am. Pharmaceutical Ass'n 181 (1971). ["APhA White Paper"].

4 "The Medications Physicians Prescribe: Who Shall Determine the Source?" Pharmaceutical Manufacturers Association, Washington, D.C., 1972, at 4. ["PMA"].

5 W. McCormick, "Attitudes of Pharmacists, Physicians,and and Consumers Toward Repeal of Antisubstitution Laws," unpublished Ph.D. dissertation, University of Wisconsin, 1972, at 3.

of the United States Pharmacopeia in 1926.[6]

Substitution, however, apparently was not considered an acceptable alternative, and, in 1928, substitution was compared to robbery in a series of articles and editorials in The Druggists Circular, a private trade publication.[7] The editor distinguished between those who substituted for their own profit and those who substituted out of a sense of "misguided philanthropy to poor customers," but urged associations to campaign against substitution in order to receive credit for helping to eliminate the practice rather than "being blamed for shielding the wolves with the lambs."[8] This action does not appear to have had any particular impact on legislation. Although substitution remained a problem, it was not until the 1950's that the issue regained prominence.

b. Post-War Developments

The pharmaceutical industry developed rapidly after World War II. A number of miracle drugs were discovered: penicillin, streptomycin, oxytetracycline, sulfa drugs, tranquilizers, and steroids. No longer were pharmacists primarily compounders or manufacturers of relatively simple pills, capsules, powders, salves and liquids. The trend away from pharmacist-compounded drugs toward newly discovered factory-made drugs accelerated, and the U.S. Pharmacopeia and the National Formulary began to change from recipe books to compendia, using generic names, of detailed standards and test specifications for prefabricated drugs. Pharmaceutical manufacturers developed a marketing system that successfully promoted these drugs by brand names: by the end of 1960, brand-name drugs had captured over 94 percent of the prescription market.[9]

Counterfeiting had not been a problem in the prewar years because many drugs were compounded by the pharmacist,[10] and

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6 Kedersha, supra note 1, at 29, 34.

7 APhA White Paper, supra note 3, at 6.

8 McCormick, supra note 5, at 4.

9 Gumbhir & Rodowskas, "The Generic-Brand Name Drug Controversy: A History," Med. Marketing & Media, November 1971, at 4-5.

10 Pharmacists compounded 10%-20% of their prescriptions in 1957, as compared to 75%-80% in 1939. Hardt, "Rx Brands and Substitution," 18 J. Am. Pharmaceutical Ass'n Practical Pharmacy Ed., No. 2, February 1957, Reprinted

(Footnote Continued)

many manufactured products were available without prescription. The spectacular growth of the brand-name industry prompted a parallel growth in the number of duplicate products: products containing the same drug entity but produced by a different manufacturer. Some manufacturers went beyond merely encouraging pharmacists to dispense their version of a prescribed drug, and clandestinely began to manufacture "counterfeit" drugs: products similar in size, shape, and sometimes packaging to the popular brand-name drug, but of unknown quality, content, and origin. These counterfeits were then passed off to consumers through unwitting or unscrupulous pharmacists. According to numerous sources, counterfeiting reached "epidemic" proportions in the early 1950's.

It is difficult to document the prevalence of substitution, because few pharmacists and no counterfeiters were willing to admit to the practice. Dr. Robert A. Hardt, then Vice President of Hoffmann-La Roche, Inc. and President of the National Pharmaceutical Council (NPC) stated in February 1957 that "the American Druggist puts the current rate of substitution on prescriptions at 4.3 percent, as contrasted with 14.7 percent in 1953."[11] It is not clear, however, to what statement in the American Druggist he was referring. A common estimate is that as many as 25 percent of all pharmacists practiced substitution;[12] surveys on individual products showed rates of substitution as high as 40 percent.[13]

American Druggist reported that the vast majority of substitutions involved counterfeit products rather than reputable duplicates:

> Whatever the merits of the brand substitution issue, there appears to be ample evidence that brand substitution accounts for only a small share

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10 (Footnote Continued)

in Hearings, "Administered Prices in the Drug Industry," Subcommittee on Antitrust and Monopoly, Committee on the Judiciary, U.S. Senate, 86th Cong., 2d Sess., 1960, at 11576 ["Administered Prices"].

11 Id.

12 "A Background Study of Antisubstitution Laws and the Brand Interchange Concept," The National Association of Retail Druggists, Chicago, Illinois, 1972, at 1.

13 PMA, supra note 4, at 5.

of the drug industry's substitution problem.[14]

For example, investigations over several years by Smith, Kline & French Labs revealed that 90 percent of all substitutors dispensed outright counterfeits of the prescribed products.[15]

Pharmacists and manufacturers gave different reasons for the increase in substitution. A nationwide poll[16] reported that manufacturers believed the major reason for substitution was "greed on the part of unscrupulous pharmacists." Most pharmacists believed the cause was the huge proliferation of duplicate products, and the resulting difficulty retailers had in stocking all the brands physicians were likely to prescribe.

Interest in public welfare, as well as a more generalized fear of injury to the reputation of the pharmacy profession, may have been partly responsible for the joint action taken in August 1952 by the American Pharmaceutical Association, the National Association of Boards of Pharmacy, the American College of Apothecaries, and the National Conference of State Pharmaceutical Association Secretaries in condemning "as unethical the dispensing of a pharmaceutical preparation or brand thereof other than that ordered or prescribed." Adoption of laws and regulations against brand substitution was urged.[17] The editor of the American Druggist pointed out that "the biggest danger in the substitution situation lies in the fact that, if the public finds out about the extent of the practice, pharmacy is liable to face the worst press campaign ever directed against the profession."[18]

Although PMA argues that to cite drug counterfeiting per se as the reason antisubstitution laws were enacted in the 1950's and 1960's is misleading without focusing on the danger arising from the use of products of lesser or unknown quality,[19] it is clear that the strong adverse reaction to counterfeiting made it easier for the pharmaceutical industry to sell the benefits

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14 Am. Druggist, July 6, 1953, at 8.

15 Id.

16 Id. at 6.

17 Am. Druggist, Sept. 1, 1952, at 5; Administered Prices, supra note 10, at 11697.

18 Am. Druggist, Apr. 12, 1954, at 5.

19 "Statement of the Pharmaceutical Manufacturers Association in Response to Federal Trade Commission Request of January 11, 1978," Feb. 21, 1978, at 1.

of strengthened antisubstitution laws. The industry had a direct economic interest in eliminating substitution as well as counterfeiting. In a 1959 letter to a prospective new member, National Pharmaceutical President Harry S. McNeil wrote that "NPC is a working organization, out to protect the sale of the products which we create," and further advised, "I know the NPC would be a highly profitable effort for your good company to join.[20]

The industry opposed efforts in New York in 1953 by pharmacists and physicians to encourage prescribing by generic name and to add the symbol "A.R.B." (meaning "any reliable brand") on all prescriptions.[21] At the same time, pharmaceutical manufacturers pressed for adoption of state antisubstitution laws. The Drug, Chemical and Allied Trades section of the New York Board of Trade launched a national program to adopt a model state antisubstitution law, which prohibited "substituting a different drug, brand of drug, or drug product of a different manufacturer or distributor for any drug, brand of drug or drug product ordered by prescription or otherwise."[22]

It must be understood that there are two distinct kinds of state antisubstitution laws or regulations: those which specifically prohibit selection by the pharmacist of a different brand for the one prescribed, and those which prohibit substitution in more general terms. Typical language for a brand-specific substitution law would be a prohibition against:

> dispens[ing] or caus[ing] to be dispensed a different drug or brand of drug in lieu of that ordered or prescribed without the express permission in each case of the person ordering or prescribing such drug.[23]

The other kind of restriction seeks in more general terms to prohibit substituting different drugs or ingredients, deviating from a formula, or deviating from a physician's instructions.[24]

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20 Administered Prices, supra note 10, at 11801.

21 APhA White Paper, supra note 3, at 7.

22 Hawkins, "APhA's Position on State Antisubstitution Law Repeal," Texas Pharmacy, February 1971, at 15.

23 Alabama Code, tit.34, § 34-23-8 (1975); § 3(d) of the Uniform State Food, Drug and Cosmetic Bill of the Association of Food and Drug Officials of the United States (1964).

24 The North Dakota provision, which may predate 1877, forbids substituting "a different article for an article prescribed (Footnote Continued)

It is unclear whether selection of a different brand of drug violates this type of law; some statutes are more ambiguous in this regard than others.

The ambiguity apparently arose because the more traditional meaning of substitution involved the dispensing of a different drug entity for the one prescribed. As Dr. George Archambault, chief of the Pharmacy Branch of the U.S. Public Health Service, stated:

> Some 28 years ago when I started to practice pharmacy, "substitution" meant one thing--the dispensing of a wrong chemical or drug, one different from that prescribed. Only occasionally did we hear "substitution" then being applied to trade vs. official name substances.[25]

Perhaps the first state to take legal action against brand substitution was California, which in 1952 empowered the Board of Pharmacy to void a pharmacist's license for substitution.[26] The first brand-specific antisubstitution law was probably the 1953 amendment to the New Jersey antisubstitution law.[27]

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24 (Footnote Continued)

or ordered" or deviating from the terms of the prescription "in consequence of which human life is endangered." N.D. Cent. Code § 43-15-43(3) and (5) (1960).

25 Archambault, "The Formulary System Versus the New Concept of 'Substitution'," Hospitals, J.A.H.A, Feb. 1, 1960, reprinted in Administered Prices, supra note 10, at 11797, 11799.

> In 1955 the National Pharmaceutical Council was kind enough to give to all the world a new defninition of substitution. Substitution previously was understood to be to substitute one drug for another. But in 1955 the National Pharmaceutical Council, as part of its program, enlarged this definition and has been pushing it ever since.

Dr. August H. Groeschel, Associate Director, New York Hospital, in Administered Prices, supra note 10, at 11576.

26 PMA, supra note 4, at 5.

27 N.J. Stat. Ann. § 45:14-16, as amended by L. 1953, c.329, § 1. In 1977, New Jersey amended this law to permit product
(Footnote Continued)

The PMA did not take any direct action, and in 1953, twelve of the largest manufacturers formed the National Pharmaceutical Council (NPC), which became the industry's primary vehicle for education and lobbying with respect to substitution in all its aspects, including hospital formulary systems.[28]

c. The NPC's Role in the Passage of Antisubstitution Laws

The National Pharmaceutical Council began a concerted effort to encourage enactment of antisubstitution laws where none existed, to convert general antisubstitution laws to brand-specific ones, and to replace brand-specific regulations with statutes.[29]

The internal operations and lobbying activities of the NPC were discussed at great length in Part 21 of the hearings conducted by Senator Estes Kefauver. NPC documents reproduced in the hearing record confirm that the industry's interest in brand-specific antisubstitution laws was due to the fact that many pharmacy boards were reluctant to act against substituting pharmacists because they were unsure of their legal authority to do so. Thus, a December 19, 1955, memorandum on substitution activity by state authorities[30] says of Arizona, "Section on substitution, but doubtful if A.G. would interpret to cover brands. If necessary, board would promulgate regulation although legality might be questioned." The same document says that Michigan "has general section on substitution previously interpreted by A.G. as not applying to brands," while Ohio "has no specific authority and

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27 (Footnote Continued)

selection by pharmacists. N.J. Stat. Ann. § 24-6E-1 et seq. (West Supp. 1978-79).

28 Other large manufacturers later joined NPC. Current member companies are: Abbott Laboratories, Ayerst Laboratories, Burroughs Wellcome Co., Ciba-Geigy Corporation, Hoechst-Roussel Pharmaceuticals Inc., Hoffmann-La Roche Inc., Johnson & Johnson, Lederle Laboratories, Eli Lilly and Company, Marion Laboratories, Merck Sharp & Dohme, Merrell-National Laboratories, Parke, Davis & Company, Pfizer Inc., Riker Laboratories, A.H. Robins Company, Sandoz Pharmaceuticals, Schering Corporation, G.D. Searle & Co., Smith Kline & French Laboratories, E.R. Squibb & Sons, Syntex Laboratories, The Upjohn Company, Warner-Chilcott Laboratories, and Winthrop Laboratories.

29 NPC's official antisubstitution program is reported in Administered Prices, supra note 10, at 11697-98.

30 Id. at 11818.

legislation will be required," and Illinois "has general authority on substitution but questionable whether it applies to brands." A more extensive compilation prepared in January 1958[31] contains similar statements about a number of states.

The NPC took a firm position in favor of statutory authority prohibiting brand substitution, but some state pharmacy boards preferred to promulgate regulations rather than recommend specific legislation. NPC's first success came in June 1955, when the South Dakota Board of Pharmacy promulgated an antisubstitution regulation adapted from language suggested by NPC:

> The furnishing or dispensing of a different drug, or a different drug product, or a drug product of a different manufacturer or distributor, in place of the specific drug, brand of drug or drug product ordered or prescribed, by any person holding a certificate of registration shall be evidence that such person is incompetent or otherwise lacking in the necessary qualifications to perform the duties of a registered pharmacist and shall constitute grounds for the revocation of such person's certificate of registration.[32]

Other states enacted specific antisubstitution laws or regulations in steady progression; including Pennsylvania in 1955, Iowa and Utah in 1957, Ohio in 1958, Nebraska and Pennsylvania in 1961, Washington in 1963, Louisiana in 1964, Kansas in 1965, Alabama in 1966, Illinois (replacing a 1962 regulation), Montana and New Mexico in 1967, Wyoming and Colorado in 1969, Arizona and Virginia (replacing a regulation) in 1970, Maryland and Missouri in 1971, and Alaska in 1972. Some state pharmacy boards apparently promulgated their first specific regulations against brand substitution during this period, among them Montana in 1956, Massachusetts in 1961, Ohio, Illinois, and New Hampshire in 1962, Nevada in 1963, and North and South Carolina in 1965. The following exchange during the Kefauver hearings between Paul Rand Dixon, subcommittee counsel and staff director, and Newell Stewart, Executive Vice President of NPC, illustrates the dominant role played by the NPC:

> Mr. Dixon. When you wanted this legislation passed you went to state associations and urged them to do it; is that correct?
> Mr. Stewart. That is right, and still do.

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31 Id. at 11802.

32 Id. at 11817.

Mr. Dixon. And you are still doing it. As I understand it, you have been successful in 44 States; is that correct?
Mr. Stewart. Yes Sir. I think we have been quite successful in the operation.
Mr. Dixon. I think you have been remarkably successful.
Mr. Stewart. Thank you.
Mr. Dixon. In a very short period of time.[33]

By 1972, virtually every jurisdiction except the District of Columbia had enacted some form of antisubstitution law or regulation.

Manufacturers did not rely solely upon the passage of anti-substitution laws, but adopted various measures of their own. These included identifying products, where practical, with distinctive symbols, letters, names, shapes, or colors; adding secret tracer ingredients; "shopping" stores to uncover substitutions; and asking doctors to report substitutions.[34] In many cases, the mere threat of shopping was probably sufficient to deter pharmacists from making substitutions. In addition, brand-name manufacturers successfully brought trademark infringement and unfair competition suits against manufacturers and distributors of counterfeit products.[35]

The National Pharmaceutical Council also launched an "educational program" against the use of hospital formularies. Under this practice, physicians using hospital facilities indicate in writing their willingness to have the hospital pharmacy dispense the drug product purchased by the hospital for its formulary, even if the prescription specifies a different brand. In this country the first hospital formulary was adopted in the early 1800's at New York Hospital.[36] The formulary's purposes are to promote rational drug therapy, reduce inventory costs by eliminating duplicate products, and permit hospitals to secure competitive pricing for drug purchases.

Mr. William E. Woods became director of hospital relations at NPC in 1958. His job description detailed some of the functions of this new office:

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33 Id. at 11725.

34 Am. Druggist, supra note 14, at 15; Kedersha, supra note 1, at 58.

35 Kedersha, supra note 1, at 58.

36 Administered Prices, supra note 10, at 11572. To work continually toward effecting the validity

> of brand name specification and to attempt to make the honoring of brand name specifications an integral part of ethical pharmacy practice in the hospitals;
>
> To slow up, if not to stop, the trend of more and more hospitals adopting a compulsory formulary system;...[37]

Dr. August Groeschel, Associate Director of New York Hospital, was asked whether a campaign of threats was employed by NPC against hospitals and hospital pharmacists using a formulary system. He responded:

> In my opinion, very definitely. However, if you ask me to produce a threat made against myself or my pharmacist or the hospital pharmacist, it is not done that way. It is done on the basis of these speeches, papers, and so forth.[38]

The effort to discourage the use of hospital formularies was largely unsuccessful, apparently in part because hospital pharmacists did not consider the practice to constitute substitution. NPC itself admitted that formularies "are here to stay" and would "eventually be adopted in all hospitals of any size."[39]

d. Reversal of the Antisubstitution Trend

As noted earlier, the incidence of substitution reportedly fell from 14.7 percent in 1953 to 4.3 percent in 1957. The "epidemic" of counterfeit drugs subsided, and with the passage of new federal laws (such as the 1962 Kefauver- Harris amendments to the Federal Food, Drug and Cosmetic Act) strict controls were placed on drug products and drug manufacturers. As a result, the appropriateness of restrictive antisubstitution laws was again questioned.

Much of the concern came with the development of state Medicaid programs. Several states adopted welfare formularies which imposed cost limits on the drug products listed in them, and

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37 Id. at 11760.

38 Id. at 11582.

39 "Study of Administered Prices in the Drug Industry," Report of the Committee on the Judiciary, Subcommittee on Antitrust and Monopoly, U.S. Senate, 87th Cong, 1st Sess., 1961, at at 239.

they further encouraged prescribing and dispensing by generic rather than brand name.

To alleviate the problems created when a physician prescribed a drug which did not meet the welfare program's requirements, the California Health and Welfare Agency in 1965 began issuing preprinted prescription forms which authorized pharmacists to dispense chemical equivalents when the prescribed product cost more than the stated maximum. A 1965 California Attorney General's opinion stated that pharmacists who followed the preprinted statement to comply with the welfare program's rules would not be held to have violated the state antisubstitution law.[40]

Similarly, in 1969, Maryland established a Medicaid formulary of "generic equivalents," and issued prescription order forms that required pharmacists to dispense generic equivalents unless otherwise specified by the prescribing physician.[41]

In 1968, physicians and pharmacists in Virginia's Albermarle County adopted a voluntary program to encourage the use of low-cost drugs.[42] A voluntary formulary was adopted by Delaware's medical, dental, osteopathic, and pharmaceutical associations in 1970.[43] Also in 1970, Massachusetts established a drug formulary commission to prepare a formulary of therapeutically equivalent drug products. Physicians who prescribed a brand-name drug listed in the formulary were required to include the generic name of the drug on the prescription order.

The American Pharmaceutical Association (APhA) played a major role in the recent trend by states to grant their pharmacists authority to dispense in certain circumstances a different brand of drug than the one prescribed. Even in 1955 and 1956, when opposition to substitution was near its height, APhA passed resolutions encouraging "the use of generic names in the prescribing and dispensing of drugs."[44] At its 1966 annual convention, APhA's House of Delegates adopted a resolution that

> state agencies utilizing a system of

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40 APhA White Paper, supra note 3, at 7.

41 Id.

42 McCormick, supra note 5, at 15.

43 Id.

44 Archambault, "The Law of Hospital Pharmacy," Am. J. Hospital Pharmacy, Aug. 16, 1960, reprinted in Administered Prices, supra note 10, at 11864.

> listing drugs by generic name or by cost, or by a combination of these factors, include a printed statement on their prescription order blanks which, when signed by the prescriber, permits the pharmacist to dispense a comparable drug from the approved list.[45]

Finally, in 1970, APhA officially committed itself to seek the repeal of antisubstitution laws to thus allow the pharmacist to select the manufacturer of the drug to be dispensed when the prescription specifies a product by brand name alone. APhA contended that counterfeiting had virtually disappeared due to the enactment of strong federal controls, and that antisubstitution laws were being applied in cases where there was no intent to deceive anyone as to the source of the drug.[46] APhA's 1971 White Paper made three principal points: use of the brand name alone on a prescription order cannot be taken to represent conscious selection by the physician of a source of supply; pharmacists should be allowed to exercise their professional expertise in selecting the source of supply; and permitting pharmacists to do so would lower the cost to purchasers of prescription drugs.[47]

2. Current Status

Only ten states[48] still have antisubstitution laws or regulations totally prohibiting drug product selection by pharmacists. The rate of antisubstitution law repeal has accelerated over the past few years; since the beginning of 1977, eighteen states have repealed their antisubstitution laws and five states have amended existing product selection laws.

As noted earlier, state antisubstitution laws range from general prohibitions on substituting a "different article for the article prescribed" to specific prohibitions on dispensing a "different drug or brand of drug" for that prescribed. Violation of these provisions typically is a misdemeanor (punishable by a fine, imprisonment or both), as well as cause for revocation or suspension of the license to practice pharmacy. In some states, prohibitions may appear both in the state's pharmacy

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45 APhA White Paper, supra note 3, at 7.

46 Hawkins, supra note 22, at 14.

47 APhA White Paper, supra note 3.

48 Alabama, Hawaii, Indiana, Louisiana, Mississippi, Nevada, North Carolina (except for Medicaid prescriptions), North Dakota, Texas, and Wyoming. See table of state laws in Ch. VII.B., infra..

code and in its Food, Drug, and Cosmetic Act. In at least one case,[49] an apparent discrepancy has been created by amendment of one prohibition without comparable amendment of the other.

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49 In Alaska, the antisubstitution provision in the Business and Professions code, Alaska Statutes, § 08.80.295(1962), was amended to permit product selection by pharmacists, but not the provision in the Alaska Food, Drug and Cosmetic Act, Alaska Stat. § 17.20.290 (1962). Presumably, the state's product selection law prevails, being the latest and most specific pronouncement by the legislature.

VII.B. Drug Product Selection Laws

Approximately 40 states and the District of Columbia[1] have enacted drug product selection laws, with nearly half of these laws adopted since 1977. As can be seen in Table 1,[2] the provisions of these laws offer a bewildering number of alternatives and permutations: it is safe to say that no two laws are identical. And in the past two or three years a "second generation" of product selection laws has developed as a number of states amend earlier laws that proved less effective than expected.

In this section we will discuss the major types of provisions listed in Table 1. We also will refer to the small but growing number of studies of the effect of these laws. In section VII.C., we will discuss separately three major studies, including a multi-state pharmacist survey conducted for the Federal Trade Commission by an independent health market research firm.[3]

1. Permissive Versus Mandatory Drug Product Selection

Most states simply permit pharmacists to select a generic product in lieu of the brand prescribed; nine states require product selection (absent contrary direction by the physician or

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1 According to 1970 census figures, these states contain almost 85 percent of the U.S. population.

2 Because the effectiveness of a state law depends upon the length of time it has operated, Table 1 indicates the date each law became (or becomes) fully effective. In some cases this differs from the date of enactment because of the time needed to develop and publish a state formulary or to require the use of preprinted prescription forms. Some estimation also is involved, particularly in those states that did not establish deadlines for publication of a formulary, or where the deadline has not been met. Other examples of useful state summaries include National Ass'n of Chain Drug Stores, "Drug Product Selection - An Overview," May 31, 1978; "Generic Substitution Laws: Innovations in State Policy," State Health News, September 1977; W. M. Dickson, University of Wisconsin School of Pharmacy, "Analysis of the Status and Characteristics of State Drug Product Selection Laws," Presented at Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13, 1978.

3 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978. ["FTC Study."]

patient).[4]

Most of the mandatory product selection laws are so recent that their effectiveness has not yet been studied. The FTC study, however, did question pharmacists in Pennsylvania, which has a mandatory provision. Only 24 percent of the pharmacists surveyed in Pennsylvania reported that their store policy was to substitute whenever possible,[5] and that they actually did substitute on only 9.5 percent of the prescriptions for which substitution was possible.[6] Ironically, these percentages are significantly lower than those for several other states that do not require product selection. For example, 60 percent of the pharmacists in Delaware and Wisconsin said that their store policy was to substitute whenever possible and that they substituted lower-cost generics 40 to 46 percent of the time.[7]

Perhaps this difference is due to pharmacists' resentment of mandatory laws and other governmental intrusions.[8] The responses of Pennsylvania pharmacists to our survey questions generally were more negative than those of pharmacists in the six states with permissive laws: for example, only 39 percent of Pennsylvania pharmacists supported the law as written whereas 31 percent favored an antisubstitution law.[9] Similarly, 82 percent of 194 pharmacists surveyed in Kentucky, another state that mandates product selection, said they did not favor the current law, even though an identical percentage also said they favored the concept of product selection.[10]

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4 Florida, Kentucky, Massachusetts, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, and West Virginia. In Florida product selection is mandated only in the sense that once a pharmacy establishes its own positive formulary of interchangeable drugs, it must substitute for those drugs listed. Fla. Stat. § 465.30, as amended by House Bill Nos. 2740 & 2950, Ch. 76-77, Laws 1976.

5 FTC Study, supra note 3, at 26.

6 Id. at 27.

7 Id. at 26-27.

8 National Analysts, "Pharmacists' Attitudes Toward Generics," Prepared for E.R. Squibb & Sons Inc., December 1976, at 5.

9 FTC Study, supra note 3, at 55. The Pennsylvania law contains a number of other restrictive provisions that probably also contribute to pharmacist opposition.

10 Barnett, "Kentucky Pharmacists and the Generic Drug Law," Kentucky Pharmacist 11 (September 1977).

Interviews with 100 Florida pharmacists showed that two-thirds of them opposed mandatory product selection.[11]

Neither the ability of state officials to enforce mandatory product selection nor the cost of such enforcement efforts has been established. Pharmacy surveys[12] demonstrating lack of compliance with the Kentucky law prompted the state Attorney General to send all Kentucky pharmacists a letter in which he explained the law's requirements and warned of the penalties for willful violation.[13] We do not know what, if any, enforcement efforts followed this letter, but it is likely that such efforts will be strongly opposed:

> [P]harmacists can be expected to be less than enthusiastic about a program that . . . does not permit them adequate latitude in their professional behaviors. The exercise of professional judgement and the freedom to do so by the professions is a highly cherished concept and one that would not be given up without a very, very lengthy fight.[14]

2. Drug Formularies

Drug product selection may be implemented with or without a drug formulary. Formularies may be either positive, listing all substitutable drugs, or negative, listing all nonsubstitutable drugs. More states (nearly 30)[15] have some kind of formulary than have a completely open system (13 states), and positive formularies

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11 Market Measures Inc., "Florida Pharmacist Substitution Study," November 1976, at 1. Florida's law, however, still permits pharmacists considerable discretion in establishing their own formularies. See note 4, supra.

12 Lexington Herald-Leader, Aug. 29, 1976, at A-1, A-12; Courier-Journal, Aug. 3, 1976, Section B.

13 Letter from Robert F. Stephens to Kentucky Pharmacists (Dec. 2, 1976).

14 Albert Wertheimer, University of Minnesota College of Pharmacy, "Alternatives for Public Policy Decisions," Presented to Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978, at 8.

15 The number is inexact because three jurisdictions, the District of Columbia, Utah, and Washington, authorize but do not require establishment of negative formularies.

are the most common (17 states).[16]

Although all drug product selection laws represent an assessment that product equivalence is not an insurmountable problem, some states use a formulary as an added safeguard. Most often the formulary is based upon information supplied by another government agency, usually the FDA, but sometimes it is based primarily on manufacturer-supplied data. Among states with negative formularies, for example, Arkansas,[17] Delaware,[18] and Maryland[19] basically have adopted the FDA's list of over 100 drugs with actual or potential bioequivalence problems.[20] Florida, on the other hand, does not adopt any existing list but considers each drug individually and lists those judged inequivalent; only 14 drugs were listed in 1977.[21] Finally, California authorizes establishment of a negative formulary, but has never listed any drugs because it has never been proven to the California Director of Health's satisfaction that any drug,

> demonstrate[s] clinically significant biological or therapeutic inequivalence and which, if substituted . . ., would pose a threat to the health and safety of patients

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16 This includes 2 states, Florida and Ohio, which require each pharmacy to compile its own positive formulary.

17 "Revised List of Drugs With Known or Potential Bioequivalence/Bioavailability Problems," State Health Officer, Arkansas Dept. of Health, Jan. 1, 1978.

18 Delaware permits product selection for products on its negative formulary only if they are manufactured or distributed by firms listed in the FDA's "Blue Book." "Non-Equivalent Drug List," Delaware Drug Advisory Board, effective Dec. 22, 1976.

19 "Interchangeable Drug Products," Dept. of Health and Mental Hygiene, effective Apr. 21, 1978. For each drug on its negative formulary, Maryland lists those manufacturers who hold FDA-approved new drug applications and whose products therefore are eligible for selection.

20 See discussion at Ch. VI.A.I.e., supra. "Compared to the numerous products on the market the list is quite brief." Dickson, supra note 2, at 23.

21 Rules of the Fla. Bd. of Pharmacy, Ch. 21S-5.01, Mar. 17, 1977.

receiving prescription medication.[22]

In the past, positive formularies have been more cumbersome to develop because they place the burden of proving equivalence upon manufacturers seeking to have their products listed. The formularies were based upon data submitted by manufacturers, including such information as the description and ingredients for each product, the identity of its manufacturer and packager, the results of FDA inspections, the product's recall history, its compendial and manufacturing standards, any bioavailability data, and the product label.[23] The burden of proving equivalence and of compiling these lists has prevented them from including more than a small number of drugs; for example, Rhode Island listed 13 drugs in 1977[24] and 32 in 1978,[25] Kentucky listed 49 in 1976,[26] and Wisconsin listed seven in 1976[27] and 23 in 1977.[28] In fact, the cost of creating a state formulary persuaded the Michigan legislature to drop its consideration of a formulary provision:

> The House Committee on Consumers and Agriculture evaluated the experience with "formularies" in Massachusetts and Kentucky and observed a multitude of problems in their operations. In addition, the estimated costs of creating a State Drug Equivalency Commission were substantial enough to raise the question of whether the product would be equivalent to the investment.[29]

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22 Cal. Bus. & Prof. Code, § 4047.7(a) (Deering 1975).

23 See, e.g., Kentucky Drug Formulary Council Questionnaire (undated); Pennsylvania Generic Law Formulary Application (undated).

24 "Rhode Island Formulary," Rhode Island Formulary Commission, Dept. of Health (June 13, 1977).

25 "Rhode Island Formulary," Rhode Island Formulary Commission, Dept. of Health (June 1, 1978).

26 "Kentucky Drug Formulary," Kentucky Drug Formulary Council, Dept. for Human Resources (July 1, 1976).

27 "Wisconsin Drug Formulary," Wisconsin Drug Formulary Council, Div. of Health, Wisconsin Dept. of Health and Social Services (October 1976).

28 "Wisconsin Drug Formulary, Vol. 3," Div. of Health, Wisconsin Dept. of Health and Social Services (September 1977).

29 H. Lynn Jondahl, quoted in 9 U. Mich. J. L. Reform 399, n.44 (1976).

Other limited formularies include Tennessee's, which lists drugs in the Tennessee Medical Assistance Drugs with Price Maximums Formulary (approximately 11 drugs in 1977),[30] and New Mexico's, which lists only federal Maximum Allowable Cost drugs.[31] Two states[32] avoid such administrative problems by requiring each pharmacy to compile its own positive formulary.

In 1978, New York adopted a positive formulary of approximately 800 drugs certified by the FDA as safe, effective and therapeutically equivalent.[33] The list includes all products approved by the agency as safe and effective and excludes those for which bioequivalence is a documented or potential problem. FDA has explained that in most cases exclusion of a product does not automatically mean that it is inequivalent; it generally indicates that an appropriate bioequivalence standard has not yet been established or that evidence that the standard has been met has not been submitted to FDA.[34] One limitation of the New York list is that it excludes pre-1938 (or "old") drugs,[35] which do not require premarketing approval by FDA. The constitutionality of the law has been challenged by the Pharmaceutical Society of the State of New York and by the PMA; the suits focus on the law's mandatory provisions.[36]

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30 House Bill No. 78, Public Ch. No. 78. eff. June 1, 1977; "Saving Dollars on Prescription Drugs," Chattanooga News - Free Press, July 3, 1977.

31 N.M. Stat. Ann. § 54-6-28.3, enacted by House Bill No.62, Ch.60, L. 1976. See Ch. VI.B., supra, for discussion of Maximum Allowable Cost drugs.

32 Florida and Ohio.

33 "Safe, Effective and Therapeutically Equivalent Prescription Drugs," New York State Dept. of Health (Apr. 1, 1978).

34 Donald Kennedy, FDA Commissioner, Letter to Robert P. Whalen, New York State Dept. of Health (Jan. 23, 1978).

35 See discussion of pre-1938 drugs in Ch. VI.A.1., supra.

36 Am. Druggist, April 1978, at 3. A federal judge denied a motion for a preliminary injunction, indicating that state court issues were involved. F-D-C Reports, June 26, 1978, at T & G 1. Eli Lilly & Co. also has brought suit on the ground that the law may force pharmacists to violate the patent laws. F-D-C Reports, June 5, 1978, at 3. PMA filed a separate suit on September 11 charging that the law promotes unfair competition, denies manufacturers the right to a public hearing, and violates the patient's privacy.

Other states, including Illinois, Massachusetts, and Vermont, are following New York's example by basing their positive formularies on FDA-supplied lists.[37] Some of these lists apparently expand the New York formulary by including several pre-1938 drugs. Requests by many states for FDA assistance have prompted that agency to work to develop a universal FDA list of approved drug products, which will be revised periodically, for use by state agencies to meet the requirements of their respective laws.[38] This list may at some point be combined with drug price information to provide a single comparative guide to prescription drugs.[39]

By eliminating formularies, open product selection systems avoid potential arguments, administrative disputes, and the need to print drug lists and enforce adherence to them. According to the FTC survey, pharmacists say they would substitute most often under either a positive formulary or an open system; very few (11%) preferred negative formularies.[40] Apparently some pharmacists want to be free to exercise their professional judgment, whereas others seek some positive guidance in product selection. But although many pharmacists say they would substitute most often if they were not restricted by a formulary, our survey found the highest substitution rates in two formulary states: Wisconsin (46%), which has a positive formulary, and Delaware (40%), which has a negative formulary. The highest rate in a state without any formulary was reported in California (20%). And even in those states without formularies, reference to drug lists may be provided in a guideline report,[41] or by requiring pharmacists to be knowledge-

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37 See, e.g., F-D-C Reports, Apr. 24, 1978, at T & G 1; NARD Newsletter, October 1978, at 7; "Massachusetts List of Interchangeable Drugs," Massachusetts Department of Public Health (July 1978).

38 Letter from Donald Kennedy, FDA Commissioner, to State Health Officers, State Boards of Pharmacy and State Drug Program Officials, May 31, 1978.

39 The New Jersey positive formulary apparently also will include comparative price information.

40 FTC Study, supra note 3, at 50. Even a negative formulary may encourage more product selection than no formulary at all. Twenty-nine percent of the pharmacists in one Florida study said the state negative formulary would cause an increase in their level of substitution, while only nine percent said it would cause a decrease. Market Measures, supra note 11, at 32.

41 Report of the Task Force on Drug Product Selection, Oregon State University School of Pharmacy, November 1975.

able of FDA's list of potentially bioinequivalent drugs.[42]

Two other types of provisions should be noted. One requires that substitutable products satisfy certain "Good Manufacturing Practices" that may be additional to those imposed by FDA; for example, limiting substitution to products marked with identification codes, requiring maintenance of 24-hour product information services, and requiring certain return and recall capabilities.[43] These provisions, which generally apply only to substitution and not to generically-written prescriptions or brand prescriptions filled as written, may unfairly discriminate against smaller manufacturers and in fact are supported by at least one large brand-name company.[44] Three states[45] have a second provision limiting refills to the same product originally used to fill the prescription. This limitation apparently is intended to reduce the possibility that patients will be confused by a change in tablet color or shape.[46] Yet because it precludes shopping around for a lower-priced generic, it may allow a dominant firm to resist price competition once it has "locked in" pharmacists. Moreover, the pharmacist may be able to avoid confusion by conferring with the patient or by determining that for certain patients or certain drugs no change should occur.[47]

3. Physician Control

As the PMA itself has noted, all state drug product selection laws "contain a safeguard permitting the physician to insist that

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42 Colo. Rev. Stat. § 12-22-118.5, added by House Bill No. 1087, 1976 Colo. Sess. Laws.

43 See, e.g., laws of Alaska, Arizona, Idaho, South Dakota, Washington, and West Virginia.

44 Letter from David M. Winer, Senior Attorney, Hoffmann-LaRoche Inc., to Peter D. Holmes, FTC, Mar. 22, 1978, at 3-4.

45 Pennsylvania, Vermont, and Wisconsin.

46 State officials were less likely to suggest bioavailability problems as a basis for the refill limitation. Those concerns may be better addressed by a state formulary. See discussion, Ch. IX.C.1.d., infra.

47 We have been told that pharmacists do not often change products when refilling prescriptions. Apparently nearly all pharmacists have heard embarrassing stories about a patient who, upon receiving a refill with a different appearance, loudly proclaims, "You've given me the wrong prescription!"

the particular brand be dispensed."[48] The laws vary, however, in their description of how this order must be given.

Slightly over half the states insist that the prescribing physician "make a conscious decison for each prescription and in his/her own handwriting order the prescription to be dispensed as written."[49] This type of provision is designated "Physician Veto" in Table 1, and simply requires that the physician write such phrases as "Medically Necessary" (the same phrase required by HEW's Maximum Allowable Cost program)[50] "Dispense as Written" (D.A.W.), or "Do Not Substitute" (D.N.S.). Many of these states specifically prohibit preprinted instructions for the obvious reason that such

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48 "Estimated Effect on the Research-Based Industry of the Spread of Antisubstitution Repeal Laws," at 2 (undated), submitted by C. Joseph Stetler, President, PMA, to Peter Holmes, FTC, Apr. 28, 1978. The one exception, possibly inadvertent, is Oklahoma. After the defeat of a product selection bill in 1975 (House Bill No. 1160), it was determined by an Attorney General's opinion that a 1961 Oklahoma law permitted substitution either with the consent of the prescriber or the patient. Letter from Larry Derryberry, Attorney General, to State Representative Mark Hammons, Opinion No. 75-160, Jan. 8, 1976. For a detailed analysis of the claims presented by opponents of the 1975 bill, see Illinois Consumer Advocate Office Analysis, "An Inventory of Deceptive Advertising by Oklahoma Opponents to Generic Substitution," January 1977; Letter from Peter D. Holmes, FTC, to Dr. Francis A. Davis, President, Oklahoma Congress of County Medical Societies, Apr. 8, 1977; Letter from Dr. Francis A. Davis to Peter D. Holmes, May 10, 1977.

49 Carolee A. DeVito, Wayne State University, "Issues and Alternatives Involved in Achieving Maximum Public Benefit," Presented at Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978, at 7.

50 See Ch. VI.B., supra. A legislative staff report notes that the use of any other phrase, such as "dispense as written" (or, of course, the use of preprinted instructions), probably would conflict with the Medicaid MAC requirements. The result would be that "pharmacists will be requested to issue a brand drug, but will be unable to obtain a full reimbursement from Medicaid." Staff Report on H.B. 1605, Committee on Commerce, Florida House of Representatives, May 15, 1978 at 2.

easily taken action would completely circumvent the law.[51] Verbal notification by the physician generally is permitted for telephone prescriptions.

The "Medically Necessary" provision has been criticized for permitting physicians to thwart the law,[52] but the provision recognizes that not all products may be suitable for a particular patient. Moreover, although a physician is not prevented from writing "Medically Necessary" on all prescriptions, "an affirmative act, indicating a conscious decision on his part, is required."[53]

Numerous studies show that only rarely do physicians find it necessary to write "Medically Necessary" or "D.A.W.". An extensive study of over 150,000 prescriptions (the "Goldberg study"), found that only 3.6 percent of prescriptions in Wisconsin prohibited substitution. In Michigan, the figures were 6.4 percent the first year the law was in effect, dropping to 4.0 percent as physicians became more familiar with the law the second year.[54] Pharmacists responding to the FTC study estimated that, in five states, substitution was prohibited on 1.4 to 5.1 percent of all prescriptions.[55] The Province of Ontario, which has had a product selection law since 1972, reported a "no substitution" rate of less than 1.0 percent.[56] A PMA Committee on the Effects of Amendments to State Antisubstitution Laws reported a prohibition rate of 1.0 percent in California, 5.0 percent in Michigan, and 2.9 percent in Florida.[57] Similar figures have been reported by

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51 U. Mich. J. L. Reform, supra note 29, at 405. California and Colorado permit preprinted indications only if they are initialed by the prescriber.

52 Id.

53 Id. at 406.

54 Theodore Goldberg, Wayne State University School of Medicine, "Cost Implications of Drug Product Selection Legislation," Presented at Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978, at 11.

55 FTC Study, supra note 3, at 29.

56 Dr. Allen E. Dyer, Ontario Ministry of Health, "Implementation and Implications of Applying Drug Product Selection to Selected Populations," Presented at Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13, 1978, at 7.

57 PMA Committee on the Effects of Amendments to State Anti-

(Footnote Continued)

other studies.[58]

The remaining 19 states require the physician to consent to product selection by signing or checking one of the alternative instructions preprinted on the prescription form: for example, one line labeled "Substitution Permitted," the other "Dispense as Written."[59] When physicians are thus required to choose between prohibiting or permitting product selection, a majority choose to prohibit it. A 1977 study in Delaware found that physicians signed on the "Dispense as Written" line 78 percent of the time.[60] This percentage was relatively uniform for each of the 45 drugs surveyed, whether they were antibiotics, diuretics, analgesics or sedatives. A subsequent Delaware study by another researcher found physicians signing "Dispense as Written" 62.1 percent of the time (56.9 percent of the cases involved single-source products for which substitution was impossible).[61] This study also reported that pharmacists felt the two signature line

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57 (Footnote Continued)

substitution Laws, "Preliminary Report on the Effect of the Repeal of Antisubstitution Laws in California, Michigan, Florida and Delaware," Apr. 25, 1977. This report was not supplied to the FTC by PMA but by the SmithKline Corp. According to PMA, this committee was disbanded and had its files destroyed in 1977. Letter from C. Joseph Stetler, President, PMA, to Peter Holmes, FTC, Apr. 23, 1978.

58 See, e.g., Letter from Richard C. Zeich, Director, Audit Research, Market Measures Inc., to Peter Holmes, FTC, May 31, 1978 (Florida rate less than 1.0 percent, California less than 2.0 percent); Letter from J.H. Ebbeler, Director, Public Affairs, Eli Lilly & Co., to Bruce J. Brennan, Vice President and General Counsel, PMA, Oct. 25, 1976 (Michigan rate 3.2 percent, California 1.0 percent): The Lea-Mendota Research Group, "Antisubstitution Repeal: Ampicillin Prescribing and Dispensing in Kentucky: Phase II," November 1974, at vii (two percent); "Perceptions on Product Selection," California Pharmacist, September 1977, at 7 (86.7 percent of California pharmacists responding said physicians "infrequently" or "never" precluded product selection).

59 Kansas permits but does not require preprinted lines.

60 Market Measures Inc., "Delaware Substitution Legislation," April 1977.

61 Fink & Myers, "Effectiveness of Drug Product Selection Legislation in Delaware," 1 Contemp. Pharmacy Prac. 6-7 (1978).

requirement was "sometimes" a barrier to substitution.[62] Similarly, pharmacists in the FTC survey estimated physician prohibitions of over 50 percent in Pennsylvania and 31 percent in Delaware, both of which require preprinted forms.[63] A Board of Pharmacy survey[64] found that 32 percent of the prescriptions the first month after New York's law became effective and 19 percent the second month[65] were written on invalid prescription forms, thus presenting pharmacists with a dilemma -- fill an invalid prescription or tell the patient that he or she must get a new prescription. Of those prescriptions that were valid, approximately three-quarters prohibited product selection. Legislative proponents stated that physicians were undermining the law's intent that prescriptions be restricted to higher priced brand names only in "unique" situations when the physician "believed it was best for his patient."[66] Opponents of drug product selection, such as PMA, have strongly recommended requiring preprinted prescription blanks.[67]

As noted earlier, Delaware studies indicate that physicians prohibit substitution at about the same rate across drug categories and for multisource and single-source drugs.[68] A Michigan study supplied to us by PMA noted that the use of "DAW" was "relatively consistent across [drug] classes, suggesting that a few physicians routinely add this legend to all of their prescriptions."[69] The

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62 Id. at 8.

63 FTC Study, supra note 3, at 29.

64 New York Times, June 2, 1978, at B6.

65 Press Release from Stanley Steingut, Speaker, New York State Assembly, June 13, 1978, in "Are Generics Safe?," Prepared by N.Y. State Assembly's Office of Legislative Oversight and Analysis, June 1978, at 223.

66 Id. at 224.

67 See, e.g., "Statement of the Pharmaceutical Manufacturers Association Before the Subcommittee on Consumer Protection and Finance of the Committee on Interstate and Foreign Commerce Concerning H.R. 1963, 95th Congress," June 22, 1978, at 11; Drug Topics, Oct. 10, 1978, at 32.

68 Supra notes 60 & 61. About half the pharmacists in the FTC study said the frequency with which substitution was prohibited did not vary by drug type. FTC Study, supra note 3, at 30.

69 Letter from C. Joseph Stetler, President, PMA, to Peter D. Holmes, FTC, Feb. 21, 1978, Appendix C, at vi.

Goldberg study in Michigan also showed that physicians wrote "dispense as written" as frequently for single-source prescriptions (for which no substitution is possible) as for multisource prescriptions and even for generically-written prescriptions (when the pharmacist must choose some brand to dispense).[70] The Goldberg researchers concluded that physicians "appear to exercise their 'veto' more often on principle (professional domain issues) than for possible quality concerns."[71] This conclusion is supported by a nationwide survey of 1700 physicians, which found that their support or opposition to product selection was most clearly associated with their attitudes toward the principles of physician autonomy.[72]

Only one state, Alaska,[73] requires that the pharmacist notify the physician each time substitution occurs. Not only is this provision a "severe restriction" on the pharmacist, it "would certainly be a tremendous annoyance to the physician."[74] A PMA document acknowledged the problems created by such restrictions:

> Some old-fashioned pharmacists will insist on obtaining the physician's permission before substituting, in spite of the new 'product selection' laws. And when the pharmacist does this, there is inevitably an additional social cost in the loss of time from the busy schedules of both health professionals. [Emphasis in original.][75]

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70 Goldberg, supra note 54, at 11; DeVito, supra note 49, at 7; Goldberg, et al., "Impact of Drug Substitution Legislation: A Report of the First Year's Experience," 17 J. Am. Pharm. Ass'n, April 1977, at 220-225.

71 DeVito, supra note 49, at 7.

72 Thomas Sharpe & Mickey Smith, University of Mississippi School of Pharmacy, "A Multivariate Analysis of Physicians' Attitudes Toward Repeal of Antisubstitution Laws," Presented before Academy of Pharmaceutical Sciences, APhA, Atlanta, Georgia, November 1975, at 8.

73 New Jersey and New Mexico require physician notification in certain circumstances.

74 Strom, Stolley & Brown, "Antisubstitution Law Controversy - A Solution?", 81 Annals Internal Med. 257 (1974). Maryland and Virginia amended their laws to remove such requirements.

75 "Estimated Effect on the Research-Based Industry of the Spread of Antisubstitution Repeal Laws," supra note 48, at 3.

4. Patient Participation

Most product selection laws refer, at least implicitly, to the patient's participation in the selection process. A number of states (17) expressly recognize the patient's right to refuse a substitute product. Even when this authority is not expressly granted, the patient's strongest veto remains his or her refusal to pay for the prescription.[76]

It is quite possible that consumers, who traditionally have had little or no choice in prescription purchasing, do not realize that choices are available. Furthermore, "professionals might argue that given the lack of funds to educate the public, consumers may not know which choices are appropriate or reasonable."[77] Therefore most states with product selection laws (22) require that the pharmacist notify the patient of the substitution.[78] A few (6) require that notification be followed by affirmative patient consent.

One goal of purchaser notification is to increase the patient's understanding of product selection; it is unrealistic to assume that all patients have sufficient knowledge to make informed decisions. Consumers infrequently request lower priced products: pharmacists in the FTC survey reported that such requests occurred about five percent of the time.[79] When notified, few patients refuse substitution: less than two percent according to the FTC study.[80] Similarly, 96 percent of the pharmacists in a California study reported that their patients "always" or "usually" concurred with their selection.[81] Thus, pharmacists apparently seldom have to refill the prescription because of patient refusal of the product selected. Increased communications (as well as lower prices) may explain why most pharmacists report

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76 Prescriptions paid by third parties are quite different since the patient may have no incentive to accept a lower cost product. See Ch. VI.B., supra.

77 DeVito, supra note 49, at 3.

78 In New York, the physician rather than the pharmacist must notify the patient that an equivalent product may be dispensed.

79 FTC Study, supra note 3, at 31. A majority (54%) of California pharmacists in one survey reported that patients "occasionally" or "frequently" asked the pharmacist to select a less expensive brand. California Pharmacist, supra note 58, at 7.

80 FTC Study, supra note 3, at 32.

81 California Pharmacist, supra note 58, at 7. A report from Florida indicates that less than one percent of patients raise any objection. Am. Druggist, February 1977, at 18.

that product selection laws have had a positive effect on their relations with patients.[82]

Although most pharmacists (54 percent) in the FTC study said the state laws had increased the time spent with patients, few thought this increase so burdensome as to cause them to substitute less often.[83] The information contained in the notification and its timing vary from state to state, however, and some laws are more burdensome than others. Several states require the pharmacist to calculate the prices of the brand prescribed and the generic dispensed and inform the purchaser of the difference. Several Delaware pharmacists said this requirement was occasionally a barrier to substitution, with a few indicating that it was often a problem.[84] Some states require that the pharmacist notify the patient of the availability of a generic equivalent prior to filling the prescription. This can inconvenience the pharmacist and the patient, especially when the prescription is telephoned in by the physician. The pharmacist then "must wait until the customer arrives at the drug store, inform him of the generic equivalent, and then fill the prescription."[85]

The effort to inform and educate consumers takes other forms. Approximately 16 states require the posting of consumer information, typically a sign indicating:

> this pharmacy may be able to substitute a less expensive drug which is therapeutically equivalent to the one prescribed by your doctor unless you do not approve.[86]

In addition, state agencies have undertaken education programs to explain the state law and to help consumers make informed decisions. The Massachusetts law directs its Department of Public Health to provide for consumer education.[87] Consumer pamphlets have been

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82 Fifty-three percent of pharmacists reported a positive effect on patient relations, 43 percent reported no effect or both positive and negative effects, and less than four percent reported a negative effect. FTC Study, supra note 3, at 34.

83 Id. at 35-36.

84 Fink & Myers, supra note 61, at 7-8. See discussion of cost savings provisions, infra at Ch. VII.B.6.

85 Staff Report on H.B. 1605, supra note 50, at 3.

86 Or. Rev. Stat. § 689.835 (1977).

87 1976 Mass. Acts, Ch. 470.

prepared by such groups as the Pennsylvania Department of Health,[88] the Ohio Commission on Aging,[89] and the New York City Department of Consumer Affairs.[90] Two-thirds of the pharmacists responding to a Kentucky poll said they wanted the state pharmaceutical association to provide them with consumer education materials.[91]

It is apparent that consumer pressure will be perhaps the most significant cause of increased product selection. A PMA-supplied study reports that most pharmacists in Michigan

> feel that the Michigan consumer will generate additional demand necessary to cause an increase in the substitution rate. [Emphasis in original.][92]

And a national poll of "pharmacy leaders" reported that 95 percent believed that consumer pressure would be an important factor in encouraging pharmacists to select lower-cost generic equivalents.[93]

5. Labeling and Recordkeeping

Twenty-six states[94] require that certain information be included on the prescription label, either for all prescriptions or only for those involving product selection. The exact nature of the information varies: the label may include only the drug name (either generic or brand, if any), the manufacturer's (or distributor's) name, or both. These labeling provisions reinforce the consumer's right to be informed about prescription dispensing,[95] although the consumer may be unfamiliar with the drug

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88 "Think Generic," March 1977.

89 "Generic Drug Bill" (undated).

90 "New York's Generic Drug Law," April 1978.

91 Barnett, supra note 10, at 32.

92 Stetler, supra note 69, at ix.

93 1 pharmaSYST reports 3, July 1976. See also Dickson, supra note 2, at 22.

94 In addition, Arkansas has an optional labeling provision and Missouri requires that the manufacturer's name be included either on the prescription label or in the pharmacists' records.

95 Prescription labeling may also aid health professonals should it be necessary, for example in an accidental poisoning case, to quickly identify the drug.

name. Certainly, brand-name companies recognize that consumers relate more to brand names than to generic names, especially to the extent that retail pharmacies type the brand name on the label.[96]

Nineteen states similarly require pharmacists to record the name of the drug or the manufacturer on the prescription file copy. Because the name of the actual manufacturer of the finished drug (as opposed to the distributor) is not always known to the pharmacist, eleven states require that the name be disclosed on all drugs supplied to pharmacies within the state. We have been told informally that states' limited resources may prevent enforcement of manufacturer labeling requirements; the proposed Drug Regulation Reform Act of 1978 would have required such labeling as a matter of federal law.[97]

Although some pharmacists have complained of difficulties in including all required information on the label,[98] pharmacists responding to the FTC study did not find paperwork requirements particularly burdensome. Although twenty-eight percent said product selection laws had increased their paperwork (presumably in part because of labeling and recordkeeping requirements), most (81 percent) did not think this had caused them to substitute less often.[99]

6. Cost Savings

Nearly all product selection laws state or imply that there must be a cost savings to consumers; often this is done simply by limiting selection to a generic equivalent lower in price than the brand prescribed.

A number of other states specify the amount of cost savings that must be "passed on" to the consumer. Some laws require that

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96 Rx OTC Research, "Propoxyphene C-65 Prescription Purchase Report," Prepared for Roche Laboratories, June 25, 1976, at 8.

97 See Ch. XI., infra. Presumably this proposed act will be reintroduced in the next session of Congress.

98 Some states permit the use of abbreviations. Vermont requires the use of the letter "S" on the prescription label as a shorthand notation that a generic product has been selected.

99 FTC Study, supra note 3, at 37-38.

all "cost savings" be passed on, but do not define this term.[100] Others specify that the savings must equal the difference in the wholesale[101] or the acquisition costs[102] of the prescribed and dispensed products. Some also prohibit the pharmacist from charging a "different fee" for the dispensed drug.[103]

One difficulty with these provisions is that they compare an actual event (the sale of the dispensed product) with a hypothetical event (the sale of the brand prescribed but not dispensed).[104] The brand prescribed but not dispensed may be available direct from the manufacturer at one price, from the wholesaler at another price, and as a part of a special "deal" at yet a third price. Furthermore, pricing systems vary among pharmacies -- some use a fixed fee, some a percentage markup, and others a combination fee and markup.[105] Pharmacists therefore may find it difficult to comply with such provisions; this difficulty prompted 89 percent of the pharmacists in a Medicaid reimbursement survey to oppose a formula requiring the calculation of actual acquisition costs.[106] And it may be impossible to enforce and monitor pass-on provisions; for example, a Michigan State Representative has stated that a representative of the Attorney General's office had "publicly admitted that the section [was] unenforceable."[107]

Mandatory pass-on provisions may even discourage pharmacists from selecting lower-cost generic equivalents. These provisions generally prohibit pharmacists from earning any additional profit

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100 E.g., Idaho, Maryland and Montana. Other states, including Colorado, Ohio, and Tennessee, refer to a pass-on of "differences in cost."

101 E.g., Connecticut, Michigan, Utah and Wisconsin.

102 E.g., California, Delaware, Iowa, Minnesota, Rhode Island, Virginia, Washington and West Virginia.

103 E.g., California, Colorado, Montana, Rhode Island and Utah.

104 Dickson, supra note 2, at 20.

105 See discussion of pricing systems, Ch. IV.B., supra.

106 R.A. Gosselin & Co., Inc., "Pharmacy Charges for Prescription Drugs Under Third Party Programs," May 5, 1971, at 7.

107 Representative Bert Brennan, quoted in U. Mich. J. L. Reform, supra note 29, at 405. We also have been told informally that some manufacturers have promoted artificially inflated list prices to pharmacists as a means of thwarting mandatory pass-on provisions.

to cover costs incurred in searching for, stocking and dispensing lower-cost products. Researchers in the Goldberg study assert that financial incentives, rather than regulatory mandates, may encourage pharmacists to engage in product selection more frequently.[108] "The dispenser of pharmaceuticals can be expected to cooperate if he or she realizes that one's livelihood is not being directly threatened or impaired."[109] Nearly one-third of the pharmacists in the FTC study said they would not substitute as often if their state required a pass-on of all cost savings.[110] The percentage was significantly higher for store owners and managers than for staff pharmacists.[111]

Some states avoid these problems by prohibiting pharmacists from charging more than their "usual and customary" or "regular" retail price for the dispensed product.[112] These provisions prevent establishment of a two-tiered pricing system -- one price for the product when used to fill a generically-written prescription or a prescription dispensed as written, and another, higher price for the product when selected as a substitute for a brand-name item--but still permit the pharmacist to establish prices in response to market competition. However, it is not apparent that competitive market forces would so vary that a pharmacy could charge the higher price in the second case but not the first. Moreover, although

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108 Drug Topics, Dec. 1, 1976, at 12; Goldberg, supra note 54, at 22.

109 Wertheimer, supra note 14, at 8.

110 FTC Study, supra note 3, at 52.

111 Id. at 85.

112 E.g., Arkansas, Kansas, New Jersey, Pennsylvania, and Vermont. Similarly, Florida apparently requires a cost savings pass-on of the difference in the retail price of the prescribed and the dispensed products: § 465.30(3)(a) requires that the pharmacist notify the purchaser of the amount of the "retail price difference" and § 465.30(3)(b) requires that the pharmacist pass-on the "full amount of the savings." Fla. Stat. Ann. § 465.30 (West 1978). For a discussion of lobbying efforts by brand-name manufacturers and others to amend the Florida provision, see The Miami Herald, Apr. 23, 1978, at 1AA, col. 1; Fla. H.B. 1605, introduced 1978. The National Retired Teachers Association and American Association of Retired Persons opposed the amendment. Memorandum to the Members of the Commerce Committee of the House of Representatives from Jack Carroll and Ed Henderson, May 12, 1978.

retail prices are easier than wholesale prices to ascertain, difficulties in interpreting "usual and customary" price still may arise.

Finally, a small number of states require pharmacists to select the least expensive product in stock when they substitute.[113] Some states in effect make this discretionary by requiring products substituted for branded items or used in filling generically-written prescriptions to be the least expensive in stock "judged equivalent" by the pharmacist.[114] These provisions also pose enforcement difficulties. They are easily thwarted because a pharmacist can comply with the requirement by pricing the lower-cost item only a penny below the brand-name price. Moreover, the Goldberg study found evidence that such provisions are ineffective. A comparison of savings on generically-written prescriptions in Michigan, which has no such provision, with those in Wisconsin, which requires selection of a product with a lower-than-average wholesale cost, showed that only 14 cents per prescription was saved in Wisconsin as compared to 74 cents in Michigan during a comparable period.[115]

7. Professional Liability

Although no liability lawsuits have resulted from legal substitution, nor have pharmacists been held liable for selecting sources in filling generically-written prescriptions, pharmacists show considerable concern about liability risks -- a concern possibly magnified through the efforts of some brand-name manufacturers.[116]

A Florida study reported that over 75 percent of responding pharmacists believed they were more vulnerable to malpractice suits under the product selection law; over 50 percent were very concerned about the possibility of such suits.[117] Fifty-six percent of the pharmacists in a Massachusetts survey believed the law subjected

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113 Kentucky and Vermont.

114 E.g., Georgia, Montana, Nebraska, and Oregon.

115 Goldberg, supra note 54, at 10.

116 See discussion, Ch. IX.E., infra. Yet a study reported by a PMA Committee found that pharmacists had encountered no problems as a result of substitution. PMA Committee on the Effects of Amendments to State Antisubstitution Laws, supra note 57.

117 Market Measures, supra note 11, at i.

them to a greater liability risk.[118] Similarly, 72 percent of the pharmacists in a Kentucky study feared the law had increased their vulnerability to lawsuits.[119] Sixty-six percent of the pharmacists in the FTC survey believed product selection laws had increased their risk of liability lawsuits,[120] and 42 percent of these pharmacists said the increased risk caused them to substitute less often than they would otherwise.[121]

> The liability issue is raised often in the pharmacy press and appears to be the focal point for other reservations about drug product selection. The liability question, probably more than any other, creates the uncertainty that limits adoption of . . . [drug product selection] by pharmacists.[122]

Sixteen state laws address the issue of pharmacist liability. One group of provisions states that the act of substitution is not evidence of negligence, particularly if the substitution was made within the "prudent practice" of pharmacy[123] or if the product selected was listed in a generally recognized formulary.[124] Most provisions state that the liability is the same as or no greater than that incurred in filling a generically-written prescription.[125]

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118 Krbec & Taubman, "Effects of the Massachusetts Drug Substitution Law on Pharmacists' Dispensing Habits," Med. Marketing & Media, July 1976, at 42.

119 Barnett, supra note 10, at 31. A survey of "pharmacy leaders" found that liability risk was expected to be a major factor in discouraging drug product selection. pharmaSYST reports, supra note 93, at 3.

120 FTC Study, supra note 3, at 39.

121 Id. at 40.

122 Dickson, supra note 2, at 25.

123 E.g., District of Columbia and Nebraska.

124 E.g., Illinois and Oregon.

125 E.g., Arizona, California, Florida, Missouri, Montana, and Tennessee. Colorado and Utah also charge the pharmacist with notice of FDA's list of drugs with actual or potential bioequivalence problems. Pennsylvania and West Virginia limit liability only to cases of incorrect substitution.

According to the FTC study, the pharmacist's fear of increased liability was unaffected by the existence of a state liability provision.[126] This may be due to the fact that most pharmacists in states with liability provisions were unaware of their existence: only 29 percent the pharmacists in California, 28 percent in Oregon and 41 percent in Pennsylvania knew their states had such provisions.[127]

Although there has been much less discussion and concern about physician liability, fourteen states address this issue. Most common are provisions exempting the physician from liability unless the drug was incorrectly prescribed,[128] or providing that failure to indicate "medically necessary" or "D.A.W." is not evidence of negligence, particularly if the physician had no reason to believe a particular brand was necessary.[129]

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126 FTC Study, supra note 3, at 108.

127 Id. at 48.

128 E.g., Florida, Ohio, Pennsylvania, and West Virginia.

129 E.g., Arizona, District of Columbia, Illinois, Nebraska, Ohio, Oregon, Utah and West Virginia. California and Washington exempt the physician from liability for the pharmacist's actions in substituting.

Table 1.

State Laws

	1. Drug Product Selection Prohibited	2. Drug Product Selection Permitted/Mandated	3. State Positive Formulary	4. State Negative Formulary	5. No Formulary	6. Refill Limitation	7. Generic Rx Provision	8. Physician Consent (Preprinted Rx Blanks)	9. Physician Veto (D.A.W., D.N.S., etc.)	10. Purchaser Consent	11. Purchaser Veto	
Alabama	S											
Alaska		S			X			X		X		
Arizona		S	X					X				
Arkansas		S		X					X		X	
California		S		X					X			
Colorado		S			X				X			
Connecticut		S			X				X		X	
Delaware		S		X				X				
D. C.		S	X	O					X		X	
Florida		S M	X 5	X					X		X	
Georgia		S			X		X	X			X	
Hawaii	S											
Idaho		R			X			X			X	
Illinois		S	X					X		X		
Indiana	S											
Iowa		S		X					X		X	
Kansas		S		X 7				O	X			
Kentucky		S M	X						X		X	
Louisiana	S											

12. Physician Notification	13. Purchaser Notification	14. Pharmacist Recordkeeping for Drugs Dispensed	15. Selected Drug Must be Lower in Cost	16. Pass-on of Entire Cost Savings to Consumers	17. Other Cost Savings Provisions	18. Pharmacist Liability	19. Physician Liability	20. Consumer Information Posted	21. Rx Container Labeling	22. Manufacturer's Labeling	23. Date Fully Effective	
												Alabama
X	X		X					X 1			9/76	Alaska
	X					X	X		X		1/79	Arizona
	X		X		X				O		12/75	Arkansas
	X		X	X		X	X		X		5/76	California
	X	X	X	X		X 2			X	X	4/76	Colorado
	X	R	X	X		X 3		X	X		10/76	Connecticut
	X	X		X					X		9/76	Delaware
		X	X 4			X	X	X	X		12/77	D. C.
	X	X	X	X 6		X	X	X			74,A 6/76	Florida
		X			X						1/78	Georgia
												Hawaii
		X	X	X				X	X		7/78	Idaho
	X	X	X			X	X				6/78	Illinois
												Indiana
	X	X	X	X						X	7/76	Iowa
			X		X						7/78	Kansas
					X			X	X		72,A 6/76	Kentucky
												Louisiana

	1. Drug Product Selection Prohibited	2. Drug Product Selection Permitted/Mandated	3. State Positive Formulary	4. State Negative Formulary	5. No Formulary	6. Refill Limitation	7. Generic Rx Provision	8. Physician Consent (Preprinted Rx Blanks)	9. Physician Veto (D.A.W., D.N.S., etc.)	10. Purchaser Consent	11. Purchaser Veto	
Maine		S			X				X			
Maryland		S		X					X			
Massachusetts		S/M	X					X				
Michigan		S 8			X				X			
Minnesota		S			X				X 9	X		
Mississippi	S											
Missouri		S		X				X			X	
Montana		S			X		X		X		X	
Nebraska		S		X			X		X		X	
Nevada	R											
New Hampshire		S	X					X 11		X		
New Jersey		S/M	X					X			X	
New Mexico		S	X						X			
New York		S/M	X					X				
North Carolina	S 14											
North Dakota	S											
Ohio		S	X 15						X			
Oklahoma		S 16			X							
Oregon		S			X		X		X		X	

12. Physician Notification	13. Purchaser Notification	14. Pharmacist Recordkeeping for Drugs Dispensed	15. Selected Drug Must be Lower in Cost	16. Pass-on of Entire Cost Savings to Consumers	17. Other Cost Savings Provisions	18. Pharmacist Liability	19. Physician Liability	20. Consumer Information Posted	21. Rx Container Labeling	22. Manufacturer's Labeling	23. Date Fully Effective	
	X		X 4						X		76,A 7/78	Maine
	X	X	X	X							7A 75 1/78	Maryland
			X						X		71,A 1/78	Mass.
	X		X	X					X		75,A 1/77	Michigan
	X		X 4	X					X	X	8/75	Minnesota
												Mississippi
		X 10	X			X			X	X	1/79	Missouri
	X		X	X		X	X	X			7/77	Montana
			X		X	X	X	X	X	X	1977	Nebraska
												Nevada
											8/73	N. H.
X 12			X		X			X	X		1979	New Jersey
X 13			X						X		5/76	New Mexico
			X					X	X		4/78	New York
												N. C.
												N. D.
	X	X	X	X	X		X		X	X	1/78	Ohio
											1961	Oklahoma
		X	X 4			X	X	X	X		9/75	Oregon

	1. Drug Product Selection Prohibited	2. Drug Product Selection Permitted/Mandated	3. State Positive Formulary	4. State Negative Formulary	5. No Formulary	6. Refill Limitation	7. Generic Rx Provision	8. Physician Consent (Preprinted Rx Blanks)	9. Physician Veto (D.A.W., D.N.S., etc.)	10. Purchaser Consent	11. Purchaser Veto	
Pennsylvania		S M	X			R		X			X	
Rhode Island		S M	X					X			X	
South Carolina		S			X			X		X		
South Dakota		S			X			X				
Tennessee		S	X					X				
Texas	S											
Utah		S		X 17					X	X 18		
Vermont		S M	X			X			X		X	
Virginia		S	X					X 19				
Washington		S		O				X				
West Virginia		S M		X				X			X	
Wisconsin		S	X			X	X		X			
Wyoming	S											

12. Physician Notification	13. Purchaser Notification	14. Pharmacist Recordkeeping for Drugs Dispensed	15. Selected Drug Must be Lower in Cost	16. Pass-on of Entire Cost Savings to Consumers	17. Other Cost Savings Provisions	18. Pharmacist Liability	19. Physician Liability	20. Consumer Information Posted	21. Rx Container Labeling	22. Manufacturer's Labeling	23. Date Fully Effective	
	X	X	X		X	X	X	X	X		5/77	Penn.
		X	X	X		X	X				76,A 5/78	R. I.
	X	X							X		1/79	S. C.
											7/78	S. D.
			X	X		X			X	X	6/77	Tennessee
												Texas
	X	X		X		X 2	X		X	X	5/77	Utah
	X		X		X			X	X		8/78	Vermont
	X	X	X	X					X	X	76,A 1/79	Virginia
		X		X			X	X			9/77	Washington
	X	X	X	X		X	X	X	X	X 20	7/78	W. Virginia
	X			X	X			X		X	10/76	Wisconsin
												Wyoming

CODES FOR CHART

M - Mandatory, R - Regulation, S - Statute, X - Affirmative Provision, O - Optional Provision, A - Amendment

FOOTNOTES FOR CHART

1/ Required only during first 2 years of Act.

2/ Same liability as incurred in filling a generic Rx, but pharmacist charged with notice of FDA bioequivalence problems list.

3/ Posting of sign and absence of purchaser veto are no defense.

4/ Selected drug must be of lower or equal cost.

5/ Each pharmacy is to prepare its own positive formulary.

6/ Pass-on of difference in retail price.

7/ Product selection prohibited for drugs FDA determines to be bioinequivalent.

8/ Purchaser can mandate product selection.

9/ Pharmacist can override veto if selected drug is made by same manufacturer as prescribed drug.

10/ Name of manufacturer must be on Rx label or in pharmacist's records.

11/ Physician must write in words "or its generic equivalent drug listed in N.H. drug formulary."

12/ Physician notification required only if physician so indicates on Rx.

13/ Physician notification required only if pharmacist changes the drug dispensed at some time after product selection has occurred (e.g. refills).

14/ Except for Medicaid Rx's, for which product selection is mandatory, absent D.A.W.

15/ Each pharmacy is to prepare its own positive formulary. Drugs cannot be considered generically equivalent if listed by FDA as having a proven bioequivalence problem.

16/ Product selection upon authority of prescriber or purchaser.

17/ Utah Board of Pharmacy empowered to adopt FDA list. Selected drugs may not be in any Drug Bioequivalence Problems List such as FDA list.

18/ Purchaser must specifically request product selection.

19/ Rx blanks required after 1/1/79. Prior to that time, physicians may handwrite "Voluntary Formulary".

20/ Product eligible for selection only if manufacturer's name appears on label.

VII. C. Studies Of Drug Product Selection

This section will review three major studies of drug product selection: the study of Michigan and Wisconsin conducted by Theodore Goldberg, et al., of Wayne State University ("the Goldberg study"), the Delaware study conducted by Joseph Fink of the Philadelphia College of Pharmacy and Science ("the Fink study"), and the study conducted for the FTC by an independent market research firm ("the FTC study"). Other, less comprehensive studies, also will be discussed briefly.

1. The Goldberg Study

Probably the most extensive study of drug product selection has been conducted by a group of researchers at Wayne State University in Detroit.[1] The Goldberg study provides calculations based on actual prescribing and dispensing information derived from an audit over a three-year period of more than 154,000 prescriptions in Michigan and Wisconsin.[2]

Goldberg found that over half of all prescriptions were written for multisource drugs,[3] thus offering significant opportunities for savings from drug product selection. Physicians rarely blocked product selection by writing "dispense as written" or

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1 Theodore Goldberg, Wayne State University School of Medicine, "Cost Implications of Drug Product Selection Legislation," Presented to Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978. ["Goldberg"]. See also, Goldberg, et al., "Impact of Drug Substitution Legislation: A Report of the First Year's Experience," 17 J. Am. Pharm. Ass'n 216 (1977); Goldberg, et al., "Evaluation of Economic Effects of Drug Substitution Legislation," Presented to the 105th Annual Meeting of the American Public Health Ass'n, Wash., D.C. Oct. 31, 1977; Moore, et al., "Evaluation of the Impact of Drug Substitution Legislation-III," Presented at the 124th Annual Meeting of the American Pharmaceutical Ass'n, N.Y.C., May 17, 1977; Aldridge, et al., "Profile of the Doubters: Pharmacists Who Doubt That Members of Their Profession Can Safely Select Among Drug Products," Presented at the 124th Annual Meeting of the American Pharmaceutical Ass'n, N.Y.C., May 17, 1977; DeVito, et al., "Development of a Comprehensive Drug Product Coding System," Presented at the 124th Annual Meeting of the American Pharmaceutical Ass'n, N.Y.C., May 17, 1977.

2 Goldberg, supra note 1, at 4.

3 Id. at 6.

"no substitution" -- this occured only 3.6 percent of the time in Wisconsin, and 6.4 percent of the time during the first year of the Michigan law, decreasing to 4.0 percent the second year.[4] The "D.A.W." notation was applied about as often to single-source and generically-written prescriptions as to multisource prescriptions.[5]

By matching the prices of prescriptions dispensed as written with those of substituted prescriptions, the study was able to document significant savings when product selection took place. Substitution produced a 20 percent savings in Michigan (or $1.15 per prescription), and a 17 percent savings in Wisconsin (or 87¢ per prescription).[6] This was greater than the savings from generic prescribing: 74 cents per prescription in Michigan and 14 cents per prescription in Wisconsin.[7]

Using this price information, Goldberg calculated potential consumer savings in Michigan alone of $11.7 to $15.3 million a year.[8] If the savings from dispensing lower-priced products when filling generically-written prescriptions were added to this, the total potential annual savings would be $13.5 to $17.6 million.[9]

Actual consumer savings in Michigan were only $200,000 to $300,000 a year,[10] however, because product selection occurred in only 1.5 percent of all multisource prescriptions.[11] In contrast, preliminary analysis of 1977-78 data in Wisconsin indicates a drug product selection rate of 18 to 20 percent.[12] One reason

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4 Id. at 11.

5 See discussion in Ch. VII.B.3., supra.

6 Goldberg, supra note 1, at 7.

7 Id. at 10. See discussion in Ch. VII.B.6., supra.

8 Id. at 18. See further discussion of cost savings, Ch. VIII., supra.

9 Goldberg, supra note 1, at 18.

10 Id. at 22.

11 Id. at 20.

12 Carolee DeVito, Wayne State University, "Drug Product Selection Legislation: Issues and Alternatives," Presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Seattle, Washington, Sept. 21-22, 1978, at 5.

given for the low product selection rate in Michigan is that the original Michigan law was interpreted to require the purchaser to request a generic equivalent before the pharmacist could select a lower-cost product.[13] Although the "purchaser request" requirement was removed from the law in 1977, Goldberg's analysis of the data during the first four months of the amended law failed to disclose any effect on the substitution rate.[14] It may be that four months was insufficient time to measure the impact of the amendment. Or it may be that lack of economic incentives for the pharmacist because of mandatory pass-ons or other restrictive provisions is the major cause of the low substitution rate.[15]

2. The Fink Study

Joseph Fink of the Philadelphia College of Pharmacy and Science audited prescription data collected from 30 of the 130 community pharmacies licensed in Delaware.[16] Baseline data were gathered for the period September 1, 1976, to December 20, 1976. Data then were gathered for the period October 1, 1977, to December 1, 1977, after the effective date of the Delaware law.

Most of the prescription forms examined contained a physician prohibition against substitution. Fink found that physicians signed on the preprinted "dispense as written" line 62 percent

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13 Mich. Att'y Gen. Op. No. 4839 (Feb. 5, 1975).

14 Goldberg, supra note 1, at 21. According to a recent mail survey of 136 retail pharmacists, about half said that they engaged in product selection "frequently" or "whenever possible." Michigan Pharmacist, November 1977, at 10-11. It is not clear whether this survey is measuring more recent responses to the amended law or whether the difference in response is due simply to differences in methodology between it and the Goldberg study.

15 Drug Topics, Dec. 1, 1976, at 12; Goldberg, supra note 1, at 23.

16 Fink & Myers, "Effectiveness of Drug Product Selection Legislation in Delaware," 1 Contemp. Pharmacy Prac. 4 (1978). See also, Joseph L. Fink III, Philadelphia College of Pharmacy and Science, "A Study of Savings Resulting from Passage of the Delaware Drug Product Selection Act: Report on Phase I Collection of Baseline Data," June 28, 1977; Fink, "A Study of Savings Resulting from Passage of the Delaware Drug Product Selection Act: Final Report," January 1978.

of the time. In 57 percent of the cases where the physician had indicated "dispense as written" the prescription was for a single-source drug for which substitution was impossible.[17]

Pharmacists did substitute a majority (56%) of the time when the opportunity was presented, i.e. when authorization was given by the physician and a multisource drug was prescribed.[18] The rate of substitution varied among pharmacies: three stores substituted 100 percent of the time when authorization was given, whereas two pharmacies never substituted when authorized.[19]

Because nearly half (47%) of all prescriptions were for multisource drugs[20] (a figure comparable to that found in Michigan and Wisconsin by the Goldberg study),[21] product selection offered significant opportunities for consumer savings. Fink measured the unit prices for ten commonly prescribed multisource drugs, finding no increase in their unit prices during the study period, in contrast to a seven percent increase in the Bureau of Labor Statistics Consumer Price Index for the same period. Fink concluded that the Delaware product selection law appeared to be holding down prices, at least for these ten drugs. The study also found statistically significant consumer savings for seven of the ten drugs when substitution was authorized; the savings ranged from 2.7 cents to 13.2 cents per dosage unit.[22]

3. The FTC Study

We contracted with IMS America, Ltd., an established health care market research firm, to conduct a multistate telephone survey of pharmacists' attitudes concerning the effects of drug product selection laws on their stores and themselves, on their opinion of product selection laws in general, and of key provisions in particular.[23] We undertook this study because existing

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17 Fink & Myers, id. at 7.

18 Id.

19 Id.

20 Id.

21 See note 3, supra.

22 Fink & Myers, supra note 16, at 8. See further discussion of cost savings, Ch. VIII., infra.

23 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978. ["FTC Study"].

surveys seldom provided evidence of the reasons pharmacists did or did not substitute lower-cost products, and because no other survey to our knowledge attempted to test the effect of various statutory provisions on pharmacists' attitudes and behavior.

We questioned 723 pharmacists[24] in seven states (Arkansas, California, Delaware, Minnesota, Oregon, Pennsylvania, and Wisconsin) with product selection laws. The states were selected on the basis of three major criteria: geographic distribution, variation in the provisions of the state's product selection law, and at least one year's experience with the law. Further, we selected two states, Delaware and Wisconsin, which were the subject of prescription audits by other researchers (Fink in Delaware and Goldberg in Wisconsin),[25] as a means of testing the accuracy of pharmacists' perceptions of their behavior. Appendix C of this Report consists of a copy of the pharmacist questionnaire used in our study, and tabulations of the responses to each question.

All the pharmacists reported that they were familiar with the generic substitution (or drug product selection) law in their state.[26] In most states less than 30 percent said their store policy was to substitute whenever possible; 60 percent of the pharmacists in Delaware and Wisconsin, however, reported a store policy of substituting whenever possible.[27] In Pennsylvania, the only state surveyed that has a mandatory substitution law, fewer than one-quarter of the pharmacists reported compliance with this provision. Pennsylvania pharmacists reported that they substituted on about ten percent of the prescriptions for

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24 The sample, drawn from the Hayes Directory of Pharmacies, was a systematic sample using a random start. A total of 1390 pharmacies were contacted, of which 52 percent participated in the study. Twenty-two percent refused to participate, and the remainder of non-respondents resulted from busy, unanswered, or disconnected telephones, and miscellaneous other reasons. In no state was there any significant difference between the distribution of chain and independent pharmacies sampled and the distribution of all pharmacies. Id. at 4 and Appendix 10. Demographics of survey respondents are discussed, id. at 7.

25 See discussion of Fink and Goldberg studies in Ch. VII.C.1. and 2., supra.

26 FTC Study, supra note 23, at 25.

27 Id. at 26. Larger pharmacies were more likely than smaller pharmacies to report that their store policy was to substitute whenever possible. Id. at 57.

which substitution was possible.[28] The median percentages were highest for two formulary states: Wisconsin (45.5%), which has a positive formulary, and Delaware (39.5%), which has a negative formulary. These reports of considerable substitution in Delaware and Wisconsin are supported by Fink's study in Delaware and by Goldberg's preliminary findings in Wisconsin.[29]

Almost three-quarters (73.7%) of the pharmacists thought the law had resulted in lower retail prices,[30] with customers realizing an average savings of about 20 percent.[31] This percentage savings is comparable to the 17 to 20 percent figure found in Goldberg's study of Michigan and Wisconsin.[32] Interestingly, although none of the seven state laws require that pharmacists select the least expensive product in stock when substituting, nearly two-thirds (65%) of the pharmacists said they did so "all" or "most" of the time.[33]

The study confirmed findings reported elsewhere[34] that physicians rarely (only 1.4 to 5.1% of the time) find it necessary to prohibit substitution by handwriting such indications as "Medically Necessary" or "Dispense as Written."[35] When physicians have to sign one of two instructions preprinted on the prescription form, however, they sign on the "Dispense as Written" line nearly half (31 to 51%) the time.[36] About half the pharmacists (49.2%) thought the frequency with which physicians prohibited substitution did not vary by drug type.[37] Few pharmacists (3.9%) were concerned that the state law had negatively affected their relations with physicians; most (77.4%) thought the law had had no effect

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28 Id. at 27.

29 See Ch. VII.C.1. and 2., supra.

30 FTC Study, supra note 23, at 43.

31 Id. at 44.

32 See Ch. VII.C.1., supra.

33 FTC Study, supra note 23, at 28.

34 See Ch. VII.B.3. and C.1., supra.

35 FTC Study, supra note 23, at 29.

36 Id. See discussion of similar findings in Ch. VII.B.3. and C.2., supra.

37 Id. at 30.

or a mixed positive and negative effect.[38]

Lack of consumer awareness of the availability of cost-saving generic drug products or of the pharmacist's ability to select a lower-cost product is reflected in the response of pharmacists that less than five percent of their patients ask about the possibility of receiving a generic substitute.[39] Yet very few patients (1.4%) refused a lower-cost substitute when it was suggested by the pharmacist.[40] Patient appreciation of the cost savings provided by generic products may be the reason a majority (53%) of pharmacists reported a positive effect of the law on their relations with patients.[41]

Perhaps because of various state requirements that the pharmacist notify the patient that a generic is being dispensed,[42] most pharmacists (54.2%) reported that the law had caused them to spend more time with patients.[43] The percentage is highest (68%) in the two states, Delaware and Wisconsin, reporting the greatest amount of substitution. This increased communication may be the reason, along with reduced prices, that pharmacists reported improved relations with patients. Of those pharmacists who reported spending more time with patients, relatively few (19.9%) said this increased time was so burdensome as to discourage them from substituting.[44] Similarly, although some pharmacists (27.7%) said their state law had created more paperwork (presumably due to labeling, posting, and recordkeeping requirements),[45] few of them (19.3%) found it so burdensome as to discourage them from substituting.[46]

Pharmacists' fears of liability lawsuits do have a significant effect on their willingness to substitute. Two-thirds of the pharmacists (65.8%) thought the law had increased their risk

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38 Id. at 33.

39 Id. at 31.

40 Id. at 32.

41 Id. at 34.

42 See Ch. VII. B.4., supra.

43 FTC Study, supra note 23, at 35.

44 Id. at 36.

45 See Ch. VII. B.4. and 5., supra.

46 FTC Study, supra note 23, at 38.

of being subject to lawsuits, and nearly half of them (41.5%) said this perceived risk caused them to substitute less often than they would otherwise.[47] Although younger pharmacists are the strongest supporters of substitution laws, they are more likely than experienced pharmacists to be concerned about the risk of liability lawsuits.[48] The existence of a state formulary or even a provision expressly defining or limiting their liability appears to have no effect on pharmacists' liability concerns.[49] This latter point is not surprising since most pharmacists (60 to 72%) in the three states with liability provisions were unaware of the existence of those provisions.[50] One-third of the pharmacists (33.5%), however, did say that a state liability provision would increase their willingness to substitute.[51]

Nearly nine out of ten pharmacists (87.4%) believed that net profits had remained constant or had increased because of their state product selection law.[52] This was so even though half (53.9%) claimed that the law had led to increased inventory

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47 Id. at 39-40.

48 Id. at 58, 60.

49 Id. at 108-111.

50 Id. at 48. This point illustrates the difficulty in correlating substitution behavior with various provisions of drug product selection laws. The FTC Study attempted a regression analysis to see if certain provisions of the state laws or the demographic characteristics of the pharmacy and the pharmacist were useful predictors of the rate of generic substitution. Six variables -- mandatory cost savings pass-ons, posting provisions, negative formularies, liability provisions, average daily prescription volume, and manager status in the pharmacy -- were positively related to the substitution rate, and one variable - years in pharmacy practice -- was negatively related. Yet all the variables explained only 25 percent of the variance in the substitution rate. The fact that existence of a liability provision, for example, was a significant variable, even though most pharmacists were unaware of the provision's existence, indicates that the regression analysis was limited considerably by the small number of states sampled. Future analyses might attempt to include additional variables and a greater number of states. Id. at 103-104, 116.

51 Id. at 47.

52 Id. at 42.

costs.[53] Almost one-third (29.3%) of the pharmacists said that a provision requiring them to pass on all wholesale cost savings to patients would adversely affect their willingness to substitute.[54] This attitude was more pronounced among owners and managers, who are most directly involved with decisions affecting store profits, than among staff pharmacists.[55] The fact that 34 to 56 percent of the pharmacists in states with mandatory cost savings pass-ons were unaware of those provisions suggests that the mandate often may not be complied with.[56]

Pharmacists in the two states, Delaware and Wisconsin, reporting the most substitution also reported the clearest preference when given the choice of a negative formulary, a positive formulary or no formulary. Two-thirds (68.4%) of the pharmacists in Delaware, which currently has a negative formulary, said they would substitute most often if there were no formulary.[57] On the other hand, a corresponding proportion (65.3%) of pharmacists in Wisconsin, which has a positive formulary, said they would substitute most often if their state continued to have a postive formulary.[58] Apparently there are a large number of pharmacists (particularly store owners) who prefer to have no state formulary either because they oppose government restrictions generally or because they view formularies as an unnecessary limitation of their ability to select generic drug products. An equally large number of pharmacists (particularly staff pharmacists) apparently prefer a positive formulary because of the guidance it

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53 Id. at 41. It is difficult to explain this response. It may be that pharmacists who responded this way considered the addition of new generic lines as an increased inventory cost, even though the new generic products presumably replaced an equal number of higher priced brand-name products. Or it may mean that significant inventory savings become apparent only after generic products replace entire lines of duplicate brand-name products. See discussion, Ch. IV.B., supra.

54 Id. at 52.

55 Id. at 60,85.

56 Id. at 53. Similarly, 20 to 36 percent of the pharmacists in states without mandatory pass-ons mistakenly believed that their laws included such a requirement.

57 Id. at 50.

58 Id.

provides in selecting drug products.[59] Pharmacists in the remaining five states were almost equally divided in preferring positive formularies or no formulary at all (with a slight preponderance preferring no formulary).[60] Regardless of the system used in their own state, very few pharmacists (6 to 15%) preferred a negative formulary.[61]

A majority (57.1%) of pharmacists in the four formulary states did not think their state formulary provided adequate guarantees of product equivalence; that percentage was lower in states with higher rates of substitution.[62] Approximately half the pharmacists (48.0%), however, thought the quality of product information from the pharmaceutical industry had improved since enactment of the state product selection law.[63] And almost three-quarters (72.1%) felt they generally had sufficient product information to exercise their authority to substitute.[64]

Pharmacists overwhelmingly (82.6%) favored the principle of generic drug substitution, and most (57.9%) indicated general satisfaction with their state substitution law.[65] Two exceptions involved states with provisions pharmacists may feel are particularly burdensome. Wisconsin, for example, limits substitutable products to those meeting certain published wholesale prices and further limits refills to the same product used to fill the original prescription. Perhaps because of these provisions, nearly as many Wisconsin pharmacists said they preferred a different substitution law (36.4%) as preferred the law as currently written (46.3%). And in Pennsylvania, which mandates substitution and imposes a number of regulatory restrictions, most pharmacists preferred either a different substitution law (30.1%) or even an antisubstitution law (30.9%).

Finally, nearly 80 percent of the pharmacists said they expected their rate of substitution to increase either "greatly"

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59 Id. at 50, 60, 83.

60 Id. at 50.

61 Id.

62 Id. at 51.

63 Id. at 45.

64 Id. at 46.

65 Id. at 55.

or "somewhat" over the next two years.[66] Presumably this change is expected to result from increasing consumer demand for lower-cost generics as well as pharmacists' increasing familiarity with and confidence in drug product selection.

4. Miscellaneous Studies

This section will briefly discuss several other surveys we have obtained from manufacturers, trade associations or other sources. In most cases, we have insufficient information about their survey methodology to evaluate them fully.

A 1975 study supplied by PMA[67] supports the findings of Goldberg, et al., that little product selection has taken place in Michigan. A prescription audit of ten multisource drug classes combined with a mail survey of 173 pharmacists found a substitution rate of about five percent, with substitution most common for antibiotics.[68] As reported in the FTC study, pharmacists disagreed about the law's effect on inventories and profits.[69] The percentage of pharmacists favoring the law increased over time, however, and most felt their substitution rate would rise in the future, primarily because of increased consumer demand.[70]

Florida pharmacists appear to be engaging in product selection to a greater degree than is occurrring in Michigan. An audit by Market Measures, an independent market research firm, of 25,000 prescriptions dispensed from July-September 1977 showed a 5.9 percent substitution rate on the 50 products surveyed.[71] For some drugs the rate was as high as 20 percent. A PMA Committee report[72] showed an even higher rate of 11 percent for October-December 1976. And although non-PMA firms only have about

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66 Id. at 56.

67 Letter from C. Joseph Stetler, President, PMA, to Peter D. Holmes, FTC, Feb. 21, 1978, at Appendix C.

68 Id. at vi, vii, x, xii.

69 Id. at viii.

70 Id. at vii, ix, xx.

71 Letter from Richard C. Zeich, Director, Audit Research, Market Measures Inc., to Peter Holmes, FTC, May 31, 1978.

72 PMA Committee on the Effects of Amendments to State Antisubstitution Laws, "Preliminary Report on the Effect of the Repeal of Antisubstitution Laws in California, Michigan, Florida and Delaware," Apr. 25, 1977. ["PMA Committee"].

a five percent share of the overall prescription market, the report showed them with 61 percent of the substitution market, thus indicating that most products selected were probably unbranded generics.

California has been the subject of several studies. A Market Measures audit of 28,000 prescriptions in February-April 1977 showed a substitution rate for 32 products of seven percent, with rates on individual products as high as 14 to 16 percent.[73] PMA reported substitution rates in May-July and August-October 1976 of 11 to 11.5 percent. Again, non-PMA firms captured most (63-67%) of the substitution market.[74]

Finally, surveys by the Ministry of Health in Ontario, Canada, demonstrate the influence of education campaigns and of increasing experience with product selection laws on substitution rates: a five percent rate in 1972, the first year of the Ontario law, had increased to 21.45 percent only four years later.[75]

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73 Zeich, supra note 71. The substitution rate for Medi-Cal prescriptions was 21 percent.

74 PMA Committee, supra note 72.

75 Dr. Allan E. Dyer, Ontario Ministry of Health, "Implementation and Implications of Applying Drug Product Selection to Selected Populations," Presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13, 1978, at 13. It may be that increasing experience with product selection laws is beginning to have some effect in this country. For example, Market Measures Inc. reported in May 1978 that its latest study of 19 states showed a 30 percent increase in substitution (to an overall rate of four percent) over a comparable study it made six months earlier. Based on this research, the president of Market Measures expressed the belief that "substitution is growing dramatically." Kellogg, "M.D.'s Update on Generic Substitution," Legal Aspects Med. Prac., May 1978, at 21.

CHAPTER VIII. MEASURING THE BENEFITS FROM DRUG PRODUCT SELECTION

Studies to estimate the amount of potential savings from drug product selection have been undertaken. As different as the sponsors, the data base and the methodology of these studies are, one finding is consistent throughout: consumers potentially can save hundreds of millions of dollars annually if pharmacists are given greater discretion to select the drugs they dispense.

For example, the FTC Bureau of Economics' analyses indicate that annual wholesale-price savings could be between $400 million and $500 million. An independent research firm using estimates of the retail price premium attributed to brand-name prescribing concluded that annual retail-price savings could amount to $323 million. A university study which examined retail prices in Michigan estimated that potential savings in Michigan alone could range from $11 to $15 million. If these potential savings were extrapolated nationwide, consumers could save from $260 to $450 million.

To arrive at an estimate of the consumer benefit to be derived from drug product selection, we reviewed eight major studies and undertook one of our own.[1] In the following discussion these reviews and the FTC work are grouped into two categories: those that used wholesale-price information, and those that used retail-price information. The former group includes the FTC analyses and reviews of three studies: two by HEW and one by IMS America, Ltd. The latter group includes two IMS studies of the price effect of brand-name prescribing, and three studies which analyzed the effects of drug product selection legislation: two dealt with Michigan, and one was concerned with Delaware.

In all these studies, estimates were involved and conclusions must be drawn carefully and qualified where appropriate.

A. Savings Estimates from Wholesale-Price Information

Wholesale prices, which represent the pharmacist's drug acquisition cost, form a good basis for savings estimates. They demonstrate directly the differences among manufacturer's prices for equivalent generic drug products. The studies set forth below using wholesale prices may come closest to providing an estimate of the upper limit on potential savings.

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1 Supplementing all of the above works are a number of "miscellaneous" studies. Some of them are limited in scope, while others bear indirectly on the savings issue. Too numerous to cover in detail, their findings are reported briefly in Appendix B.

1. FTC Estimates

The staff of the Bureau of Economics undertook its own study to measure the potential consumer savings from drug product selection.[2]

The next two sections of this report, "Nationwide Savings: 60 Drugs" and "32 Drugs," present the FTC studies in detail. The following sections present our review of the other eight studies.

a. Nationwide Savings: 60 Drugs

To estimate savings, an initial search was made among leading brand-name drugs to find those for which alternative sources of supply existed. From a dollar volume ranking of the leading 200 prescription drugs, we identified 60 multisource brand-name drugs. These 60 multisource brand-name drugs were distributed fairly evenly in terms of rank among the top 200. To get three different "generic" price proxies for these 60 drugs to compare with the brand-name price, we used: 1) the lowest price of all generic equivalents, 2) the price of Wolin's Pharmacal, a low-cost generic drug supplier, and 3) the unweighted average price of all equivalents to a brand-name drug, including the brand-name price itself.[3] 1974 wholesale price information was obtained from the Drug Topics Red Book[4] and the Wolin's Price catalog. By using these different proxies, we were able to estimate the range of

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2 These savings were estimated using the traditional "monopoly-loss" methodology, aspects of which are discussed technically in Appendix A.

The two type of benefits, transfer and welfare, were estimated from the following formulas:

$$TB = Q(P-C) \quad \text{---------} \quad (1)$$

$$WB = 1/2\ PQ\ nt^2 \quad \text{-----} \quad (2)$$

where P = monopoly price; Q = monopoly quantity; C = Marginal cost (also equals average cost); n = elasticity of demand; t = (P-C)/p

The model presumed a demand for each given brand-name drug (in essence presuming that this drug is an industry unique to itself). Marginal cost was assumed constant and defined to be represented by the price of a low-cost generic equivalent, following the example of Green; see James R. Green, "The Welfare Effects of an Antisubstitution Law in Pharmacy on the State of Oklahoma" unpublished Ph.D. dissertation, Oklahoma State University, 1972.

3 Weights were available for only one drug.

4 Drug Topics, Red Book (1974).

potential savings. We then derived prices per tablet.[5]

With these price data, unit price savings were calculated by subtracting in turn each of the three generic price proxies from the brand-name price. To complete the savings calculation these unit savings were multiplied by estimates of the number of brand-name tablets sold. To get this figure, we used 1967 data on the quantity of new and refill prescriptions and on the average prescription size. The use of 1967 quantity figures with relative 1974 prices introduces potential bias because the market success of individual drugs can change substantially over a period of seven years. If each drug experienced sales growth, then benefits will be underestimated. If the sales of some grew while others declined the net effect and direction of bias would be unclear. The use of catalog wholesale prices introduces a probable bias into the results as well by failing to account for special deal prices and discounts that manufacturers offer pharmacies from time to time. This bias is most difficult to measure. Deals and discounts vary from firm to firm, and change as market conditions warrant. For some firms, deals represent one shot promotions. For others, deals are offered more frequently.

By calculating and summing the savings for each of the 60 brand-name drugs we derived the annual totals presented in Tables 1 and 2. Sales of these drugs totaled about $460 million. Table 1 shows that the annual transfer benefit ranged from $208 million, if the averaged priced "generic" was selected, to $341 million, with the lowest priced generic. These savings are underestimated because they apply only to the multisource drugs found among the leading 200 drug products. Additional savings may be possible for those multisource brand-name drugs of lesser sales importance. The extent of this omission is difficult to measure from available data sources. A rough extrapolation suggests, however, that additional transfer benefits ranging from $38 million to $67 million are possible.[6] Added to the "60-drug" savings, potential transfer

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5 In selecting a price where different dosage forms, strengths, and package sizes were offered, the following procedures were followed: the most common dosage strength was chosen, only dosage forms involving pills, tablets, or capsules were used, and for different package sizes, the price of 500's, 100's and 1000's were used in that order of preference.

6 Estimating the proportion of multisource drug volume relevant to these analyses is difficult. Goldberg, et al., "Evaluation of Impact of Drug Substitution Legislation: A Report of the First Year's Experience," 17 J. Am. Pharm. Ass'n, April 1977, estimate multisource volume to be as much as 50 percent of total prescription volume in Michigan. Nationwide, IMS estimates multisource prescription volume to be about 33 percent.

(Footnote Continued)

benefits from all multisource drugs could then range from $246 million to $408 million.

Table 1: Potential One-Year Transfer Benefits (Consumer Savings) Assuming Product Selection at Three Alternative Prices[7]

Alternative Substitute	Transfer Benefits (TB) for 60 Brand-Name	TB as a proportion	Additional Transfer Benefits for Other Multisource Brand-Name	Total Transfer

6 (Footnote Continued)

But these estimates include sales of products marketed without a trademarked brand name and low-priced brand-name drugs, both of which are the potential low-price substitutes for the high-priced brand names. What is relevant is the sales volume of the high-priced brands against which the selection of lower-priced equivalent drugs is possible. Presumably, these drugs occupy a relatively higher proportion of sales among the leading 200 drugs than among drugs of lesser importance, because the latter will contain many brands that represent potential substitutes for a "leading" brand.

Estimates of the appropriate proportions require some arbitrary judgment. In 1971 sales of the 60 brand-name drugs were $459,112,493, or 25 percent of the leading 200 drug products' volume of $1.8 billion. For the remaining $0.9 billion of prescription drug sales (total sales were $2.7 billion in 1971), we assume 10 percent, or $90 million, is accounted for by sales of high-priced brands that are available on a multisource basis. Because a 25 percent weight would be a probable upper limit, we feel that 10 percent represents a conservative choice. Selection of this weighting procedure means that total sales of the high-priced multisource brands would be 20 percent of total prescription drug volume, 13 percentage points below the IMS estimate of the total multisource drug proportion.

7 To economists, these calculations represent attempts to measure the monopoly profits earned by the brand-name drug, profits that are potentially transferable to consumers if cheaper drug products are selected. See Appendix A for additional discussion of this measurement. The data base is such that these estimates necessarily exclude Alaska and Hawaii.

Prices	Drugs ($)	of Revenues[8] (%)	Drugs[9] ($)	Benefits ($)
Average Price of Equivalent Drugs	207,776,356	42.1	37,890,000	245,666,356
Wolin's Price	321,888,327	70.1	63,090,000	384,978,327
Lowest Price of Equivalent Drugs	341,315,761	74.3	66,870,000	408,185,761

In addition to measuring the transfer benefit of drug product selection, that is, the savings from buying the same drug at a reduced price, we also attempted to measure the welfare benefit derived from drug product selection for these 60 drugs. The welfare benefit is the net gain to society that results when a reduction in price causes consumers who previously were deterred from filling prescriptions by monopolistic high prices to now fill them. The net gain arises because consumers are now able to purchase and consume needed medications and because manufacturers can expand volume to meet the additional demand, yet still earn a reasonable return on their investment. Taken together, the transfer benefit and welfare benefit represent the total potential savings to consumers from drug product selection.

The welfare benefit is frequently not considered in estimating the benefits to be derived from drug product selection, in part, because it is a small segment of the total benefit (the proportion of unfilled prescriptions is thought to be relatively small) and, in part, because it is difficult to measure (an accurate measure of welfare benefit requires a clear knowledge of the total range of drug quantities that consumers would buy at different market prices). Nonetheless, to get as clear a picture as possible of the total benefit to be derived from drug product selection, our study attempts to estimate the welfare benefit.[10]

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8 Total revenues of the 60 brand-name drugs amounted to $459,112,493.

9 The calculation procedure for these figures is explained in note 6, supra.

10 More technically, estimating the welfare benefit requires knowledge of the demand function and of the price elasticity of demand. For the traditional monopoly model, with an assumed profit-maximizing firm facing a linear demand function,

(Footnote Continued)

The size of the welfare benefit depends upon the extent to which a prescription price reduction will increase the quantity of prescription drugs consumers demand. Economists refer to this relationship between changes in price and the quantity consumers demand as elasticity of demand. A low elasticity of demand (between 0 and 1) means price changes will not have much effect on the quantity demanded. Conversely a high elasticity (between 1 and infinity) means even small price changes will greatly affect the quantity consumers demand.

Unfortunately, the price elasticity for prescription drugs is not known. In arriving at a value for price elasticity, we presumed that the quantity of drugs purchased is relatively unresponsive to price changes. Hence we used a relatively low value (0.3) for price elasticity in calculating the welfare benefits. The resultant figures, which are additional to the transfer benefits of Table 1, are presented in Table 2. These welfare benefits represent the gains arising from filling prescriptions previously unfilled. The welfare benefit ranges from $30 million to $50 million.

As with the transfer benefits for the 60-drug sample, these welfare benefits are underestimated because of the exclusion of multisource brand-name drugs that rank below the leading 200 products in sales volume. A rough extrapolation indicates that additional welfare benefits ranging from $15 million to $25 million are possible. Total welfare benefits could then range from $37 million to $61 million.

To complete the process, all that remains is to add the transfer and welfare benefits together to get the total potential savings. This addition yields a range of potential savings from $283 million to $469 million.

Tables 1 and 2 estimate the nationwide benefit for just one year, assuming that equivalent drug products are selected for brand-name products whenever possible. The actual rate of product selection, however, depends upon the physician's willingness to

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10 (Footnote Continued)

a biased overestimate of welfare benefits is generated (see Appendix A for further discussion of this point). For this reason also, the focus of the analysis is upon the more substantial transfer benefit (so named because the price reductions from the erosion of monopoly power would constitute in effect a transfer of future income from the monopolist to consumers).

permit pharmacists to select products[11] and upon the pharmacist's propensity to select lower-cost generic equivalents.[12] If the probable "selection" rate is 50 percent, annual savings to consumers would range from $142 million to $234 million, under the Table 1 cost assumptions. If the selection rate is lower, say, at 25 percent, the range of savings would be halved.

Table 2: Potential One-Year Welfare Benefits Assuming Product Selection at Three Alternative Prices[13]

Alternative Substitute Prices	Welfare Benefits (WB) for 60 Brand-Name Drugs ($)	WB as a proportion of Revenues[14] (%)	Additional Welfare Benefits for Other Multisource Brand-Name Drugs[15] ($)	Total Welfare Benefits ($)

11 Surveys show that up to 38 percent of all physicians favor repeal of antisubstitution law. Thomas R. Sharpe, "The Economic Issues in the Antisubstitution Controversy," American Journal of Pharmacy (forthcoming).

12 Surveys of pharmacists indicate that as many as 66 percent favor repeal of the antisubstitution laws. Sharpe, id. at 3; Aldridge, Goldberg, DeVito, Moore & Vidis, "Profile of the Doubters: Pharmacists Who Doubt that Members of their Profession can Safely Select Among Drug Products," Unpublished paper presented at the Annual Meeting of the American Pharmaceutical Association, 1977, at 4.

13 To economists, these calculations represent an attempt to measure the deadweight monopoly-loss inherent in the loss of output to society from the presence of high monopolistic prices. See Appendix A for additional discussion of this concept. These estimates assume a price elasticity of demand of 0.3.

14 Total revenues of the 60 brand-name drugs amounted to $459,112,493.

15 The calculation procedure is described at note 6, supra.

Average Price of Equivalent Drugs	31,166,453	6.8	6,120,000	37,286,453
Wolin's Price	48,282,799	10.5	9,450,000	57,732,799
Lowest Price of Equivalent Drugs	51,206,364	11.2	10,080,000	61,286,364

b. Nationwide Savings: 32 Drugs

The above analysis of 60 drugs estimated considerable benefits from dispensing lower-cost equivalent products for those brands actually prescribed. A preferred data base, however, would be that for which all data were drawn from the same time period. Because the analysis used price and quantity data from different time periods, we also derived estimates using more current quantity data, but for fewer multisource drugs.

By screening the list of 60 multisource drugs for products that were among the market leaders in both 1975 and 1977, we attempted to gauge the sensitivity of the estimated benefits to change in a drug's market position over time. From the same list of 60 brand-name drugs, we found only 32 that were among the leading 200 products (in dollar volume) in 1975 and 1977. Using this sub-sample then, we estimated the quantity of tablets dispensed by multiplying the number of prescriptions in 1975 and 1977 by the average prescription size in 1967.[16] By multiplying the annual quantity figures for each brand-name drug by 1974 "brand-generic" price differences, we estimated transfer benefits for each of the two years.

Table 3 presents the potential savings (i.e., total transfer benefits) for 1975 and 1977. Focusing on 1977, the estimated savings for the 32 brands range from $136 million to $252 million

16 The only year for which data were available to the staff.

under two alternative price assumptions.[17] Extrapolation of these benefits to the universe of all prescription drugs is difficult for this period because we lack a figure for the proportion of multisource drug volume accounted for by high-priced brands for which selection of cheaper alternative products is possible. By employing a weighting procedure similar to that developed to derive the total benefits shown in Table 1 for an earlier period, we estimate that the total potential transfer benefits in 1977, for example, could range from $444 million to $817 million under alternative price assumptions.[18]

Table 3: Transfer Benefits for Multisource Brand-Name Drugs in 1975 and 1977, Assuming Product Selection at Alternative Prices[19]

Alternative Substitute	Transfer Benefits (TB) for 32 Brand-	TB as a percent of "32-Drug"	Total Transfer Benefits for Multi-source Brand-Name

17 Because the "brand-generic" price differences were assumed to be constant over time, the decline in the "32-Drug" benefits from 1975 to 1977 results from a 20 percent decrease in the total number of prescriptions (new and refill) for these sample drugs: from 299 million in 1975 to 191 million in 1977. Of course, if the "brand-generic" price differences have narrowed over time, the benefits are overestimated; conversely, underestimation will result if the price difference has widened. Also, if pharmacists' propensity to substitute is less than 1.0, as the Michigan experience indicates, the benefits must be adjusted downward.

18 These benefits are derived in accord with the weighting procedure explained in note 6, supra. Sales of high-priced multisource brands are assumed to be 25 percent of the leading 200 drug product sales and 10 percent of the remaining drug product sales. The savings rates shown in Table 3 were then applied to the estimated volume of "high-priced" brands. Relevant figures for these calculations are as follows: total prescription drug sales in 1975 = $4,636,810,000; total prescription drug sales in 1977 = $5,369,284,000; sales of the leading 200 drugs in 1975 = $3,170,748,000; and sales of the leading 200 drugs in 1977 = $3,916,384,000.

19 Wholesale catalog prices for 1974.

Year	Prices	Name Drugs ($)	Revenues[20] (%)	Drugs[21] ($)
1975	Average Price of Equivalent Drugs	165,534,770	39.7	372,899,400
	Lowest Price of Equivalent Drugs	301,711,774	72.4	680,048,277
1977	Average Price of Equivalent Drugs	136,731,229	39.5	444,132,470
	Lowest Price of Equivalent Drugs	251,801,545	72.7	817,428,622

c. State Savings Estimates

Because state laws govern drug product selection, we estimated potential savings for each state, for both the 60 and 32-drug samples, using as weights estimates of the number of prescriptions dispensed in each state in 1970.[22] By determining each state's proportion of the national totals, weights were derived and applied to the benefits presented in Table 1.

The Table 4 estimates of consumer savings in each state are based upon the 60-drug sample total benefit of $341 million. Savings range from $458,000, in Wyoming, to $31,491,000, in California.

Similarly, Table 5 estimates state benefits for the 32-drug sample and a nationwide savings total of $252 million. All state estimates presume selection of the lowest cost equivalent product.

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20 Estimated revenues for 1975 and 1977 were $416,836,959 and $346,571,237, respectively; 13.1 percent and 8.9 percent of the top 200 drug product volume in those years.

21 The calculation procedure is explained in note 18, supra.

22 J.F. Cady, Drugs on the Market 118-119 (1975). Weights based upon prescription dollar volume were highly correlated with the prescription weights.

Table 4: Estimated State Savings--60 Drug Sample

State	Savings[23] ($000's)
ALABAMA	5385
ARIZONA	2575
ARKANSAS	4186
CALIFORNIA	31491
COLORADO	4089
CONNECTICUT	5464
DELAWARE	701
DISTRICT OF COLUMBIA	2151
FLORIDA	12049
GEORGIA	7331
IDAHO	1518
ILLINOIS	21363
INDIANA	8760
IOWA	4404
KANSAS	4168
KENTUCKY	5341
LOUISIANA	6233
MAINE	1487
MARYLAND	5843
MASSACHUSETTS	10511
MICHIGAN	14049
MINNESOTA	6168
MISSISSIPPI	3826
MISSOURI	7984
MONTANA	581
NEBRASKA	2472
NEVADA	622
NEW HAMPSHIRE	1162
NEW JERSEY	11010
NEW MEXICO	1614
NEW YORK	27289
NORTH CAROLINA	11013
NORTH DAKOTA	1074
OHIO	16826
OKLAHOMA	4147
OREGON	3279
PENNSYLVANIA	19592
RHODE ISLAND	1894
SOUTH CAROLINA	4941
SOUTH DAKOTA	998
TENNESSEE	8035
TEXAS	21931
UTAH	1590
VERMONT	725

23 Savings of $512,000 for Alaska and $1,195,000 for Hawaii were estimated independently using 1970 population weights.

VIRGINIA	7977
WASHINGTON	4965
WEST VIRGINIA	3173
WISCONSIN	6548
WYOMING	458
TOTALS	341375

Table 5: Estimated State Savings--32 Drug Sample

State	Savings[24] ($000's)
ALABAMA	3972
ARIZONA	1899
ARKANSAS	3074
CALIFORNIA	23228
COLORADO	3016
CONNECTICUT	4030
DELAWARE	517
DISTRICT OF COLUMBIA	1586
FLORIDA	8888
GEORGIA	5407
IDAHO	1120
ILLINOIS	15758
INDIANA	6461
IOWA	3248
KANSAS	3074
KENTUCKY	3939
LOUISIANA	4598
MAINE	1097
MARYLAND	4310
MASSACHUSETTS	7753
MICHIGAN	10363
MINNESOTA	4550
MISSISSIPPI	2822
MISSOURI	5889
MONTANA	724
NEBRASKA	1823
NEVADA	459
NEW HAMPSHIRE	857
NEW JERSEY	8121
NEW MEXICO	1190
NEW YORK	20128
NORTH CAROLINA	8123
NORTH DAKOTA	792
OHIO	12411
OKLAHOMA	3059
OREGON	2419

24 Savings of $377,000 for Alaska and $881,000 for Hawaii were estimated from 1970 population weights.

PENNSYLVANIA	14451
RHODE ISLAND	1397
SOUTH CAROLINA	3644
SOUTH DAKOTA	736
TENNESSEE	5927
TEXAS	16176
UTAH	1173
VERMONT	535
VIRGINIA	5884
WASHINGTON	3662
WEST VIRGINIA	2340
WISCONSIN	4830
WYOMING	338
TOTALS	251801

2. HEW's 1968 Task Force on Prescription Drugs

In the mid 1960's the Department of Health, Education, and Welfare (HEW), concerned about the government's bill for drug reimbursement, formed a Task Force to investigate the cost of drugs dispensed to the elderly.[25] Of 409 frequently prescribed drugs, 63 were available at the time of the investigation from multiple sources. For these 63 drugs, the Task Force found that $41.5 million (6.1 percent of the drug program's cost) could be saved annually if lower-cost equivalent drugs had been dispensed.[26] These savings represented differences between the wholesale prices paid by pharmacists for brand-name and generic-name products.[27]

Public reaction to HEW's findings was mixed. The American Pharmaceutical Association (APhA), in its 1971 White Paper advocating repeal of the antisubstitution laws, responded favorably.[28] The Pharmaceutical Manufacturers Association (PMA), on the other hand, was critical and alleged that HEW overstated the savings by $15 million.[29] Even accepting these criticisms, the savings are

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25 U.S. Department of Health, Education, and Welfare, Task Force on Prescription Drugs, The Drug Users (1968).

26 Id. at 36.

27 The savings were based upon the volume of prescriptions dispensed and assumed a dispensing fee of $1.81.

28 American Pharmaceutical Association, "The Pharmacist's Role in Product Selection," 1971.

29 Pharmaceutical Manufacturers Association, "Review of Inaccuracies in Task Force Material Relating to 'Cost Savings' Allegedly Resulting from Generic Prescribing" (Mimeographed, undated).

(Footnote Continued)

considerable. Furthermore, these findings stimulated debate concerning drug costs and the relevance of state antisubstitution laws and were the critical force behind the recent establishment of HEW's Maximum Allowable Cost (MAC) program.

3. The MAC Plan and Estimated Savings

Established in 1976 to control rising expenditures, the MAC plan was designed to establish reimbursement prices for multisource drugs believed to be widely and consistently available.[30] Drug products are ranked by acquisition cost and the price of the product at the lowest end of the scale becomes the basis for reimbursement. Usually using HEW data, the states administer the program by determining the estimated acquisition costs (EAC's), and adding on an acceptable dispensing fee for the pharmacist to establish the MAC price. This price sets the maximum reimbursement a pharmacist can receive for filling a publicly funded prescription. The MAC plan is implemented on a drug-by-drug basis, however, and to date few drugs have been affected.

a. HEW Estimates

HEW estimates that Medicaid consumers alone would save $700,000 for the first MAC drug, ampicillin (see Tables 6 and 7).[31] If extrapolated to reach the entire market, the consumer savings would total almost $8 million annually on this drug alone: savings equivalent to about 32 percent of national sales of the two dosage

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29 (Footnote Continued)

The PMA criticism is also subject to challenge. For example, HEW alleges about $7 million in savings on a long-acting dosage form of pentaerythritol tetranitrate. Although PMA correctly points out that there is no other long-acting dosage form that could be substituted, it fails by implication to consider to what extent substantial savings could be achieved because more frequent consumption of a "short-acting dosage form might be a suitable substitute for the long-acting form."

30 See further discussion of the MAC program, Ch. VI.B., supra.

31 "Report on the Suitability of Ampicillin Trihydrate for MAC limits," Memorandum from Vincent R. Gardner to Dr. Mark Novitch, Executive Secretary, Pharmaceutical Reimbursement Board, Social Security Administration, U.S. Department of Health, Education, and Welfare, Sept. 10, 1976.

Table 6: HEW's MAC Savings on Ampicillin Trihydrate 250 mg Caps.

Ampicillin Trihydrate
250 mg caps

Brand	Company	Price per 100		Price per 500	Volume $(000) 100s	Volume $(000) 500s	Savings if MAC is set at $7.25/100 caps $(000)	
		Survey price	Redbook price				100s	500s
Polycillin	Bristol	*$18.74	$18.93	$92.30	$1901	$843	$105	$47
Alpen	Lederle	* 14.84	14.49		377		17	
Penbrittin	Ayerst	* 14.54	14.54	69.32	624	429	28	19
Pen-A	Pfizer	* 9.72	9.72		2204	1172	50	27
Amcill	Parke Davis	* 9.55	11.27		1263	749	27	16
Pensyn	Upjohn	* 8.06	13.69		245	192	2	2
SK-ampicillin	SKF	* 7.25	7.25		311	936		
Principen	Squibb	* 6.00	15.05	72.05	566	1792		
Ampi Co	Coastal		13.80		8			
Totacillin	Beecham		13.75	64.87	137	160	6	7
QID Amp	Mallinckrodt		12.75		19		1	
Amplin	Winston		12.50					
	Cenci		12.50					
	Stayner		12.50					
Ampifort	Fort David		10.65					
Amp-D	Daniels		9.60					
	Town, Paulson		8.15					
	Purepac		7.81	34.94	92	3		
	Premo		7.40					
	Columbia Medical		6.95	32.95				
	McKesson		6.85					
	United Research		6.75					
	Approved		6.50					
*Survey price					Total Savings		$236	$118
					Grand Total		$354	

Table 7: HEW's MAC Savings on Ampicillin Trihydrate 500 mg Caps.

Ampicillin Trihydrate
500 mg caps

Brand	Company	Price per 100		Price per 500	Volume $(000) 100s	Volume $(000) 500s	Savings if MAC is set at $11.90/100 caps $(000)	
		Survey price	Redbook price				100s	500s
Polycillin	Bristol	*$36.20	$36.52	$155.94	$1865	$346	$113	$21
Alpen	Lederle	* 24.63	28.25	103.84	248		12	
Amcill	Parke Davis	* 18.70	21.83	103.84	1263	749	41	25
Pen-A	Pfipharmecs	* 18.47	18.47		2792		89	
SK-ampicillin	SKF	* 13.90	13.90	62.55	444	680	6	9
Pensyn	Upjohn	* 13.08	24.10		276		2	
Ampicillin	Purepac	* 11.90	15.31		83			
Principen	Squibb	* 9.99	29.49	141.25	774	1133		
Ampi Co	Coastal		27.50		18		1	
Totacillin	Beecham		26.82	126.04		119		6
QID Amp	Mallinckrodt		24.63	116.75	13			1
Amplin	Winston		24.00					
Supen	Reid-Provident		23.90		70		3	
	Pharmecon		22.90					
	Cenci		22.16	70.45				
Ampifort	Fort David		20.50					
	Zenith		15.84					
	Premo		14.55					
	McKesson		13.75	66.95	6	9		
	Columbia Medical		13.50	64.40				
	United Research		12.90					
	West-Ward		12.40					
	Approved		12.10					
	Sherry		9.65	47.35				
Penbritten	Ayerst			134.94		469		24
	Generix			53.92				
*Survey price					Total Savings		$267	$86
					Grand Total		$353	

strengths examined.[32] The nationwide savings on one brand of ampicillin, Polycillin, amount to $3.2 million, 64 percent of a sales volume of $5 million. The HEW figures are slightly lower than those derived for this drug by the FTC. Using different data for approximately the same time period, FTC staff estimated savings of $5.3 million for 1975, an amount roughly 66 percent of estimated revenues of $8 million.

b. IMS Estimates

Another estimate of the potential savings from the MAC plan is provided by the PMA-sponsored IMS America, Ltd. (IMS) study. IMS is a private market research firm with considerable expertise in the gathering and analysis of prescription drug statistics. At the FTC's request, PMA supplied this study and other unpublished PMA-sponsored work that pertains to brand-generic price differences. Each of these will be discussed in turn.

Using 1973 drug purchase (wholesale-price) data gathered from pharmacies through nationwide sampling techniques, IMS estimated the Medicaid drug volume of 33 multisource drugs to be about $70 million.[33] By selecting the lowest-cost equivalent for each of the 33 drugs, the pharmacists' acquisition costs could be reduced an estimated $17 million per year, or 24 percent of the government's outlay on these drugs alone. For the sample drugs, Medicaid and non-Medicaid sales amounted to $594 million. If the benefits from designating a MAC price at the lowest cost level were to spill over and extend to the non-Medicaid market because pharmacists would stock and select the lower-cost alternatives, then the total market savings could amount to $142 million. Extrapolating the 24 percent savings rate to sales of multisource drugs (estimated to be $859 million) would mean potential savings of about $206 million.[34] This figure is close to the savings estimates by FTC

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32 Experience with a MAC-type plan in Ontario, Canada, has generated annual retail-price savings ranging from $2.5 to $10.5 million; see Allan E. Dyer, Ministry of Health, Ontario, "Implementation and Implications of Applying Drug Product Selection to Selected Populations," Paper presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978.

33 Letter from Stephen C. Chappell, Vice-President, IMS, to Armistead Lee, PMA, Oct. 7, 1974.

34 IMS estimated multisource dollar volume to be about 25 percent of all prescription drug sales (see the letter from Stephen C. Chappell to Armistead Lee, PMA, Aug. 30, 1974). In later years, they raised this estimate to about 33 percent. Only a proportion of all multisource drugs represent

(Footnote Continued)

Bureau of Economics staff for about 32 drugs using different data for about the same time period.[35]

The relative importance of these dollar savings depends upon the points of comparison. The savings are 24 percent of the Medicaid drug cost outlay for these 33 drugs, a reduction of considerable interest to the taxpayers who fund the Medicaid program through general tax revenues. Certain PMA staff note that these savings are only 3 percent of all Medicaid drug sales, including single-source drugs.[36] But single-source drugs should not be part of any savings estimate because neither MAC nor independent product selection by pharmacists can extend to single-source drugs.

Indeed, a PMA staff member recognized the impropriety of including single-source drugs in the base:

> To extrapolate the savings . . . to the universe of single and multisource drugs appears to me to lack logical statistical support. Everyone recognizes that a number of drug products are only available from a single source . . . to calculate the percentage savings on a universe, to which the savings is not applicable, is not normal statistical practice and appears to me to be an obvious attempt to play down the extent of legitimate savings.[37]

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34 (Footnote Continued)

high-priced brands against which drug product selection will produce benefits. Using the Table 1 weighting procedure for estimating benefits (see note 6, supra), we assume that 20 percent of total prescription drug sales, or $859 million, represents the relevant multisource volume. For these savings to be realized, one presumes bioequivalence among generic versions of each drug, a necessary ingredient of the MAC program. In this regard, eight of the 33 drugs presented potential bioequivalence problems.

35 Using quantity estimates for 1975 and Red Book catalog prices for 1974, the FTC estimated that total savings for 32 drugs could range from $166 million to $302 million. See Table 3.

36 Armistead Lee, PMA, "The Potential Saving from Generic Prescribing," Internal PMA staff Discussion Paper, Aug. 8, 1974, at 8.

37 Memorandum from R. Monteith to H. Binkley, Aug. 16, 1977, at 2-3.

The FTC, HEW, and IMS work discussed above used wholesale prices in estimating savings. We turn now to examine some studies that estimate savings based upon retail price data.

B. Savings Estimates from Retail-Price Information

In this section, five studies are reviewed; the first two of these were conducted by an independent research firm that applied the same methodology to data for two time periods, 1973 and 1976.

1. IMS Studies of Savings from Generic Prescribing-1973, 1976

In this PMA-sponsored effort, IMS attempted to identify the potential savings from generic prescribing. The first study involved 30 drugs using data for 1973; the second involved 37 drugs using 1976 data. These studies used retail figures based upon IMS' National Prescription Audit (NPA), which gathers data on prescriptions dispensed from a nationwide sample of retail pharmacies. Both studies attempted to determine the weighted brand to generic price ratio for equivalent generic items.

The brand price was derived by taking a weighted average of individual brand prices.[38] The generic price was that determined for prescriptions written by the established generic name. This latter price may be biased upward because pharmacists frequently dispense brand-name drugs at relatively high prices even when prescriptions are written generically.

This practice was noted by PMA:

> It is a well known fact that the IMS 'Generic Unspecified' category is a hybrid containing a large number of brand-name products which were dispensed for generically-written prescriptions. With the current low level of generic prescribing for many products, this is an understandable behavior for pharmacists.[39]

Only 12 percent of all prescriptions were written generically in 1977. Hence, pharmacists probably stock only the few popular brands of a given drug and when a generic prescription does permit the pharmacist to select the drug product, the choice will probably be for a brand priced higher than available lower-cost generics. Thus, the brand to generic price ratio derived by IMS is undoubtedly biased downward, and potential savings derived from this technique

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38 The number of prescriptions written for each brand was used as the appropriate weight.

39 Supra note 37, at 2.

will be underestimated. The extent of this distortion, however, is impossible to gauge. The results showed a brand-generic price ratio in 1973 of 110.62. For 1976, the brand-generic price ratio had greatly increased to 119.08. We will focus on the 1976 study, which used the same methodology and more recent data.

The 1976 study indicates that brand prescription prices are 19.08 percent higher than the prices of prescriptions written by the generic name of the drug.[40] IMS estimated that the potential savings to consumers, if the brand-name prescriptions had been written by the generic name, would amount to $323 million, a figure in line with FTC estimates that use wholesale-price data. Further estimating the retail dollar volume of all multisource drugs to be about $2,780 million,[41] IMS concluded that the potential savings would represent about 11.6 percent of all multisource brand-name prescription sales.[42]

IMS's procedure for deriving a brand/generic price index was to construct a price index for prescriptions written by brand names and divide it by a price index of prescriptions written by the generic name of the same drug. An alternative indexing procedure discussed by PMA staff compares a brand price index, an index that assumes that all prescriptions had been written by brand name, with a generic price index, one that assumes all prescriptions are written by the generic name and results in a lower brand-generic price ratio of 115.4. But the IMS index of 119.08 is the more relevant measure. The salient factor in arriving at drug product selection benefits is the savings that would be realized by replacing prescriptions currently being written by brand name with prescriptions written by generic name.

We will now consider studies measuring the effect of a change in a state's law concerning drug product selection on drug prices in that state. Two studies of Michigan, and one of Delaware will be reviewed. An IMS study of Michigan, contracted by the PMA, will be considered first.

2. IMS Study of Savings from Drug Product Selection in Michigan

The PMA sponsored an IMS study of the effects of the Michigan drug product selection law. From the information submitted to the

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40 Conversely, under generic prescription writing, consumers would have paid about 83 percent (100 divided by 119.08) of the brand price, thereby saving 17 percent.

41 About 33 percent of total retail prescription dollars.

42 IMS, Untitled Report to PMA on Brand-Generic Prescribing, 1977.

FTC, the study methodology is not clear. Consequently, the results cannot be evaluated fully. The aim of the study, however, was to assess before and after prices in Michigan on a small sample of products, and compare these changes with national price trends for these drugs. Prescription prices for ten drugs were sampled from about 70 retail stores in Michigan before and after the law was modified. The base-line period covered three months, November 1974 - January 1975. The post-repeal period covered three months, June - August 1975. The results suggested that the change in the law caused drug prices to increase less in Michigan than in the rest of the country. In its preliminary figures submitted to the PMA, IMS staff noted, "These tables do suggest that the Michigan law is exerting some downward pressure on price increases in that state."[43] And again, in transmitting follow-up data about one month later, the research director wrote, "As you can see, the trend shown in the preliminary tables holds up; the change in the law is having a definite dampening effect on price rises in Michigan."[44]

PMA staff questioned whether a price effect of this kind could ensue if drug product selection were occurring at only a three percent rate, and also questioned whether sample sizes from both Michigan and the nation were such that valid comparisons could be made.[45] Without more information, we cannot tell whether this appraisal is based upon appropriate scientific evaluation of the study. However, a later, more extensive study of the Michigan experience complements the results of the IMS study.

3. Savings from Substitution in Michigan: The Goldberg Study

Working with a large grant from HEW, a group of scholars at Wayne State University, led by Theodore Goldberg, studied the price effects of the Michigan law change. Details of this study are available in various papers.[46] Briefly, the research team gathered

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43 Letter from Lynn A. Downing, Director, Lea-Mendota Research Group of IMS, to Mr. William Patton, PMA, Oct. 30, 1975.

44 Letter from Lynn A. Downing, Director, Lea-Mendota Research Group of IMS, to Mr. William Patton, PMA, Nov. 20, 1975.

45 See Memorandum from Armistead Lee to Bruce Brennan, Nov. 7, 1975; Memorandum from Mr. Russo to Mr. Brennan, Feb. 17, 1976.

46 See Theodore Goldberg, "Cost Implications of Drug Product Selection Legislation," Paper presented at the Invitational Dissemination Workshop on Drug Product Selection, Detroit, Michigan, Apr. 13-14, 1978; Goldberg, Aldridge, DeVito, Vidis,
(Footnote Continued)

data on about 150,000 retail prescription prices for a three-year period. Pharmacies were sampled using a multistage, stratified cluster process (factors such as size, ownership, type of store, and geographic location were selection variables).

To determine whether savings accrued from substitution, a "prescription matching" technique was employed. The retail price of an actual substituted prescription was matched with the retail price of a randomly selected comparable prescription for any brand of the same chemical entity. Prescriptions were matched within each dispensing pharmacy and across pharmacies. Data were gathered for the year prior to the change in the law and for two successive years, during which product selection was permitted. The average price of selected generics was about 20 percent lower than the average price of the prescribed brand matched. Using these price data, the researchers estimated that annual savings to consumers in Michigan from substitution could range from $11,730,000 to $15,295,000 on new prescriptions alone if product selection occurred whenever possible.[47] The exclusion of refill prescriptions from these calculations means that these savings estimates are biased downward. Savings are also possible on prescriptions written generically, because the lower-cost products may not be dispensed despite the opportunity to select them. Adding the potential savings from generic prescriptions is estimated to raise the total potential savings on new prescriptions to between $13,538,000 and $17,647,800.[48]

In both the first and second years following the law change, only about 1.5 percent of prescriptions for multiple source drugs

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46 (Footnote Continued)

Moore,& Dickson, "Impact of Drug Substitution Legislation: A Report of the First Year's Experience," 17 J. Am. Pharmaceutical Ass'n, April 1977, at 216-226; Goldberg, Moore, Koontz, Facione, Aldridge, Vidis, Vadasy,& Jones, "Evaluation of Impact of Drug Substitution Legislation," 16 J. Am. Pharmaceutical Ass'n, February 1976, at 64-70, 90; David Smith and Gerald Aldridge, "Probability Sampling of Prescription Order Forms," Paper presented at the Annual Meeting of the American Pharmaceutical Association in New York, May 17, 1977; Carolee A. DeVito, "Issues and Alternatives Involved in Achieving Maximum Public Benefit," Paper presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978.

47 Theodore Goldberg, "Cost Implications of Drug Product Selection Legislation," id. at 18.

48 Id. at 18.

were substituted. Estimating the volume of new prescriptions dispensed in Michigan to be between 26 and 34 million annually, the study concluded the actual savings being realized were between $200,000 and $300,000, far short of the full potential.

The Goldberg research upon the effects of a modification of a state's law indicates that savings do result from substitution and at a full potential are considerable. If the same savings potential per prescription is possible throughout the country, calculations suggest that the total savings nationwide may indeed be large, ranging from $260 million to $450 million. Although these estimates are derived from a simple extrapolation, the figures are in line with estimates derived from procedures described earlier.[49] For example, IMS's 1976 study for the PMA estimated savings from generic prescribing of $323 million in retail dollars, and this figure may well be biased downward.

4. Savings from Drug Product Selection in Delaware: The Fink Study

At the request of the state of Delaware, Professor Joseph L. Fink III,[50] studied the impact of the Delaware product selection law. The object of the study was to gather prescription price data from a sample of Delaware pharmacies prior and subsequent to the act, and to estimate resultant savings, if any, for 12 frequently prescribed multisource drugs. Drug product selection became possible on December 22, 1976, and base-line data were gathered for the period September 1, 1976 to December 20, 1976. The "after" data were gathered for the period October 1, 1977 to December 1, 1977. The study found statistically significant savings for seven

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49 The figures are derived as follows: Multisource new prescription volume in Michigan ranges from 13.1 to 17 million (from Goldberg). Nationwide, the number of multisource new prescriptions for 1976 (at the 51 percent rate estimated by Goldberg for Michigan) is 382 million. Michigan, then, represents between 3.4 and 4.5 percent of the national total. These proportions are in line with drug store sales and population proportions: 4.1 percent (from Cady's data), and 4.4 percent, respectively. Goldberg, supra note 46, at 18, estimates that potential savings in Michigan range from $11.7 to $15.3 million. Dividing by 0.034 and 0.045, to establish range limits, the potential savings estimates for the nation, based upon the Michigan data lie between $260 million and $450 million.

50 Joseph L. Fink, III, "A Study of Savings Resulting from Passage of the Delaware Product Selection Act," A Report to the Pharmacy Control Office of the Division of Public Health for the State of Delaware, January 1978.

drugs, ranging from 2.7 to 13.2 cents per dosage unit (tablet or capsule, for example). These savings ranged from 32.9 to 64.1 percent of the drug retail prices charged when pharmacist product selection did not occur. For three other drugs, average retail prices were lower for "selected" drugs, but the differences were not statistically significant. For the remaining two drugs, all prescriptions were written generically and did not provide data useful to the study. Extrapolation of these findings into an aggregate dollar benefit for all multisource drugs is not possible. The findings, however, further support the assertion that benefits do accrue from drug product selection and may represent a substantial proportion of actual consumer outlays.

A number of other studies have implications for the potential savings from drug product selection. These are presented briefly in Appendix B.

C. Conclusion

The various studies, though different in methodology and scope, provide a clear message: the potential for the realization of consumer savings is substantial. This potential has not been overlooked by these studies and by state actions taken to modify constraints against drug product selection. The federal government, conscious of potential savings, has intervened, through the implementation of the MAC plan, to attempt to realize savings on Medicaid reimbursements. By contrast with direct intervention of this kind, removal of legal constraints against drug product selection offers a policy alternative wherein market forces are given the opportunity to generate savings without associated regulatory costs. The consumer benefits to be realized speaks persuasively for the repeal of restrictive antisubstitution laws.

CHAPTER IX. COUNTERING ALLEGED DISADVANTAGES OF DRUG PRODUCT SELECTION

This Report has thus far documented that drug product selection offers significant benefits to consumers of prescription drugs. Busy physicians are primarily concerned with diagnosing the patient's condition and determining which drug, if any, will improve it. Most physicians do not know the prices of competing sources of a particular drug, and generally prescribe by easy-to-remember, heavily-promoted brand names (Ch. II. and Ch. III., supra). Pharmacists are well qualified to select drug sources efficiently and have economic incentives to do so (Ch. IV., supra). If antisubstitution laws were replaced by drug product selection laws allowing pharmacists to select low-cost therapeutically equivalent products in lieu of the more expensive brands prescribed, consumers potentially could save $400 to $500 million a year (Ch. VIII., supra). Moreover, FDA extensively regulates bioavailability and other measures of product equivalence to assure the quality of marketed drug products (Ch. VI., supra).

This Chapter will now discuss the major arguments raised by opponents of drug product selection.

A. Will Drug Product Selection Reduce Research and Development Efforts by Manufacturers?

The impact of existing governmental policies upon pharmaceutical innovation centers around a trade-off between fostering innovation and increasing competition. Economist William Comanor described the problem in the following way:

> The issue of public policy with regard to the drug industry is concerned precisely with the existence of a trade-off between high levels of research and high prices at one end of the spectrum and low research and prices at the other. If patents, trademarks and advertising were not permitted, I think most of us would agree that drug prices would be much lower. At the same time, little research would be carried on. And if we had a patent system which permitted a hundred year restriction on competition rather than the current figure of 17 years, more research would probably be carried on. At the same time, prices would be even higher than they are currently. The interesting question then is what combination of research and prices is optimal given

that neither extreme is optimal?[1]

Acknowledging this trade-off between prices and research[2] we undertook to estimate what impact, if any, the lower prices resulting from drug product selection might have on drug research. The first part of this section examines whether the modification of antisubstitution laws would be likely to lower significantly the expected rate of return on drug research. To answer this question we asked the major brand-name drug manufacturers for their views and consulted with economists from the academic community for their evaluations. On the whole, the answers were mixed; some companies expressed general fears that the repeal of antisubstitution laws would lower the profitability of research, others doubted it would have an impact. Similarly the consulting economists envisioned some reduction in profitability, but differed in the extent to which this would occur; their estimates varied from a negligible effect to a 10 percent reduction in profitability.

The second part of this section explores what effect reduced profitability arising from drug product selection might have on drug research. Whether the value to society of any foregone research that might result would outweigh the savings from lower drug prices is an empirical question that no one will be able to answer until effective product selection laws are passed in a substantial number of states and their effects studied. This section concludes, nonetheless, that antisubstitution laws are an

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1 Cited in The Economics of Drug Innovation (J.D. Cooper ed. 1969), at 225. Professor Comanor is now Director of the FTC's Bureau of Economics. At the time of this statement he was Professor of Economics at Harvard University.

2 Professor Jadlow describes the correlation between R & D profits as follows:

> If public policy, such as repeal of state antisubstitution laws causes the expected net income from the produoduct to be reduced for certain years, ceteris paribus, the expected present value for the project is lowered and the firm's incentive to to the research is reduced.

Jadlow, "The Effects on Research Incentives of Eliminating Drug Antisubstitution Laws," Mar. 1, 1978, at 25, (Paper presented to FTC). See also Grabowski & Vernon, "The Effect of Repealing Anti-Substitution Laws on Pharmaceutical Innovation," Mar. 5, 1978, at 1, 36 (Paper presented to FTC).

inefficient and excessively costly way to foster drug innovation. If drug research needs additional fostering, there are a number of ways (government grants, patent extension, etc.) to accomplish this without preserving antiquated antisubstitution laws. One more efficient way, for example, would be to change the patent laws. But amending the patent laws is properly the concern of Congress, not the states nor the FTC. Altering patent protection as it applies to the drug industry could address the need for stimulating drug research without, as we shall see, foregoing the benefits from lower prescription prices on existing drugs. We conclude, therefore, that any likely impact on R & D does not undercut the case for product selection laws.

1. Views of Industry

We asked several leading pharmaceutical firms to assess the impact of drug product selection laws upon, among other things, their R & D efforts. All firms indicated that so far the laws permitting product selection have had no impact upon their research activities.[3] This response may be because many of these laws have not been in effect long enough to have any discernible impact upon R & D. American Home Products Corp., for example, prefaced its remarks by cautioning that it is very difficult at this time to assess the likely effects of these laws on its operations.[4]

One firm, E. R. Squibb, Inc., stated that it did not antici-

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3 Letter from Charles F. Hagan, General Counsel, American Home Products Corp. to Peter D. Holmes, FTC, June 8, 1978; Letter from John M. Cullen, Attorney, Smith Kline Corp., to Peter D. Holmes, FTC, Feb. 16, 1978; Letter from D.S. Brooks, Counsel, Merck, Sharp & Dohme to Peter D. Holmes, FTC, Feb. 23, 1978; Letter from Hugh A. D'Andrade, Vice President--Administration and Counsel, Pharmaceuticals Division, Ciba-Geigy Corp., to Peter D. Holmes, FTC, Apr. 6, 1978; Letter from David M. Winer, Senior Attorney, Hoffmann-LaRoche, Inc., to Peter D. Holmes, FTC, Mar. 22, 1978; Letter from R.O. Clutter, Assistant General Counsel, Eli Lilly and Co., to Peter D. Holmes, FTC, Apr. 25, 1978; Letter from Robert C. Johnston, Assistant General Counsel, E. R. Squibb, Inc., to Peter D. Holmes, FTC, Mar. 31, 1978.

4 Letter from Charles F. Hagan, supra note 3. Smith Kline Corp. commented:

> It is too difficult at this time to predict the effect of such legislation on the proportion of resources allocated to research and development until the overall effectiveness of such legislation is ascertained.

pate any changes in its R & D and marketing activities under drug product selection.[5]

Three firms, Eli Lilly & Co., Merck & Co., Inc., and Hoffmann-LaRoche Inc., expressed general fears regarding the future impact of changes in state product selection laws on their company's R & D efforts.[6] But these firms did no more than conclude that widespread drug product selection might result in less innovation because of the expectation that it would decrease the rate of return from innovation.

Eli Lilly urged that the impact of the drug product selection policy proposal be considered in the context of other regulatory policies. It noted that "repeal of antisubstitution laws has regulatory implications when thought of as changing the environment upon which the current institutional structure of the pharmaceutical industry is based."[7] The company maintained that permitting product selection would reduce R & D "by limiting the sales of existing drug products and cause research decisions to be based on even higher anticipated risk (and an expected lower rate of return) than currently is the case."[8] Lilly argued that drug product selection would reduce cash flows that are used to finance R & D.[9]

Similarly, Merck and Co. asserted "that product selection will have a significant adverse impact on future innovative research and development," particularly "high risk research and the development of important therapeutic products which have limited markets."[10]

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5 Letter from Robert C. Johnston, supra note 3.

6 Letters from R.O. Clutter, D.S. Brooks, and David M. Winer, supra note 3.

7 Eli Lilly and Co., "Comments on Federal Trade Commission Drug Substitution Inquiry," April 1978, at 21 (submission to FTC).

8 Id. at 22.

9 Id. at 21.

10 Letter from D. S. Brooks, supra note 3. The effort to get approval for a new epilepsy-control drug, sodium valproate, (Depakene) illustrates, among other things, the problem of developing interest on the part of manufacturers to market drugs having limited commercial value. Wall Street Journal, Mar. 1, 1978, at 4. The proposed Drug Regulation Reform Act of 1978 would have authorized a National Center for Clinical Pharmacology to conduct and support research of drug products for diseases of low incidence. See H.R. 11611, 95th Cong., 2d Sess., § 1802(a).

Drug product selection laws, according to Merck, "encourage manufacturers to reduce costs at the expense of funding desirable research."[11] The trade-off as perceived by Merck should be as follows:

> What is clearly necessary is a balance between the perceived short-term economic needs of the consumer and the long-term benefits of fostering an atmosphere in which research can flourish--and we submit that substitution laws do not represent such a balance.[12]

Lastly, Hoffmann-LaRoche indicated that product selection could create further disincentives "for continued investment in new product development":

> The cost of new product development has markedly increased over the years, currently averaging tens of millions of dollars per new chemical entity. The added development time required to bring new chemical entities to market from the time of discovery has effectively reduced the period of patent protection for commercial products. There is a significant risk that research-oriented firms will be discouraged from committing significant resources toward new products if substitution could further significantly erode return on this investment.[13]

These comments by Lilly, Merck, and Hoffmann-LaRoche imply that the repeal of the antisubstitution laws would reduce research activity, and, therefore, the rate of new drug innovation. Indeed, one can interpret their remarks as suggesting that the losses would exceed the gains from lower prices. But their views are simply general impressions, and we must turn elsewhere for quantitative projections. Consequently, we now consider the findings of four economists who were commissioned to address this question.

2. Views of Four Economists

Because of the dearth of research on this question, we asked four economists with different views on the economics of the drug

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11 Letter from D. S. Brooks, supra note 3.

12 Id.

13 Letter from David M. Winer, supra note 3.

industry to estimate the possible effect of the repeal of anti-substitution laws upon new drug innovation. The economists, Leonard G. Schifrin, College of William and Mary, Joseph M. Jadlow, Oklahoma State University, and a team made up of Henry G. Grabowski and John M. Vernon, Duke University, all have written extensively on the pharmaceutical manufacturing industry. Their three estimates of the possible impact upon R & D are described below.

Schifrin concluded that the likely impact on R & D is outweighed by the anticipated savings to consumers. Developing a model using three different estimates of the projected market growth of multisource drugs, Schifrin estimated that manufacturers could suffer revenue losses by 1984 of 4.08 percent to 11.04 percent a year if price competition from multisource drugs increased. The corresponding revenue losses, which equal the "consumer savings," ranged from an estimated $524 million to $2376 million. Schifrin also calculated that .6 to 1.7 fewer new single chemical entities (compounds not previously known or marketed)[14] might be introduced each year out of an annual average of 15. He concluded that this loss is not "too high a cost to incur for consumer savings that range from $524 million to $2376 million per year." The foregone new drugs presumably "will be those that offer less commercial pay-off . . . [and] are of less societal importance than those that come into the marketplace."[15] Schifrin qualified this statement, however, by noting that any reduction in R & D "also means less basic R & D and thus drugs of great commercial and therapeutic value may be among those lost."[16]

The estimates of Jadlow, and Grabowski and Vernon rely on a model developed by economist David Schwartzman to estimate the expected rate of return on pharmaceutical R & D. Schwartzman's model estimates the present value to the firm of profits that may be received in the future from an investment made today. The present value, which is determined by discounting expected future earnings, is crucial to the decision to invest. As Jadlow states,

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14 See Paul de Haen, "New Products Parade 1975, Annual Review of New Drugs," February 1976; H. Grabowski, Drug Regulation and Innovation 17 (1976), Kennedy, "A Calm Look at 'Drug Lag'", 239 J. Am. Med. Ass'n, 423 (1978); and Wardell, "A Close Inspection of the 'Calm Look', Rhetorical Amblyopia and Selective Amnesia at the Food and Drug Administration," 239 J. Am. Med. Ass'n 2004, 2007 (1978).

15 Schifrin, "The Effect of Repeal of Retail Anti-Substitution Laws on Drug Research and Development and New Drug Innovation," Feb. 28, 1978, at 19 (Paper presented to FTC).

16 Id.

"[p]ublic policy which raises or lowers the present value of individual research projects could in some instances have an effect on whether firms decide to undertake these projects."[17] Schwartzman estimated the expected rate of return after taxes for a new drug to be 3.3 percent.[18] He assumed that the average new drug had a commercial life of 15 years and earned a gross profit margin of 15.4 percent (after taxes). Applying alternative assumptions to Schwartzman's model, Jadlow, and Grabowski and Vernon sought to determine whether the rate of return would be reduced by increasing product selection.

Jadlow estimated that drug product selection will have only a negligible impact on drug research. Using Schwartzman's model, Jadlow estimated the profits which would be lost to an innovating firm because of increased drug product selection.[19] He adopted many of Schwartzman's assumptions for the average new chemical entity (NCE), including an R & D period of 10 years, and an average commercial life of 15 years.[20] Jadlow also followed Schwartzman's assumed income pattern: income rises the first 2 years an NCE is on the market; then levels off and remains constant for the next 11 years; and finally declines the last 2 years of commercial life.[21]

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17 Jadlow, supra note 2, at 24.

18 Schwartzman, The Expected Return from Pharmaceutical Research: Sources of New Drugs and the Profitability of R & D Investment 36 (1975).

19 Jadlow, supra note 2, at 25.

20 Id. at 26-28. This leaves a commercial life after patent expiration of 2 years. If the commercial life of an NCE is 15 years and its "effective" patent life is 13 years, the innovator will continue to earn profits on an NCE for 2 years after its patent expires. Thus, under Jadlow's analysis the profits in the final 2 years of product life are the ones most threatened by increased substitution. Jadlow's estimates thus attempt to determine "the relative importance to a firm of the final two years of expected profits of an NCE." Id. at 28.

21 Id. at 27-31.

> The slow initial rise in profits is because of nonrecurring promotional and other introductory costs, and because it takes time for physicians to become informed about a new drug and begin to prescribe it.

Id. at 31.

The only major adjustment made by Jadlow to Schwartzman's model was to use a higher net profit margin--25.6 percent after taxes--in his calculations.[22] He found that increased drug product selection would eliminate less than 4 percent of the present value of the expected stream of profits from an average NCE, an amount Jadlow describes as "trivial."[23] He concluded his analysis by stating:

> The elimination of antisubstitution laws would have only negligible effects on drug research incentives and little or no effect on the rate of introduction of new chemical entities.[24]

Grabowski and Vernon also relied on the basic Schwartzman model, but they conclude product selection may have "non-negligible effects"[25] on drug research profitability. To assess the impact of increased substitution on the incentive to conduct research and development, they focused on the expected rate of return. Grabowski and Vernon did not address the level of the rate of return, instead they focused on changes (or sensitivity) in the rate of return caused by increased substitution. Unlike Jadlow, however, Grabowski and Vernon used an alternative version of Schwartzman's model which assumes a 20-year commercial life

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22 To estimate the average profit margins on new chemical entities, Schwartzman used overall company profit margins. But overall company profits also reflect profit margins earned by a company on older products (some of which do not have patent protection). The profit margins on these older drugs usually are lower than the margins earned on NCE's still having patent protection. "Therefore, Schwartzman's procedure of applying the average company profit margin to NCE's [rather than applying the average profit margins for NCE's alone] seems likely to understate the true profit margins of these drugs." Consequently, according to Jadlow, Schwartzman's net income estimates for an average NCE are too low. Jadlow believes that a more realistic net profit margin for NCE's is 25.6% (30.8% gross profit margin) twice as high as that calculated by Schwartzman 12.8% (15.4% gross profit margin). Jadlow, supra note 2, at 36. See also Grabowski, supra note 14, at 42.

23 Jadlow, supra note 2, at 42.

24 Id. at 43. Jadlow surmises that the reduced research incentives "would only be expected to cause research projects which were marginally profitable (before repeal) not to be attempted." Id. at 44.

25 Grabowski & Vernon, supra note 2, at 41, 44.

(instead of 15 years). With a 20 percent (after taxes) gross profit margin, this version produces a 7.5 percent expected rate of return. They believe that these assumptions are more realistic for conditions that prevail in the drug industry today.[26] Grabowski and Vernon then tested the sensitivity of the 7.5 percent return to increasing drug product selection[27] by reducing the net income in the year the patent expires and succeeding years to reflect the reduction in net income from drug product selection.

With a 7.5 percent rate of return as the standard of comparison, Grabowski and Vernon calculated for what they believe to be the most plausible case (one which assumed a 30 percent reduction in post-patent net income [cash flow] from lower sales caused by substitution and a 12-year patent life), a 6.7% return.[28] They

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26 Schwartzman's "best estimate" of a 3.3% (after-tax) expected rate of return was based on product life of 15 years and a gross profit margin of 15.4% (after-tax). Grabowski and Vernon agree with Jadlow that Schwartzman's profit margin was too low; that a more realistic alternative would allow for much higher values on profit margins and product lives. So they chose an alternative version of Schwartzman's model which uses more "optimistic" data. Specifically, they believe that a commercial life of 20 years and a gross profit margin of 20% (after-tax) are more reasonable. Using these assumptions results in a 7.5% (after-tax) expected rate of return, which is much higher than Schwartzman's best estimate, but still "a relatively low rate of return." In comparison to Jadlow, Grabowski and Vernon use a longer commercial life assumption (20 years vs. 15 years), but a lower gross profit margin assumption (20% vs. 30.8%) in their model.

Telephone interview between Henry G. Grabowski and John Vernon, Duke University, and Robert Zwirb and Peter Pitsch, FTC, June 21, 1978. See also Grabowski & Vernon, supra note 2, at 11-12, 37.

27 "That is to say, if repealing anti-substitution laws brings about a 30% reduction in sales of new drug after patent expiration, is the 7.5% return reduced by half or it is [sic] basically unaffected?" Grabowski and Vernon, supra note 2, at 37.

28 Id. at 40, 41. The 7.5 return corresponds to a 0% reduction in net income. Alternative rates of return for alternative percentage reductions in net income and alternative patent lifes are:

(Footnote Continued)

estimated that this ten percent reduction in the rate of return would reduce industry R & D expenditures by $46 million from a total domestic R & D budget of $900 million.[29] Grabowski and Vernon concluded that this reduction "is certainly not negligible and, other things held constant, may be expected to make some R & D projects no longer attractive to pharmaceutical manufacturers."[30]

All three models are based on a chain of assumptions that raise some questions. Schifrin, for example, stated that only about 20 percent of the 200 most widely used products are multi-

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28 (Footnote Continued)

Percentage Reduction in Net Income Stream	Patent Life 10 Years	12 Years	17 Years
-10	7.1	7.2	7.4
-30	6.4	6.7	7.2
-50	5.6	6.1	7.1

Notes: (1) The standard against which the above rates should be compared is a 7.5% return. This is Schwartzman's result for a 20-year commercial life and a 20% margin.

(2) It is assumed that at the end of patent life, repealing antisubstitution laws will result in alternative reductions in net income given above for the remaining years of the 20-year commercial life.

(3) The net income referred to is not that which the lay man is accustomed to. It includes profits plus R & D expenditures less the cost of financing working capital and plant and equipment after adjustment for taxes. See Schwartzman, supra note 18, at 32.

29 Id. at 42. Grabowski and Vernon estimate total industry domestic sales to be $8 billion, half of which are from multisource drugs. Substitution would reduce sales of multisource drugs by 10 percent or $400 million (10% of $4 billion). They estimate the R & D-to-sales ratio to be 11.5% and apply it to the $400 million reduced sales figure to obtain $46 million in reduced R & D expenditures. PMA estimates that its total domestic R & D budget for human-use pharmaceuticals in 1976 was $902.9 million. Pharmaceutical Manufacturers Association, Annual Survey Report, 1976-77 17 (1977). (See Ch.II.B.2., supra).

30 Id. at 41.

source.[31] Reliance on this low estimate[32] similarly lowers the share of the market affected by product selection and therefore understates the revenues subject to future losses. It should be noted, however, that Schifrin's estimate of consumer savings is already very large, so that this weakness does not undercut his conclusion that the value of the possible loss in innovation is outweighed by benefits to consumers. Jadlow relied on a 35 percent estimate for multisource market share, which is still lower than the actual percentage.[33] He further assumed that elimination of antisubstitution laws would "cause only a relatively small increase in substitution."[34] If this latter assumption is wrong, Jadlow's estimate of the drug sales that might be affected by drug product selection may be too low. The accuracy of Grabowski and Vernon's conclusions, on the other hand, turns partly on their assumption of a 20-year commercial life. Had they used a 15-year life-cycle, their results would more clearly approximate Jadlow's. There is, however, no precise data available on the commercial life of an average NCE, although it is often thought to be increasing as fewer new drugs enter the market each year. Whether Grabowski and Vernon's estimate of 20 years is more realistic than Jadlow's 15 years is an open question, although there are other estimates suggesting that a 20-year life may not be unrealistic.[35]

To sum up, our inquiry on the impact of repeal of antisubstitution laws on the profitability of R & D was based on the views of some members of the industry and those of four economists familiar with the industry. Some manufacturers anticipated little or no

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31 Schifrin, supra note 15, at 7.

32 IMS America, Ltd., "A Study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs" Final Report Submitted to Federal Trade Commission, July 28, 1978, at 3, estimates that for the 200 drugs most frequently prescribed in 1977, 54% of all prescriptions are written for multisource drugs.

33 See IMS, id.

34 Jadlow, supra note 2, at 41. Substitution would not increase significantly, according to Jadlow, because 1) many pharmacists are unwilling to substitute and 2) many of those pharmacists who do favor substitution already substitute even where it is illegal.

35 One study of the actual sales histories for a large number of drugs concluded, "[a]ny drug product that was economically significant exhibited a lifetime of at least fifteen years, possibly considerably longer." Stauffer, "Profitability Measures in the Pharmaceutical Industry," in Drug Development and Marketing 108 (R.B. Helms.ed. 1975).

D, while others expressed a general fear that repeal would reduce the profitability of R & D. The economists predicted some effect, but differed on its significance. Two of the analyses concluded that the potential adverse effects on R & D would be minimal, while the third predicted they would be "non-negligible."

3. "Worst Case" Analysis and Conclusion

Certainly, antisubstitution laws are one form of regulation that is beneficial to the large research-oriented portion of the industry. Removal of such protection absent any offsetting regulatory changes should reduce the anticipated profits available for R & D by, for example, increasing the risks to which research-oriented firms are subjected. There are, however, no studies that assess the role these laws play in the R & D process. The three analyses we obtained indicate that some negative impact upon R & D might result from removal of these laws, but only one concluded that the impact would significantly lower the industry's expected rate of return on R & D.

Moreover, antisubstitution laws are only one of a number of forces that influence pharmaceutical innovation, and "it would be wrong," warn Grabowski and Vernon, "to consider the impact of removal of these laws 'in isolation'." In other words, antisubstitution laws interact with other governmental policies as well as economic and marketing forces that make cost/benefit calculations imprecise at best.

Consequently, even if the expected rate of return on drug research fell by about 10 percent, the highest estimate, we do not know the extent to which this might reduce innovation. Furthermore, a reduction in research and development is not necessarily socially harmful. That would be the case only if the patent system and regulatory environment -- after drug product selection is in effect -- provide an insufficient return on R & D. Otherwise, adequate resources would continue to be attracted to drug research. Further, the least financially attractive projects would presumably be the first to be cut. Finally, even if some socially desirable R & D would be lost, it is entirely possible that the loss would be outweighed by the savings to consumers from reduced prescription prices.

In the worst possible case, drug product selection could eliminate some socially beneficial R & D. We recommend, nevertheless, that states modify their antisustitution laws for two fundamental reasons. First, assessing the existence of any shortfall in drug research is the proper domain of Congress--not the states. Second, if in fact more research is needed, other remedies such as extending the effective patent period (that is, assuring drug companies full 17-year protection), for example, would foster innovation more efficiently (at less cost) than would preserving antiquated antisubstitution laws.

First, Congress is the most appropriate forum for addressing any such problem. Traditionally, Congress has had exclusive jurisdiction over the issue of fostering innovation. Indeed under Article One of the Constitution only Congress can grant patent protection.[36] The major societal goal of the patent system is encouraging innovation and the anticompetitive nature of the system is tolerated only to foster that overriding objective. Certainly, antisubstitution laws were not intended either to foster innovation or increase competition. As documented in Ch.VII.A., supra, antisubstitution laws were enacted primarily through the efforts of manufacturers seeking to protect the sales of their brand-name products from the substitution of outright "counterfeit" drugs of unknown quality, content and origin. With the virtual disappearance of these illicit counterfeit drugs due to the enactment of strong federal controls, the major rationale behind the passage of antisubstitution laws also has disappeared. Antisubstitution laws never were intended to foster drug innovation at the expense of price competition. Congress is the proper forum for the resolution of these competing goals that so vitally affect the national interest; moreover, using the antisubstitution laws to facilitate drug research is to change patent policy artificially. Furthermore, Congress is better equipped than is an individual state to resolve whether there is in fact a need to stimulate more drug research and to what extent. These questions are as difficult as they are controversial, and reliable answers will require considerable expertise and resources. Congress can more readily and fully explore this issue. (In contrast, that there will be large benefits from drug product selection is more predictable.) Therefore, Congress is both better suited and equipped to address whether any shortfall exists in drug research.

Second, if more drug research is needed (a conclusion we do not reach), assuring a full patent period on new drug products for example, may be a more precise, efficient, and less costly means of reaching that end. This could be accomplished simply by beginning the patent period when the product is marketed, as proposed for consideration by HEW Secretary Califano,[37] rather than when it is discovered. Both extending the patent period and preserving antisubstitution laws would mean higher drug prices than would prevail in their absence. But the repeal of antisubstitution laws would stimulate competition in the pricing of all drugs already developed.

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36 U.S. CONST. art. I, § 8, cl. 8: "The Congress shall have power . . . To promote the Progress of Science . . . by securing for limited times to . . . Inventors the exclusive Right to their . . . Discoveries."

37 Address by Joseph A. Califano, Jr., Secretary of Health, Education, and Welfare, Public Citizen Forum (Oct. 5, 1977), at 16. See also Drug Topics, Nov. 15, 1977, at 26.

Whereas the anticompetitive impact of antisubstitution laws is potentially perpetual, an extended patent period limits the rewards for innovation. Existing multisource drugs would be affected immediately and single-source drugs would face more competition as their patents expire. The profitability of these existing drugs, however, logically should have no effect on the prospective profitability of current and future research projects. Extending the patent period prospectively, then, would more narrowly focus on stimulating current drug research without foregoing the benefits from lower prescription prices on all existing drugs. The likely savings from lower prices on these existing drugs is great. In fact, the multi-million dollar estimates found in our discussion of potential benefits (Ch. VIII, supra) were based on the present universe of multisource drugs. And these benefits from drug product selection would continue as existing single-source drugs go off patent.

In sum, while some industry members have argued that drug product selection laws will reduce beneficial R & D, there is no consensus on this point, even among industry members themselves. Moreover, even if we were convinced that there was a need to stimulate R & D, we would not urge retention of antisubstitution laws as a means of doing so because antisubstitution laws seem a relatively imprecise and inefficient means of fostering innovation. If convincing evidence of an adverse effect on beneficial R & D were shown, we would instead urge the Congress to consider remedies other than retention of antisubstitution laws.

IX.B. Will Drug Product Selection Interfere with Physician Control of Patient Therapy?

Drug product selection will not encroach on the physicians' control of patient therapy. When prescribing, doctors have numerous decisions to make, one of which is deciding whether a chemically equivalent drug product will affect therapeutic value. Even under antisubstitution laws, physicians can and often do delegate product selection authority to a pharmacist by prescribing generically.[1] Although drug product selection laws will make it easier for physicians to delegate product selection authority to pharmacists, such laws will not undercut the physician's prerogative to require a pharmacist to dispense a particular drug product.

Drug product selection laws will allow the physician who is most familiar with or finds it easier to work with the brand name to prescribe generically by writing the brand name.[2] However, when the physician thinks a particular brand necessary and so indicates, all drug product selection laws provide that the pharmacist cannot dispense otherwise.[3] It appears that the criticism that pharmacists do not know the patient's idiosyncrasies is largely misplaced. The AMA, for example, has pointed out that the physician may know

> that a patient has great difficulty in swallowing capsules but that coated tablets give him no problem, or that a patient is allergic to a normally inert ingredient of a topical preparation, whereas a similar preparation that does not contain the offending material would be well tolerated.[4]

It is for these infrequent instances that the physician's veto power is designed. In the vast majority of cases the pharmacist can use his expertise to dispense therapeutically equivalent drug products at marked savings. We have seen that pharmacists' training qualifies them to select drug products. This conclusion is corroborated by objective tests given both doctors and pharmacists. And most physicians and pharmacists believe that pharmacists are competent to select drug products. Finally, the formulary will define the scope of permissible substitution and may assist pharmacists in selecting particular products. For a full

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1 See Ch. IV.A., supra.

2 See discussion of brand name promotion in Ch. III.C., supra.

3 See Ch. X.A., Section 2(b) of the Model Act, infra, and Ch. VII.B. supra.

4 217 J.A.M.A. 818 (1971). See also 223 J.A.M.A. 552 (1973).

discussion of pharmacists' competence for this task see Ch. IV, supra.

IX.C. Are Generic Drug Products Therapeutically Equivalent?

In this section we will discuss our review of the literature and of expert opinion about bioavailability and other measures of product equivalence (this review did not seek to independently evaluate the technical evidence underlying the views expressed). Although opinion varies about the frequency and importance of bioavailability differences, there is general agreement that for most drugs such differences have no clinical effect. Consequently, evidence of bioequivalence is necessary and desirable only for a small minority (perhaps 10-15%) of all drugs.

The recent FDA bioavailability/bioequivalence regulations seek to identify those drug classes for which evidence of bioequivalence is critical and to impose additional standards to assure their equivalence. Our review found general support among the scientific community for the FDA approach. FDA has taken additional steps to improve the quality of marketed drugs. And as noted in Ch. VI.B., supra, a federal court examining the MAC program concluded that FDA could assure the quality of the vast majority of drugs on the market and that bioinequivalence was not a major or insurmountable problem.

Furthermore, our review found considerable support for FDA's statement that there is no substantial evidence of significant differences, either in bioavailability or general quality (in terms of purity, potency or other measures of quality control), between brand-name and unbranded products, or between products made by large and by small manufacturers. There is therefore no inherent reason to choose a more expensive product simply because of brand-name familiarity. Absent some medical reason for the physician to indicate otherwise, the pharmacist is in the best position to select the drug source. Indeed, information provided by FDA should assist the pharmacist in improving the quality of the drug products dispensed to patients.

1. Drug Bioequivalence

a. Studies of Bioinequivalence

Several major studies have concluded that in some instances past standards have not ensured the bioequivalence of chemically equivalent drug products. Some literature surveys, however, have overstated the extent of bioequivalence problems by comparing products with different chemical or dosage formulations. Drug product selection laws do not permit selection of such products, but instead restrict substitution to chemically equivalent drug products of the same dosage form.

The 1969 report of the HEW Task Force on Prescription Drugs did much to stimulate debate on the bioequivalence question (for an explanation of bioavailability, see discussion at Ch. VI.A.4., supra). The Task Force concluded that research had

established instances of bioinequivalence among chemical equivalents, but that such inequivalence had been "grossly exaggerated as a major hazard to the public health."[1] The Task Force recommended further study by HEW on a high priority basis.[2]

In 1974 an expert Drug Bioequivalence Study Panel convened by the Office of Technology Assessment (OTA) issued its report. This major study has been cited by both opponents and proponents of drug product selection. It concluded that compendial standards and regulatory practices did not ensure bioequivalence for chemically equivalent drug products.[3] In at least two cited cases, digoxin and thyroid, bioinequivalence had produced clinically significant effects.[4] Nevertheless, the OTA panel indicated that the goal of interchangeability was achievable within most, if not all, drug classes and made recommendations for achieving this goal.[5] Other recommendations included replacement of the U.S. Pharmacopeia (U.S.P.) and the National Formulary (N.F.) by a single organization to set standards, elimination of exemptions in the Food, Drug and Cosmetic Act for drug products based on their year of introduction, strengthening of compendial standards and Good Manufacturing Practice regulations, and development of *in vitro* tests that are correlated with *in vivo* bioavailability.[6]

The panel noted that it is neither feasible nor ethically justifiable to perform *in vivo* bioavailability tests for all

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1 HEW Task Force on Prescription Drugs, *Final Report* 31 (1969).

2 *Id.* at 33.

3 Office of Technology Assessment Drug Bioequivalence Study Panel, *Drug Bioequivalence* 11 (1974). ["OTA Report".] The Report noted, at 11, that bioinequivalence has been shown in different batches from the same manufacturer, as well as among products of different manufacturers. The Panel listed 24 drugs for which bioavailability differences had been demonstrated. *F-D-C Reports*, July 15, 1974, at A-3.

4 *Id.* at 13-14.

5 *Id.* at 57-60.

6 *Id.* at 2-3. For further discussion of the findings and recommendations, *see* "Brand Names and Generic Drugs, 1974," Hearing before the Subcommittee on Health of the Committee on Labor and Public Welfare, U.S. Senate, 93rd Cong. 2d Sess., July 22, 1974. ["Brand Names and Generic Drugs".]

marketed products.[7] Moreover, such tests are unnecessary for the vast majority of drugs. Every drug requires a minimum concentration in the blood to be therapeutically effective. And for almost every drug there also is a higher level at which toxic effects begin to appear. For the few drugs for which this margin of safety is very narrow, bioequivalence can have serious therapeutic consequences. Examples of such drugs include certain cardioactive agents (e.g. digoxin), anticonvulsants (e.g. phenytoin) and antibiotics (e.g. chloramphenicol).[8] Most drugs, however, are taken in standardized doses without regard for the size of the patient--the same dose might be used for a patient weighing 80 pounds as for one weighing 300 pounds. For such drugs, the blood level concentration is not critical. As the OTA Panel Chairman stated, "it is very important to point out . . . that two drugs may differ in bioavailability, that is be bioinequivalent, but may still be therapeutically equivalent."[9] Panel members estimated that roughly 85 percent to 90 percent of all prescription drugs were not critical dose drugs for which bioavailability studies were necessary.[10]

The OTA Panel recommended establishment of an official list of interchangeable drug products.[11] They indicated that experts would not have difficulty distinguishing between those drugs for which evidence of bioavailability was not essential, and those for which it was critical. Panel members indicated that the list of interchangeable products could be established without waiting for the improvement of compendial standards, but that it would be more conservative than would be the case if improved standards were developed first. Furthermore, they feared that some of the impetus for improved standards might be lost once a list of interchangeable products had been established.[12]

The OTA Panel Chairman stated that if the Panel's recommendations

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7 Id. at 21. See discussion of in vivo testing, Ch.VI.A.4., supra.

8 Id. at 23.

9 Dr. Robert W. Berliner, Statement in "Competitive Problems in the Drug Industry," Hearings before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, Part 26, 1975, at 11656. ["Competitive Problems".]

10 F-D-C Reports, supra note 3, at B-11 and B-14; Brand Names and Generic Drugs, supra note 6, at 82.

11 OTA Report, supra note 3, at 57.

12 Competitive Problems, Part 26, supra note 9, at 11657.

were implemented, the physician

> need not concern himself with the specific brandname of the products that he prescribes; . . . and that . . . the cost of the drug would then become a relevant consideration.[13]

Numerous reviews in the literature confirm the OTA Report's finding that instances of bioinequivalence have occurred among chemically equivalent products. Dr. John Wagner, of the Upjohn Center for Clinical Pharmacology at the University of Michigan, found that prior to 1971 twelve drugs had been studied in man under controlled conditions, and that large differences in bioavailability were reported for seven of the twelve.[14] Several publications have attempted to list drugs according to high, moderate or low potential risk of bioinequivalence.[15] The American Pharmaceutical Association (APhA) has published a series of bioavailability monographs, reviewing available scientific data and presenting conclusions in a form useful to pharmacy practitioners in making judgments about the suitability of various drug products.[16]

Some industry-produced literature, on the other hand, has been criticized for its reliance on poorly designed studies or comparisons of different drug formulations. For example, the HEW

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13 F-D-C Reports, supra note 3, at B-11.

14 Wagner "Generic Equivalence and Inequivalence of Oral Products," 5 Drug Intelligence & Clinical Pharmacy 118 (1971).

15 See, e.g., "Report of the Ad Hoc Committee on Drug Product Selection of the Academy of General Practice of Pharmacy and the Academy of Pharmaceutical Sciences," 13 J. Am. Pharm. Ass'n, June 1973; "Report of the Task Force on Drug Product Selection," published by the Oregon State Board of Higher Education, November 1975; Dept. of Pharmaceutical Sciences, Pharmaceutical Society of Great Britain, "Biological Availability," 7 Drug Intelligence & Clinical Pharmacy 116 (1973); "The Battle Over Bioequivalence," Med. World News Nov. 8, 1974, at 73, 81.

16 See, e.g., "The Bioavailability of Drug Products," J. Am. Pharmaceutical Ass'n, July 1973; "The Bioavailability of Drug Products," J. Am. Pharmaceutical Ass'n, (with Supplement 1, December 1975; Supplement 2, July 1976); "Meprobamate," 17 J. Am. Pharm. Ass'n, March 1977; "Sustained Release Papaverine Hydrochloride," 17 J. Am. Pharm. Ass'n, May 1977; "Ferrous Sulfate," 17 J. Am. Pharm. Ass'n, June 1977; "Acetaminophen," 17 J. Am. Pharm. Ass'n, August 1977; "Digoxin," 17 J. Am. Pharm. Ass'n, October 1977.

Task Force on Prescription Drugs examined the PMA's 1968 Bibliography on Biopharmaceutics, and discovered that of 221 studies conducted in human subjects, only 76 were, by PMA's own evaluation, "adequately designed or controlled experiments." Of the 76, only 12 compared different brands of the same chemical equivalent, and most of these 12 compared different dosage forms, salts or coatings.[17]

The Upjohn Company published a book listing 370 scientific articles about bioavailability problems in some 73 drugs.[18] Dr. Allan E. Dyer, Director of Drugs and Therapeutics of the Ontario Ministry of Health, noted that most of these studies also involved "unlike" dosage formulations:

> We are aware of much of the literature quoted in Upjohn's paper and, as you probably know, most of it is not relevant to the subject of interchangeability of comparable dosage forms. It is unfortunate that data like this is presented as representing comparative bioavailability of like formulations since indeed most of the references relate to "unlike" formulations.[19]

Similarly, a recent article published in the Journal of the American Medical Association relied on a comparison of two different

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17 M. Silverman & P. Lee, Pills, Profits & Politics 154-5 (1974). One drug company official complained, "The PMA should be charged with treason in time of war. Their damn bibliography merely gave aid and comfort - and a lot more ammunition - to the enemy."

18 D. Chodos & A. DiSanto, Basics of Bioavailability (1974).

19 P. Brooke, Resistant Prices 41-42 (1975). An official of the Abbott Co. complained about bias in bioavailability studies performed by Upjohn:

> The main point that we wish to make is that Upjohn is using bioavailability studies for promotional purposes. To do this they are designing their bioavailability studies to be biased in favor of their product and negatively biased toward competitive products.

Competitive Problems, Part 26, at 11660. See also Varley "The Generic Inequivalence of Drugs," 206 J.A.M.A. 1745 (1968); Heller, "A Practitioner's Approach to Standards Setting," Drug Information Bull. 105 (January/June 1969); R. Burack, The New Handbook of Prescription Drugs 106 (1976).

dosage forms--capsules and tablets--of tetracycline to show bioinequivalence.[20]

b. Therapeutic Effects of Bioinequivalence

As the OTA Panel emphasized, few instances of bioinequivalence have been shown to have any clinical significance. The Panel identified only two drugs with documented therapeutic problems (one such drug, digoxin, has been discussed earlier).[21]

Azarnoff and Huffman,[22] of the University of Kansas Medical Center and the Veterans Administration Hospital in Kansas City, reviewed articles documenting therapeutic consequences of differences in bioavailability, concluding that "documentation of therapeutic consequences of differences in bioavailability have been few."[23] Several studies, however, did demonstrate that the potential for alteration of clinical effect due to bioinequivalence is "quite significant." Consequently, they recommended development of compendial standards to minimize the problem. Small differences in bioavailability were likely to produce therapeutic problems for drugs with either a steep dose-response curve or a narrow range separating effective and toxic levels. Most clinically useful drugs have relatively flat dose-response curves; therefore, only large differences in bioavailability were likely to alter their therapeutic effect.

Most scientists seem to agree that a large majority of drugs should present no therapeutically significant bioavailability problems. As discussed above, this was the conclusion of the OTA Panel. The Director of Pharmacy Research at Wyeth Laboratories stated that "there is general agreement that a large number of drugs can be excluded from high-priority consideration because they are freely soluble and readily absorbed."[24] The head of

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20 Both products were brand names (Achromycin and Tetrachel). Wood, Flora & Duma, "Tetracycline: Another Example of Generic Bioinequivalence," 239 J.A.M.A. 1874 (1978).

21 See discussion, Ch. VI.A.4.d, supra. For a discussion of factors influencing therapeutic equivalence, see Wagner, "Biologic Availability, Determinant Factor of Therapeutic Activity of Drugs," 7 Drug Intelligence & Clinical Pharmacy 168 (1973).

22 Azarnoff & Huffman, "Therapeutic Implications of Bioavailability," 16 Ann. Rev. Pharmacology 53 (1976).

23 Id. at 63.

24 Schneller, "The Hazard of Therapeutic Non-equivalency of (Footnote Continued)

Ontario's Ministry of Health has stated that the most critical of the "limited number of drugs" considered noninterchangeable are those, such as digoxin and anticoagulants, requiring doses tailored (or "titrated") to the response of each patient.[25] That statement is supported by several Canadian studies.[26] Ontario's Drug Benefit Formulary, for example, lists only oral contraceptives and about eight other drugs as noninterchangeable.[27] Similarly, FDA notes that the most significant problems are likely to occur when interchanging critical dose drugs that require patient titration.[28] FDA has found very few examples of therapeutic inequivalence:

> Most examples of bioinequivalence among drugs, while demonstrable by modern analytical techniques and deserving of resolution, are not severe enough to produce recognizable therapeutic inequivalence.[29]

A Canadian scientist[30] has argued that bioavailability

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24 (Footnote Continued)

Drug Products," Drug Information Bull. January/June 1969, at 101. The article discusses several drugs thought to present definite hazards.

25 Dr. Allan E. Dyer, "Implementation and Implications of Applying Drug Product Selection to Selected Populations, Presented to Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13, 1978, at 14.

26 A report by the Providence of Manitoba noted that therapeutic inequivalence has been shown for only a small number of drugs. Province of Manitoba, Manitoba Drug Standards and Therapeutics Formulary, 1st ed., January 1974, at 9. Earlier Canadian studies of several drugs reported that 92 to 97 percent of the products studied were sufficiently absorbed to be clinically equivalent. Boyd, "The Equivalence of Drug Brands," 2 Rx Bull. 101 (1971).

27 Ontario Ministry of Health, Drug Benefit Formulary and Parcost Comparative Drug Index (1978).

28 Biron, "Dosage, Compliance and Bioavailability in Perspective," 115 C.M.A.J. 102 (1976).

29 Id. at 103.

30 Bernard E. Cabana, Director, Div. of Biopharmaceutics, FDA Bureau of Drugs, "Bioavailability/Bioequivalence Issues Concerning Drug Interchangeability," Presented to Food

(Footnote Continued)

is less important in causing insufficient blood concentrations than incorrect dosage and inadequate patient compliance. Citing a 1973 report by Health and Welfare Canada that very few of the 137 drugs studied failed tests for bioavailability, he recommended:

> Much more energy and financial support should be directed towards educating physicians in prescribing correct dosage and obtaining proper compliance, rather than towards increasing the number of sophisticated and costly bioavailability trials.[31]

Scientific opinion on the extent of therapeutic inequivalence is not unanimous. John Wagner, for example, argues that it is imprudent to assume equivalence among any drug products with the same active ingredients, and that every manufacturer must prove the equivalence of its products.[32] James Doluisio, Dean of the University of Texas School of Pharmacy and a member of the OTA Panel, states, however, that although therapeutic inequivalence may have been a problem a decade ago, FDA activities and new regulations make this argument no longer valid. He advises:

> What you should seek is whether anyone can give you a specific example of a currently available product that is not therapeutically equivalent. [Emphasis in original.][33]

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30 (Footnote Continued)

and Drug Law Institute Seminar, Washington, D.C., June 8, 1977, at 31.

31 "FDA Analysis of Statement of C. Joseph Stetler, President, Pharmaceutical Manufacturers Association," Presented Before the Subcommittee on Monopoly and Anticompetitive Activities, Select Committee on Small Business, U.S. Senate, Nov. 16, 1977, at 6. ["FDA Analysis".]

32 Wagner, "Drug Bioavailability Studies," Hospital Prac., January 1977, at 127.

33 James Doluisio, Professor and Dean, College of Pharmacy, Univ. of Texas, Statement before the Texas State Senate Human Resources Committee re House Bill 10, Apr. 13, 1977, at 4. Others have noted the frequent use of generic products in hospitals, where inequivalence is assumed to be limited. Strom, et al., "Antisubstitution Law Controversy - A Solution?," 81 Annals Internal Med. 255 (1974); Milton Silverman, Health Policy Center, Univ. of California at San Francisco,
(Footnote Continued)

c. FDA Bioavailability/Bioequivalence Regulations

FDA's recent bioavailability/bioequivalence regulations (discussed earlier at Ch. VI.A.4.) implement several of the OTA Panel's recommendations. The regulations establish criteria for distinguishing drugs for which bioequivalence is critical from those for which it is not, require evidence of bioequivalence for critical dose drugs, and emphasize development in in vitro tests as indicators of in vivo bioavailability. Using the criteria established by the regulations, FDA also has developed a list of drugs presenting actual or potential bioequivalence problems (see discussion of list at Ch. VI.A.4.e., supra). Published articles, as well as our discussions with a cross-section of scientists expert in biopharmaceutics,[34] indicate general support for the regulations.

The experts we contacted, who represented a range of opinion about drug product selection, approved of the FDA approach

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33 (Footnote Continued)

Testimony Presented to the Special Hearing of the California Senate Health and Welfare Committee on Drug Product Selection, Nov. 15, 1972, at 6-7.

34 Telephone conversations between Peter D. Holmes, FTC, and Daniel Azarnoff, Dept. of Pharmacology, Univ. of Kansas Medical School, June 13, 1977; Leslie Z. Benet, School of Pharmacy, Univ. of California at San Francisco, July 20, 1977; Lewis W. Dittert, College of Pharmacy, Univ. of Kentucky, June 30, 1977; James T. Doluisio, Dean, College of Pharmacy, Univ. of Texas, Aug. 1, 1977; Edward R. Garrett, College of Pharmacy, Univ. of Florida, July 7, 1977; Louis Lasagna, Dept. of Pharmacology and Toxicology, School of Medicine and Dentistry, Univ. of Rochester, July 13, 1977; Marvin C. Meyer, Dept. of Medicinal Chemistry, College of Pharmacy, Univ. of Tennessee, Oct. 18, 1977; Sidney Riegelman, Chairman, Dept. of Pharmacy, Univ. of California at San Francisco, July 29, 1977; Victor F. Smolen, School of Pharmacy and Pharmacal Sciences, Purdue Univ., July 13, 1977; John Wagner, Upjohn Center for Clinical Pharmacology, Univ. of Michigan Medical School, July 13, 1977; and Peter Welling, Pharmacy School, Univ. of Wisconsin, July 6, 1977. Several other scientists who were contacted, including three from the pharmaceutical industry, were unwilling to be cited in this Report. We identified this cross-section of biopharmaceutics experts based on their published studies as well as the recommendations of other scientists in this field.

as a reasonable allocation of resources.[35] They believed that the criteria used to develop the FDA list of drugs with actual or potential bioavailability problems represented the best scientific judgment possible at this time. Similarly, the Director of Pharmacy Research at Wyeth Laboratories has characterized the guidelines presented in the regulations as "accepted by most workers in the field as generally sound and reasonable and . . . a major step forward."[36] Several experts[37] noted that not enough was known yet to "guarantee" that all problem drugs had been included on the FDA list; a few,[38] on the other hand, stated that the list was overinclusive and that only a small percentage of the drugs would ultimately be shown to present problems.

There is general agreement with FDA's assertion that bioequivalence usually is related to differences in rates of dissolution.[39] John Poole of Wyeth Laboratories has stated[40] that a discriminating dissolution test, especially if correlated with in vivo data, is a useful "first approximation" of bioavailability (although in certain situations other complications can destroy the utility of the test).

Most criticism of the FDA regulations involves the complexities of in vitro dissolution testing. Some scientists[41] believe that

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35 Azarnoff, Benet, Dittert, Doluisio, Garrett, Lasagna, Meyer, Riegelman, Wagner and Welling, id.

36 John Poole, "Bioavailability/Bioequivalence Regulations -- How Will They Impact on Product Development?," Presented to APhA Academy of Pharmaceutical Sciences, Phoenix, Arizona, Nov. 14, 1977, at 4-5.

37 Dittert, Garrett, Lasagna, Meyer, Riegelman, Wagner, and Welling, supra note 34. See also Stanley Kaplan, "Bioequivalency/Bioavailability Regulations: An Industrial Impression of the Regulations," Presented to Food & Drug Law Institute, Washington, D.C., June 8, 1977, at 12. Kaplan, a scientist with Hoffmann-LaRoche, also criticizes a number of the cut-off points in the FDA regulations as "arbitrary."

38 Azarnoff, Benet and Doluisio, supra note 34.

39 Azarnoff, Benet, Dittert, Doluisio, Wagner, and Welling, supra note 34.

40 Poole, supra note 36, at 6.

41 Benet, Garrett, Smolen and Wagner, supra note 34; Wagner, supra note 14, at 126. For further discussion of in vitro/in vivo correlations, see, e.g., Smolen & Weigand, "Optimally

(Footnote Continued)

dissolution testing is useful only when correlated with in vivo data, and, in fact, that this correlation must be established for each formulation of the same drug entity.[42] Others believe, however, that the correlation need not be established for those drugs for which bioavailability is not critical.[43] A subcommittee of the Policy Advisory Committee of the Drug Efficacy Study, for example, stated:

> In the majority of cases . . . [in vitro] tests should suffice, but in every case in which there may be doubt of biological equivalence . . ., biological tests should be required.[44]

Finally, an Upjohn scientist has argued that values obtained in dissolution tests can vary as much as 100 percent or more across laboratories, and that in vitro requirements therefore should not be imposed until methodological problems are resolved.[45] Indeed, FDA has acknowledged the need for standardization of dissolution procedures. It therefore will require firms sponsoring drug applications to demonstrate instrument proficiency when

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41 (Footnote Continued)

Predictive In Vitro Drug Dissolution Testing for In Vivo Bioavailability," 65 J. Pharm. Sci. 1718 (1976); Smolen & Erb, "Predictive Conversion of In Vitro Drug Dissolution Data Into In Vivo Drug Response versus Time Profiles Exemplified for Plasma Levels of Warfarin," 66 J. Pharm. Sci. 297 (1977); Poole, "Some Experiences in the Evaluation of Formulation Variables on Drug Availability," Drug Information Bull., January/June 1969, at 8. Poole noted that up to that time Wyeth Laboratories had found no change in the rank order for formulations evaluated both in vitro and in vivo.

42 Benet and Wagner, supra note 34; A. DiSanto, "FDA's Bioequivalency/Bioavailability Regulations: Impact From a Research Oriented Manufacturer," Presented to Food & Drug Law Institute, Washington, D.C., June 8, 1977, at 4.

43 Azarnoff, Doluisio, and Meyer, supra note 34.

44 Castle, et al., "White Paper on the Therapeutic Equivalence of Chemically Equivalent Drugs," 208 J.A.M.A. 1172 (1969); see also Dittert, "Dosage Form Performance: A Major Factor in Clinical Medicine," 40 Connecticut Med. 336 (1976).

45 DiSanto, supra note 42, at 3. See also Meyer and Wagner, supra note 34.

submitting dissolution data.[46]

d. Bioavailability of Brand-Name Versus Generic-Name Products

A few scientists have expressed the belief that large or brand-name manufacturers generally have fewer bioavailability problems than smaller, generic firms. John Wagner, for example, asserts that

> many small-sized manufacturers are capable of significantly reducing the bioavailability of almost any drug, owing apparently to lack of knowledge about biopharmaceutics and pharmacy research. Some older products of some larger manufacturers also have bio-availability problems.[47]

Wagner also contends that an innovator's product is safest because of its years of clinical testing.[48] Similarly, Louis Lasagna, professor of pharmacology at the University of Rochester, argues that larger firms are likely to have better quality control.[49] Most of the scientists we contacted, however, did not think bioavailability problems could be generalized as one of brands versus generics, or large versus small companies.[50] As Dr. Walter Modell of Cornell University Medical College has stated,

> trademarked brands of the same drug may differ as widely as some generics may from some trademarks or from one another. And different batches of the same trademarked drugs may

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46 Jerome Skelly, Chief, Pharmacokinetics and Biopharmaceutics Branch, FDA Bureau of Drugs, "Dissolution Proficiency Testing," Presented at the 17th Annual International Industrial Pharmacy Conference, Austin, Texas, Feb. 20-24, 1978, at 2, 12.

47 Wagner in The Scientific Evaluation of Drug Equivalency (A. Brest ed. 1974), at 80.

48 Wagner, supra note 34. But see FDA's arguments that, to the contrary, ANDA requirements often are more stringent that those imposed on the original manufacturer. Ch.VI.A.1.e., supra.

49 Lasagna, supra note 34.

50 Benet, Dittert, Garrett, Meyer and Welling, supra note 34.

not have the same biologic availability.[51]

Two groups of scientists have reached similar conclusions. First, scientists at the Tennessee College of Pharmacy[52] studied six different nitrofurantoin (50 milligram) products, six nitrofurantoin (100 milligram) products, 10 propoxyphene (65 milligram) products, and 15 tetracycline (250 milligram) products to determine whether drug prices could be correlated with bioavailability. They found that the more expensive drug products studied did not necessarily produce higher blood levels than the less expensive products: "cost, high or low, . . . was not found to be a good indicator of a drug's bioavailability."[53]

The National Research Council's Drug Research Board, which included scientists from several large pharmaceutical manufacturers as well as from schools of pharmacy and medicine, unanimously adopted a resolution and background statement concluding that absent contrary information it is "unreasonable" to assume that the less expensive product is less desirable.[54] In the absence

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51 Modell, "Drug Equivalence and Fixed Combinations," Modern Med., Sept. 6, 1971, at 43. See also Barr, "Factors Involved in the Assessment of Systemic or Biologic Availability of Drug Products," Drug Information Bull., January/June 1969, at 38.

52 Slywka, et al., "Relationship of Price to Bioavailability for Four Multiple-Source Drug Products," 17 J. Am. Pharm. Ass'n. 30 (1977).

53 Id. at 32.

54 Drug Research Board, National Research Council, Resolution and Background Statement adopted in Washington, D.C., on Jan. 16, 1975. The resolution was passed unanimously by the members of the DRB with one abstention, that of J. Richard Crout, Director, Bureau of Drugs, Food and Drug Administration, whose agency had not taken an official stand on the issue. Chairman of the DRB was Frederick E. Shideman, head, department of pharmacology, University of Minnesota. Other members were Daniel L. Azarnoff, professor of medicine and pharmacology, University of Kansas Medical Center; James A. Bain, director, division of basic health sciences, Emory University; Mitchell B. Balter, chief special studies section, psychopharmacology research branch, National Institute of Mental Health; Allan D. Bass, associate dean for biomedical sciences, Vanderbilt University School of Medicine; Paul Calabresi, physician-in-chief, Roger Williams General Hospital, Brown University; Victor A. Drill, director, scientific and professional affairs, G.D. Searle, & Co.,
(Footnote Continued)

of contrary data, the Board found "no inherent reason for choosing the more expensive product simply because of the familiarity of the physician or pharmacist with the brand name." In that event, "cost would often be the deciding factor and the pharmacist is often in the best position to make this final choice." Daniel Azarnoff, a member of the Board, has noted that prescribing by brand name does not guarantee quality or bioavailability:

> Thus, when the physician has no reason to suspect bioavailability or other special problems with his patient, there appear to be no cogent reasons for not letting the pharmacist select the cheapest, quality product.[55]

FDA officials also have stated that brand-name products do not necessarily provide greater bioavailability than unbranded equivalents:

> It should be noted, however, that it is not an issue of "brand name" versus "generic brand" since . . . there is no apparent scientific basis suggesting that the patient is offered greater protection by dispensing one brand in preference to another.[56]

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54 (Footnote Continued)

Skokie, Illinois; Robert M. Hodges, vice president, research and development, Park, Davis & Company, Ann Arbor, Michigan; Hugh H. Hussey, editor emeritus, American Medical Association, Chicago, Illinois; Werner Kalow, chairman, department of pharmacology, University of Toronto; Thomas D. Kinney, professor of pathology, Duke University Medical Center; Kenneth G. Kohlstaedt, professor of medicine, Indiana University; Emanuel M. Papper, dean, University of Miami School of Medicine; James A. Pittman, Jr., dean, School of Medicine, University of Alabama; James M. Price, vice president, corporate research and experimental therapy, Abbott Laboratories, North Chicago, Illinois; David P. Rall, director, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina; and George W. Thorn, physician-in-chief, emeritus, Peter Bent Brigham Hospital, Boston, Massachusetts.

55 Azarnoff, "In Defense of the Drug Research Board," 233 J.A.M.A. 426 (1975).

56 Cabana, supra note 30, at 30. See also Marvin Seife, quoted in "Generic Drugs," The MacNeil/Lehrer Report, Apr. 28, 1977.

For example, six of the first 13 bioequivalence problems identified by FDA were associated with innovator's brand-name products.[57] The agency's review of 500 bioavailability studies in the last three years has provided evidence of bioinequivalence with NDA-innovator products such as acetazolamide tablets, triple sulfa supension, and chlorothiazide tablets.[58]

Most of the scientists we contacted also supported some form of drug product selection by pharmacists.[59] Even the two experts[60] who generally opposed product selection thought it acceptable if carefully limited to a positive formulary based on the results of scientific testing. Others also supported the use of a drug formulary,[61] some proposing a national FDA formulary. Indeed, the FDA has announced that it will be providing states with a formulary of therapeutically equivalent drug products.[62]

2. Product Quality

a. FDA Enforcement of Drug Quality

The bioequivalence issue involves the question of whether existing quality standards ensure the bioavailability of drug products. Even where existing standards are sufficient, there has been some criticism that FDA has not adequately enforced those standards. Past problems with FDA enforcement of Good Manufacturing Practices (GMP's) have been documented, but FDA in recent years has devoted considerable effort to improving its enforcement

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57 FDA Analysis, supra note 31, at 5.

58 Id. at 8.

59 Azarnoff, Benet, Dittert, Doluisio, Garrett, Meyer, Riegelman, Smolen and Welling, supra note 34.

60 Lasagna and Wagner, supra note 34.

61 Benet, Dittert, Doluisio, Garrett, Meyer, Riegelman, Smolen and Welling, supra note 34. Some scientists also supported a provision limiting refills to the drug source originally dispensed (thus minimizing problems resulting from interchange during the course of therapy), but Professor Meyer noted that a good formulary, unlike a refill limitation, could control such variables as changes in the manufacturer's source of supply.

62 Donald Kennedy, FDA Commissioner, Statement Before the Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, July 27, 1978.

program.

A 1973 General Accounting Office (GAO) report[63] found that FDA had not always enforced GMP compliance nor had it inspected all producers as often as required by law (at least once every two years). GAO made several recommendations, including establishment of guidelines for FDA offices to encourage aggressive enforcement, establishment of a schedule system to ensure inspection of all producers at least every two years, and establishment of an accurate list of current drug producers. A House Appropriations Committee investigation reported similar findings and made similar recommendations.[64]

HEW concurred in all the GAO recommendations[65] and in 1975 reported their implementation.[66] It further reported that a GAO follow-up audit disclosed that FDA had consistently acted to correct problems where critical GMP violations occurred.[67] In response to suggestions by the OTA Panel[68] FDA also proposed to update its GMP regulations:[69] those updated regulations will become effective March 28, 1979.[70] FDA Commissioner Kennedy has stated that a system of quality assurance profiles established in 1975 shows that FDA is inspecting virtually every registered plant at least once every two years, and every registered drug formulator at least once a year.[71]

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63 Comptroller General of the U.S., "Problems in Obtaining and Enforcing Compliance with Good Manufacturing Practices for Drugs," Report to the Congress, Mar. 29, 1973.

64 Surveys and Investigations Staff, "A Report to the Committee on Appropriations, U.S. House of Representatives, on the Programs of the Food and Drug Administration, Department of Health, Education, and Welfare," February 1975.

65 Comptroller General, supra note 63, at 5.

66 40 Fed. Reg. 32286 (1975).

67 Id.

68 See discussion, Ch. IX.C.1.a, supra.

69 41 Fed. Reg. 6878 (1976); Caspar Weinberger, Statement Before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, Mar. 19, 1975, at 7-8.

70 43 Fed. Reg. 45014 (1978).

71 Donald Kennedy, FDA Commissioner, Statement Before the Subcommittee on Monopoly, Select Committee on Small Business,

(Footnote Continued)

b. General Quality of Brand-Name Versus Generic-Name Products

As in the case of bioavailability, some critics of drug product selection have claimed that the general quality of brand-name products (in terms of purity, potency, or other measures of quality control) is superior to generic equivalents, or that large (or research-oriented) manufacturers produce higher quality products than do small manufacturers. Yet FDA has consistently stated that there is no substantial evidence showing significant quality differences between brands and generics, or between large and small firms. FDA further notes that there are relatively few instances of drug products reaching the market with serious quality problems.

Industry statements about the quality of brands versus generics have been inconsistent. For example, the President of the PMA recently stated the "PMA has never taken the position that products marketed under a brand name are inherently superior to those marketed under a generic name alone."[72] Yet, PMA has implied just that:

> [N]ot only are unbranded generic drugs often not bioequivalent to branded drugs with the same active ingredients, but also . . . generic

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71 (Footnote Continued)

U.S. Senate, Nov. 14, 1977, at 6. Recently, the PMA claimed that FDA accomplished only 22% of its planned GMP inspections between July 1976 and March 1977, 19% of its planned inspections of imported drugs, and 55% of its planned drug sample examinations. FDA responded that the PMA had "become hopelessly confused by our internal reports of progress and by the extra quarter in FY 1977." The figures in FDA's memorandum represented accomplishments at the nine month juncture within a 15-month period, at which point 60% of planned operations should be accomplished. The total of GMP inspections exceeded 60% of the target, and at the end of fiscal year 1977 exceeded 100%. Fifty-five percent of planned domestic sample examinations were completed by the end of nine months and 60% of the samples had been collected (by the end of the fiscal year, 100% had been collected and 96% examined). Because a scheduled expansion of the import sampling program did not take place in fiscal year 1977, the program operated at the same level as the previous year. FDA Analysis, supra note 57, at 21-24.

72 "Statement of the Pharmaceutical Manufacturers Association in Response to Federal Trade Commission Request of Jan. 11, 1978," Submitted by C. Joseph Stetler, President, PMA, to Peter D. Holmes, FTC, Feb. 21, 1978, at 4.

> drugs have serious bioequivalency problems even among drugs produced in the same batch, because of the lack of quality control which often accompanies unbranded generic drug production.[73]

FDA officials consistently have stated that there is no evidence to suggest serious quality differences between generic and brand-name products.[74] Commissioner Kennedy notes that such differences are found neither in FDA drug assays, drug recalls, nor drug problem reports.[75] For example, as early as 1966 an FDA potency study of 5,000 samples in 20 drug categories reported no significant difference in the percentages of generic and brand products outside compendial potency limits: 4.9 percent of generic products and 6.7 percent of brand products violated potency standards.[76] The PMA criticized the study methodology, claiming that internal reanalysis by PMA members of 102 of their products found defective by FDA showed only 18 were deficient.[77]

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73 "Promotion Overview," Submitted by C. Joseph Stetler, id, at 21a.

74 Donald Kennedy, FDA Commissioner, in "FDA's Kennedy - Friend or Foe?" Drug Topics, Jan. 3, 1978, at 39; Sherwin Gardner, FDA Deputy Commissioner quoted in Drug Topics, Jan. 3, 1978, at 16; Henry Simmons, Director, FDA Bureau of Drugs, "Brand vs. Generic Drugs: It's Only a Matter of Name," FDA Consumer, March 1973, at 6; 40 Fed. Reg., supra note 66, at 32285. At least one economist has argued that low-priced sellers have little incentive to economize on quality control, because the potential cost savings are too small to justify a procedure that would result in drug law violations. Steele, "Monopoly and Competition in The Ethical Drugs Market," 5 J. Law & Economics 144 (1962).

75 Kennedy, supra note 71, at 3-5. See discussion, Ch. VI.A.6., supra.

76 "Competitive Problems in the Drug Industry," Hearings Before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, 90th Cong., 1st Sess., Part 2, 1967, at 480. ["Competitive Problems".]

77 PMA News Release in Congressional Record, July 30, 1969, at 21488-89. An APhA official has stated that he was not aware of any FDA retraction of the study results. Edward G. Feldmann, Associate Executive Director for Scientific Affairs, APhA, in "Prescription Drug Labeling and Price Advertising," Hearings Before the Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign

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It is difficult for studies to assess objectively the recall records of branded and unbranded products. The results of such comparisons vary greatly depending on whether recalls are reported as a percentage of the number of brand-name or generic firms, or as a percentage of their dollar sales.[78] Because major brand-name companies have had their products recalled for serious quality control problems,[79] and because these recalls often

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77 (Footnote Continued)

Commerce, House of Representatives, 94th Cong., 2d Sess., on H.R. 882, H.R. 884, and All Identical Bills, 1976, at 201.

78 For example, PMA data shows that from June 1966 to August 1970 70% of the approximately 130 PMA firms had recalls as compared to 30% of the remaining 700-800 non-PMA firms. Council on Economic Priorities, "In Whose Hands?," 4 Economic Priorities Report 12 (1973). See also Competitive Problems, supra note 76, Part 2, at 787. PMA prefers to report recalls as a percentage of dollar sales: for example, $30 million sales per recall for PMA firms versus $500,000 for non-PMA firms from June 1966 to September 1969. Council on Economic Priorities, id.

79 For example, an APhA spokesman notes that an FDA inspection report recommended prosecution of the E.R. Squibb Company for "operating under conditions whereby their entire output is open to question." Feldmann, supra note 77, at 201-202. See also Competitive Problems, supra note 76, Part 2. FDA also recommended closing Sterling Drug's plant in Rensselaer, New York. Feldmann, id. at 202. A 1971 recall of an Abbott Laboratories product reportedly was associated with 50 deaths. Feldmann, id. See appendix of recalls provided by Kennedy, supra note 71. The Council on Economic Priorities, supra note 78, at 46, reported the following recall record of 16 major manufacturers:

Company	Recalls	Recalls/$100 Million Sales	Rank
Hoffmann-LaRoche	3	1.1	1
American Home Products	15	6.8	5
Merck	22	10.7	11
Eli Lilly	9	4.8	4
CIBA-Geigy	4	3.0	3
Warner-Lambert	10	8.2	9
Smith Kline & French	2	1.7	2
Squibb	10	9.1	10
Chas. Pfizer & Co.	19	18.0	15

(Footnote Continued)

involve many more units than do those of smaller generic firms, a more accurate comparison might report the number of units recalled per sales dollar. Even with this comparison, it is also necessary to define the universe of drugs and recalls to be considered.

Eli Lilly, for example, recently issued a study of FDA recalls and other drug quality data from January 1974 to December 1977.[80] Lilly claimed that 23 "research-intensive" firms had only 72 Class I or II recalls as compared to 280 recalls for all other firms. Based on prescription volume, Lilly claimed that other firms were seven times more likely than research-intensive firms to have recalls.

FDA has not yet completed its review of the Lilly report. Comnmissioner Kennedy, however, has criticized the report because it arbitrarily defines "research-intensive" firms and omits at least one research firm with a poor recall record; it counts large recalls, involving national and international distribution, as equivalent to small recalls, thus understating the greater adverse health impact of the larger recalls; it specifically emphasizes products not listed by FDA as therapeutically equivalent; and it measures all Class I and II recalls, most of which are not related to drug quality.[81] Commissioner Kennedy has stated:

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79 (Footnote Continued)

Bristol-Myers	17	17.9	14
Searle	7	7.8	7
Upjohn	12	14.2	12
Abbott	38	46.5	16
Burroughs-Wellcome	5	6.2	6
Schering	6	9.1	8
Sterling	7	17.8	13

Source: Compiled from Food and Drug Administration data and estimated sales figures.

Note: Recalls are for prescription drugs only, 1966-June 1973, excluding recalls for ineffectiveness. Rank is based on recalls/$100 million sales, lowest to highest.

80 Pauls & Kloer, Eli Lilly & Co., "FDA Enforcement Activities Within the Pharmaceutical Industry; Analysis of Relative Incidence," June 1, 1978.

81 Kennedy, supra note 62, at 4. See also Donald Kennedy, FDA Commissioner, Speech Presented to the National Center for Health Service Research & Development, Seattle, Washington, Sept. 21, 1978.

> The fact is that we have seen no defensible challenge to FDA's assertions about therapeutic equivalence. There may indeed be differences among drug plants, or among drug companies; but we do not believe that any analysis conducted according to the criteria I have just described will yield consistent differences between generic and brand-name firms or products. [Emphasis in original.][82]

Finally, this dispute may obscure the fact that only a small fraction of marketed products, brand or generic, have presented quality problems.[83] For example, an FDA study of results for 123 drugs assayed between 1970 and 1974 concluded that most drugs tested had a low average percentage of dosage units outside potency limits.[84] Only 4 drugs (3%) had more than five percent of the units outside the limits: these problem drugs then underwent further testing by FDA. Thus, not only does the evidence fail to show significant quality differences between brand-name and generic-name products, but it also shows the high quality of most marketed drug products.

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82 Kennedy, supra note 62, at 4.

83 40 Fed. Reg., supra note 66, at 32285.

84 Madden, et al., FDA Office of Planning and Evaluation, "A Statistical Analysis of Drug Analytical Data," November 1977.

IX.D. Will Pharmacists Select Lower-Cost Products and Pass on Cost Savings to Consumers?

Pharmacists are willing to select lower cost drug products and over time will be spurred by competition to pass on a substantial portion of these savings to consumers. As we have seen earlier,[1] numerous studies show pharmacists believe generic products are generally equivalent and should be substituted if significantly cheaper. And although drug product selection by pharmacists has been slow in starting (because of fears of increased liability and possibly counterproductive features of state laws) there is growing evidence that product selection is and will continue to increase. Finally, the evidence is that product selection by pharmacists lowers prices to consumers.

First, most pharmacists are in favor of modifying antisubstitution laws and allowing drug product selection. A nationwide poll of 1,000 pharmacists found that they overwhelmingly favored the substitution of a cheaper generic drug for a brand name product, 69 to 28 percent.[2] Similarly, the FTC study found that only 17.4 percent of the pharmacists polled preferred antisubstitution laws to drug product selection laws.[3] We also examined studies by Goldberg and by pharmaSYST that found pharmacists favor the repeal of antisubstitution laws[4] -- indicating that pharmacists at least want the option of selecting drug products. Another survey found that most pharmacists will substitute less expensive equivalent products when the savings per prescription are on the order of one or two dollars.[5]

We also know that the initial reluctance of pharmacists to select drug products may have resulted from their cautious approach to liability, physician opinion, and inopportune

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1 Ch. IV.A., supra.

2 20 Am. Med. News 5 (1977).

3 IMS America, Ltd., "A study of Pharmacists' Attitudes Towards the Generic Substitution of Drugs," (Final Report submitted to the Federal Trade Commission), July 28, 1978, at 55 ["FTC Study"].

4 See Ch. IV.A., supra.

5 Nelson, "The Saliency of Price in the Acceptance of the Pharmacist Substituting Chemically Equivalent Drugs on a Prescription," July 1973 (unpublished Ph.D. Thesis, University of Iowa) at 106-110.

provisions of state laws.[6] Evidence of the role that concern over liability and physican opinion has played was found in a 1975 study in Massachusetts.[7] Although the long term effects of these factors are not known, over time their impact may diminish with favorable experience. (For a fuller discussion see Ch. IX.E., supra, on pharmacist liability). Counterproductive provisions of state product selection laws can also discourage selection. In the first years in Michigan, for example, few pharmacists selected drug products as permitted under the modified law. Part of the problem in Michigan was the confusion over whether the consumer had to make an unsolicited request for a generic product.[8] A more important example of a counterproductive provision may be the mandatory pass-on which likely increases the paperwork costs of product selection at the same time that it undercuts the profitability of promoting and selecting less expensive products. (For a fuller discussion of the mandatory pass-on provision see Ch. X.A., Section 2(c)).

Notwithstanding an admittedly slow start in some states there exists growing evidence that product selection will catch on. According to the FTC study, significant substitution is occurring in some states.[9] For example, 72 percent of the pharmacists responding said their store's policy was either to substitute "whenever possible" or "sometimes;" only 8.6 percent said their store had a policy of "never" substituting. Moreover, 80 percent of the pharmacists polled in the FTC study believed that substitution would increase moderately to greatly over the next two years and less than two percent overall thought that substitution would decrease.[10]

The most promising reasons for the eventual widespread acceptance of drug product selection, particularly if state

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6 Siegelman "How Chains Look at Their Prescription Depts. Today," Am. Druggist, November 1977, at 6.

7 Krbec & Taubman, "Effects of the Massachusetts Drug Substitution Law on Pharmacists' Dispensing Habits", Med. Marketing & Media 42 (July 1976). See also, pharmaSYST reports, July 1976, at 3.

8 Curran, Reynolds Securities, "Multi-Source Drugs: An Acceleration in the Use of Lower Costing Substitutes?", May 13, 1977, at 7-8.

9 FTC Study, supra note 3, at 9-10, 26.

10 Id. at 17.

laws are made more effective, are the strong incentives at work.[11] Many pharmacies -- especially chains -- are beginning actively to promote generic products.[12] No doubt the initial attraction of product selection is the lower acquisition cost of many unbranded products. As we saw in the benefits section the difference in price can be tremendous, often more than 100 percent.[13] These lower acquisition costs[14] can both reduce inventory costs and by lowering retail prices attract greater sales volume. (For a fuller discussion see Chapter IV. B.) Moreover, in the beginning pharmacies may be able to earn higher profit margins (percent) on unbranded products. As this process matures, however, numerous pharmacies competing to offer consumers generic products should lead to effective price competition. Indeed, a survey of pharmacy leaders revealed that 95 percent believed that consumer pressure and price competition will provide the most encouragement to engage in product selection.[15]

Finally, to persuade consumers to buy generic products pharmacies will have to pass on some of their cost savings.[16] In fact, contrary to the claims of some opponents,[17] where it has

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11 Reynolds Securities, supra note 6, at 6-16.

12 See, e.g., Giant Pharmacy Advertisements in The Washington Post, July 19, 1978, at A-7 and July 12, 1978, at A-10 and A-11; Reynolds Securities, supra note 6, at 9-10.

13 Ch. VIII., supra.

14 A study of the Massachusetts law found that 63 percent of pharmacists felt that the state formulary lowered acquisition costs. Krbec & Taubman, supra note 7, at 44.

15 pharmaSYST reports, July 1976, at 3.

16 See Giant ads, supra note 11.

17 For example, William B. Patton, Assistant General Counsel of the Pharmaceutical Manufacturers Association testified before Congress that a substitution law in Saskatchewan, Canada led to a 19 percent price increase where substitution occurred. "Hearings on H.R. 882, H.R. 884," Before the Subcomm. on Consumer Protection and Finance, Comm. on Interstate and Foreign Commerce, U. S. House of Rep., 94th Cong., 2d. Sess., Serial No. 94-153 Apr. 22, 1976, at 301. Elsewhere this claim of a 19 percent price increase in Saskatchewan was coupled with the assertion that pharmacists' malpractice insurance also increased. Letter to Peter D. Holmes, FTC, from Francis A. Davis, M.D., Editor, Private Prac., May 10, 1977, at 7. Both of these claims have been found to

(Footnote Continued)

occurred drug product selection has lowered prices.[18] For example, in Michigan substitution produced a 20 percent savings ($1.15) per prescription and in Wisconsin the savings were 17 percent

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17 (Footnote Continued)

be misleading or unsubstantiated. Professor Tindall is one of the authors of the study on which both claims rely. The statement that prices increased by 19 percent, he believes is misleading because

> it leaves out the fact that the number of tablets per prescription decreased from 1971 to 1972 as a result of a government prescriber awareness program. Because virtually all Canadian pharmacists use a fixed fee rather than a markup system, that fee is spread over a smaller number of tablets, so that the increase was 19% per tablet.

Telephone conversation between Peter D. Holmes, FTC and Professor William Tindall, Creighton University School of Pharmacy, Omaha, Nebraska, June 1, 1977. See also Tindall, Hunter, & Kotzan, "A Quantitative Analysis of Antisubstitution Repeal," Med. Marketing & Media, May 1975, at 20; and Illinois Consumer Advocate Office, "Analysis: An Inventory of Deceptive Advertising by Oklahoma Opponents to Generic Substitution," January 1977, at 5. Not only is the claim that prices increased misleading, but it ignores the fact that the study found a significant price reduction on substituted prescriptions (which averaged $4.06 per prescription in 1972) as compared to nonsubstituted prescriptions (which averaged $4.81 per prescription in 1972). Tindall, Hunter & Kotzan, supra at 20. Regarding any impact on the cost of malpractice insurance, Professor Tindall said,

> As nearly as I can recall there was nothing at all in the study about malpractice insurance cost. The majority of malpractice insurance in Saskatchewan comes from a group which 100% of the pharmacists join, and the premiums are minimal. In the U.S., group insurance through APhA costs $30 for $200,000 coverage ($20 ten years ago).

Tindall telephone conversation, supra.

18 Kunin & Dierks, "A Physician - Pharmacist Voluntary Program to Improve Prescription Practices," 280 New England J. Med. 1442 (1969); see also Krbec & Taubman, supra note 6, at 44.

($.87) per prescription.[19] Likewise, pharmacists polled in the FTC Study also believe drug product selection will lower prices: 74 percent indicated prices have decreased and over one-third said the savings have been between 26-50 percent.[20] (For a fuller discussion of these price savings see Ch. VII.C., supra). Eventually as the competition to provide low priced generic drug products intensifies and as more consumers become familiar with drug product selection the aggregate savings could amount to hundreds of millions of dollars.[21] The result should be that pharmacies will earn only a competitive remuneration for their promotional and retailing efforts, with most of the savings being passed on to consumers.

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19 Theodore Goldberg, Wayne State University School of Medicine, "Cost Implications of Drug Product Selection in Legislation," Presented to Invitational Dissemination Workshop on Drug Product Selection Legislation, Detroit, Michigan, Apr. 13-14, 1978.

20 FTC Study, supra note 8, at 14.

21 See Ch. VIII., supra.

IX.E. Will Drug Product Selection Increase Pharmacist Liability?

1. Professional Liability

It has been argued that drug product selection will dramatically increase the incidence of lawsuits against pharmacists. Although a large majority of pharmacists favor the concept of drug product selection, this fear of liability apparently has deterred some pharmacists from engaging in product selection in states where antisubstitution laws have been repealed.[1] Opponents have alleged that drug product selection will increase existing liability or create new forms of liability.[2] The argument has been made that

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1 See, e.g., IMS America, Ltd., "A Study of Pharmacist' Attitudes Towards the Generic Substitution of Drugs," Final Report Submitted to the Federal Trade Commission, July 28, 1978. This survey shows that many pharmacists fear that drug product selection increases their risk of malpractice lawsuits. A majority (65.8%) of interviewed pharmacists believed that product selection laws increased the risk of suits. In the three states with provisions limiting or defining pharmacists' liability, most pharmacists were unaware of the existence of these liability provisions. See Ch. VII.C.3., supra. Other studies have reported similar concerns about liability. For example, a survey of 194 Kentucky pharmacists found that 71.6% believed that the state product selection law had increased their professional liability. Barnett, Kentucky Pharmacist, September 1977, at 8, 31. A study of 68 pharmacists in Massachusetts reported that 56% felt that state product selection law subjected them to a greater risk of being sued. Krbec & Taubman, Med. Marketing & Media, July 1976, at 40, 42. Of 100 Florida pharmacists interviewed, 77% thought they would be more liable to malpractice suits as a result of the state substitution law, and over half indicated strong concern about this possibility. Market Measures Inc., "Florida Pharmacist Substitution Study," November 1976, at 8. And 89% of 166 Minnesota pharmacists thought legal risks would discourage substitution either to "some" or a "considerable" extent. pharmaSYST reports, August 1976. Such fear and lack of understanding might stem partly from brand-name firms' public statements exaggerating the risks attending drug product selection.

2 Note, "Generic Drug Bill," 30 Ark. L.Rev. 376 (1976); Sonnenreich & Menger, "State Substitution Laws - A Lawyers View", U.S. Pharmacist, April 1977, at 19. Hammel, "Some Perspectives on the Proposed Repeal of Pharmacy's Anti-substitution Laws," Wisconsin Pharmacist, March 1972, at

(Footnote Continued)

consumers who sue pharmacists will have available to them new legal theories in negligence, express and implied warranties, and strict liability. The message of the opponents of drug product selection is that product selection creates unwarranted risks of liability, and that these risks outweigh any possible benefits. In fact, however, these claims of potential liability have been greatly exaggerated. Pharmacists' potential increase in liability appears insubstantial, whereas the potential benefit to them from drug product selection is great. Pharmacists' professional associations have enthusiastically supported drug product selection.[3]

Drug product selection under statutes permitting substitution should create no new forms of liability for pharmacists. Neither should it require pharmacists to perform their services in a manner significantly different than they have over the years, since pharmacists have already been selecting sources for generic prescriptions. Pharmacists have been, and will continue to be, held to a high standard of care in dispensing drugs.[4] In filling

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2 (Footnote Continued)

64; "Pharmacy and the Law," a film produced for Roerig-Pfizer of a Dade County, Florida, symposium on Pharmacy and the Law (final script dated Aug. 11, 1977). The symposium was co-sponsored by Roerig-Pfizer, the National Association of Retail Druggists and the Dade County Pharmaceutical Association of Florida.

3 See, e.g., American Pharmaceutical Association, A White Paper on the Pharmacist's Role in Product Selection," March 1971; Letter from Robert J. Bolger, President, National Association of Chain Drug Stores, Inc., to Peter D. Holmes, FTC, Mar. 29, 1978; Letter from Robert B. Greenberg, Legal Counsel, American Society of Hospital Pharmacists, to Peter D. Holmes, FTC, Jan. 24, 1978.

4 For example, it has been held that a pharmacist who sells a drug which is harmless in itself, but which the pharmacist knows will be used in a connection with another drug, which in combination with the first, will produce an injurious effect, has the duty to exercise a high degree of care in advising the purchaser of this injurious effect. Fuhs v. Barber, 140 Kan. 373, 36 P. 2d. 962 (1934). In a more recent case, it was alleged that a pharmacist did not adequately warn a patient about the severe side effects of a drug. The patient's injury allegedly occurred after excessive use of the product. This resulted in an out-of-court settlement, in which the manufacturer and the physician, as well as the pharmacist, contributed. Tonnessen v. Paul B. Elder Co. (Docket No. 286-356, Superior Court, Santa Clara County

(Footnote Continued)

any prescription, pharmacists must dispense the prescribed product in the correct dosage and form.[5] They must use due care when labeling the container and providing instructions for use.[6] Traditional legal theory has held that they must be aware of obvious defects (such as visible contamination or decomposition) in the products they dispense, and are responsible for correctly maintaining the product while it is under their control.[7] These principles apply equally to any product dispensed, regardless of whether it is the one prescribed or a substituted generic equivalent.

Arguably, drug product selection, although probably creating no new legal bases for liability, does provide more opportunities for the pharmacist to mistakenly dispense the wrong product.[8] But similar potential liability is present whenever a pharmacist fills a generically-written prescription, a function pharmacists have been

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4 (Footnote Continued)

Mar. 8, 1974). According to some commentators, a pharmacist has a duty to warn when "dire consequences" are "likely to result" from use of a particular drug. Salisbury, "The Pharmacist's Duty to Warn the Patient of Side Effects of Drugs," J. Am. Pharm. Ass'n, February 1977, at 97.

5 See Annot., 79 A. L. R. 2d 301, 315-320 (1961). See also Potter v. Known Drug, 214 S. 2d. 198 (La. Ct. App. 1968) Watkins v. Jacobs Pharmacy Co., 48 Ga. App. 38, 171 S.E. 830 (1933).

6 See generally Prosser, The Law of Torts, § 31 (4th ed. 1971).

7 See also Howard v. Jacobs' Pharmacy Co. 189 S.E. 373, 374 (Ga. Ct. App. 1937). The court noted: "The retailer owes to the consumer the duty to supply goods packed by reliable manufacturers, and such as are without inperfections that may be discovered by an exercise of the care, skill, and experience of dealers in such products generally." However, this duty of care does not require the pharmacist to inspect drugs or medicines purchased for resale where he or she sells the products in the original sealed package. See generally "Products Liability for Prescription Drugs -- the Effect of Generic Substitution on the Consumer and the Pharmacist," 23 Syracuse L. Rev. 887, 902 (1972).

8 See Chadwick, "Physician Controlled Source Selection: The Potential Impact on Manufacturers," Remarks Prepared for Medical Service Representative Conference, Nov. 6, 1975.

performing for years without incurring additional liability. In any event, as we detail below, malpractice insurance is readily available to offset the risk of liability arising from this and other causes.

Selecting an appropriate drug source both in filling generically-written prescriptions and, more recently, prescriptions for brand-name drug products in states permitting substitution, is an integral part of the profession of pharmacy. Yet even though pharmacists have filled millions of prescriptions, (over 90 million in 1977)[9] requiring them to select an appropriate source, we are unaware of any pharmacist ever being held liable for inappropriate source selection or of any insurance claim being made against any pharmacist for product selection.[10] None

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9 Pharmacy Times, April 1978, at 41, 42.

10 Myers & Fink, "Liability Aspects of Drug Product Selection," J. Am. Pharm. Ass'n, January 1977, at 33; Telephone interviews between Mary Alice McKeen, FTC, and executives of four major insurance companies, July 11-12, 1977. Extensive legal research conducted by FTC staff members, with the aid of computers, failed to reveal a single case where a pharmacist was held liable for product selection. Pharmaceutical manufacturers and their trade associations also were unaware of any such suits against pharmacists. We asked several brand-name manufacturers and their trade associations:

> What information do you have concerning the existence or nature of any lawsuit filed within the last ten (10) years against a pharmacist for legally dispensing a chemical equivalent for a prescribed brand-name, or for selecting a chemical equivalent for a prescription written by the generic name alone?

Neither the manufacturers, the Pharmaceutical Manufacturers Ass'n, nor the National Pharmaceutical Council had information concerning any such suit. Letter from Charles F. Hagan, American Home Products Corporation, to Peter D. Holmes, FTC, June 8, 1978; Letter from R.O. Clutter, Eli Lilly, to Peter D. Holmes, FTC, Apr. 25, 1978; Letter from Hugh A. D'Andrade, Ciba-Geigy, to Peter D. Holmes, FTC, Apr. 6, 1978; Letter from David M. Winter, Hoffmann-LaRoche, to Peter D. Holmes, FTC, Mar. 22, 1978; Letter from John M. Cullen, SmithKline Corporation, to Peter D. Holmes, FTC (undated); Letter from Donald S. Brooks, Merck Sharp & Dohme, to Peter D. Holmes, FTC, Feb. 23,

(Footnote Continued)

of the major brandname manufacturers and trade associations we contacted knew of any lawsuit filed against a pharmacist for legally substituting a generic drug product for the brand prescribed or for selecting the product used to fill a generically-written prescription. Neither did the major pharmacy insurers we contacted know of any insurance claim filed against a pharmacist for generic drug substitution.

We are aware of only one lawsuit in which drug product selection appeared to be an issue. In Bichler v. Willig, suit was brought on behalf of a purchaser's child to recover for injuries allegedly caused by the prescription drug diethylstibestrol (DES).[11] The physician and drug manufacturer, as well as the pharmacist, were named defendants. The plaintiffs alleged that the physician prescribed DES by its generic name and that the defendant pharmacist decided which brand of DES to give plaintiff. The pharmacist's defense was that he merely dispensed DES pursuant to a physician's prescription and did not prepare or compound the drug himself.[12] The court held that the plaintiff could not recover from the pharmacist on a negligence theory, noting that the pharmacist could not be held liable for choosing a particular brand of the drug in the absence of a "difference" between the brand chosen and "other available brands," absent evidence of such a difference; "his choice of the particular name brand of DES cannot be classified as negligence." [Emphasis added.][13] The court also held that the pharmacist could not be held liable for a breach of an express warranty, in the absence of evidence that he gave any written or oral warranty concerning the safety or side effects of DES. A theory of implied warranty was also rejected by the court, noting that

> implied warranties are conditioned on the buyer's reliance upon the skill and judgment of the seller but when a consumer asks a druggist to fill a prescription, thus enabling him to obtain

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10 (Footnote Continued)

1978; Letter from Robert C. Johnston, E.R. Squibb & Sons, Inc., to Peter D. Holmes, FTC, Mar. 31, 1978; Letter from C. Joseph Stetler, PMA, to Peter D. Holmes, FTC, Mar. 21, 1978.

11 58 A.D. 2d 331, 397 N.Y.S. 2d 57, (App. Div. 1977).

12 Record at 12, Bichler v. Willig, 58 A.D. 2d 331, 397 N.Y.S. 2d 57 (App. Div. 1977).

13 397 N.Y.S. 2d at 58.

> a drug which is not otherwise available to the public, he does not rely on the druggist's judgment as to whether that particular drug is inherently fit for its intended purpose but rather he places that confidence to reliance in the physician who prescribed the remedy.[14]

Citing the Restatement of Torts,[15] the court also held that the pharmacist could not be held liable under a theory of strict products liability.

It has been argued that pharmacists will be subject to greater risks of liability under theories of strict liability, express and implied warranty, and negligence for drug product selection.[16] Bichler is the only case which we have found that deals with generic substitution and addresses the above theories. Although Bichler is a lower court opinion, not universally applicable, the case may serve as some indication of the way in which courts will treat drug product selection cases should they arise in the future.

Thus, in instances where a legal product selection is made, no liability has yet resulted due to product selection. Furthermore,

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14 397 N.Y.S. 2d at 59.

15 "Comment k., [of the Restatement of Torts, Second, §402A] in relevant part, provides as follows:

> 'Unavoidably unsafe products. There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs . . . Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it unreasonably dangerous . . . . The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.'" Id.

16 Supra note 2.

it appears that product selection will continue to pose little or no additional liability for pharmacists. As a spokesman for the American Society of Hospital Pharmacists has stated:

> Drug product liability based exclusively upon brand selection may arise only if an injured party established that injury was caused by the difference in the product prescribed and that dispensed, not the action of the therapeutic entity on the body . . . [W]e believe it impossible [for plaintiffs to establish this] in almost all cases . . . Given FDA's NDA procedures and bioavailability regulations, we do not perceive "product quality" as a very material or special liability problem.[17]

In any event, as the following section shows, there are ways for pharmacists to offset any liability that might be incurred.

2. Protection for the Pharmacist

Several avenues of protection exist for the pharmacist who engages in drug product selection. Professional liability insurance, offered by pharmaceutical associations as well as the private market, is available to cover the pharmacist's professional functions as well as the drugs and products he or she dispenses.[18] Premiums for such policies are extremely low. Policies providing adequate coverage can be obtained for under $50 per year.[19] Not only has professional liability insurance for pharmacists been readily available and inexpensive, but it has also remained relatively stable in terms of premium costs. This is further indication that the risk of law suits against pharmacists, even with the repeal of antisubstitution laws, remains low.[20]

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17 Letter from Robert B. Greenberg, supra note 3.

18 Beardsley & Wertheimer, "The Dynamics of Malpractice Insurance for Pharmacists," Best's Review, April 1977, at 24.

19 Id. at 25. For example, the American Pharmaceutical Association has offered a $200,000/$600,000 policy for $35/year in 1976 and $46/year in 1977.

20 > While the cost of malpractice insurance for physicians and certain other health care professionals has skyrocketed, premiums for pharmacists have remained relatively unchanged. If it is reasonable to conclude that insurance rates represent an accurate barometer of pos-

(Footnote Continued)

In addition to the various professional liability insurance plans, a number of pharmaceutical manufacturers offer liability protection to pharmacists.[21] Although liability protection policy statements vary, such statements typically represent that the manufacturers will stand behind the pharmacist to assist in the defense of a lawsuit if the pharmacist correctly dispenses a product which it distributed.[22] These policy statements are dis-

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20 (Footnote Continued)

> sible liability, it seems clear that, at least until now, the potential for malpractice actions against pharmacists has been minimal.

Berns, "Pharmacists and the Sword of Damocles," Scalpel and Quill, May 1977, at 2. See also Haddad & Fensterer, "No Liability Increases Under New York's Drug Substitution Law," Special Report to Honorable Speaker Stanley Steingut and Assemblyman Harvey L. Strelzin, New York State Assembly, July 25, 1978.

21 More than 25 pharmaceutical manufacturers offer this type of protection. For a detailed treatment of manufacturers' policies, see Fink, "Evaluating Manufacturers' Liability Protection Policies," U.S. Pharmacist, February 1978, at 10. According to a study prepared for E.R. Squibb & Sons, "liability guarantees are universally appreciated but not [every pharmacist] recognizes that even the larger generic companies offer them." [Emphasis in original.] National Analysts, "Pharmacists' Attitudes Toward Generics -- An Exploratory Study," Prepared for E.R. Squibb & Sons Inc., December 1976, at 7.

22 Joseph L. Fink III, Statement Before the Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, July 27, 1978, at 5.

The policy statement of SmithKline & French is illustrative:

> If a claim is made against a pharmacist or a pharmacist's employer as a result of the pharmacist dispensing a SK&F product, we will, subject to the following conditions, provide legal defense -- including the payment of all reasonable expenses and attorney fee -- and assume any judgment liability. This guarantee is conditioned on SK&F being promptly notified of any claim, or the service of any complaint, and the full cooperation of

(Footnote Continued)

tributed to pharmacists by state pharmaceutical associations and manufacturers' representatives. They also appear in institutional advertisements in the professional press.[23] Such offers of voluntary indemnity by pharmaceutical houses provide an added incentive to pharmacists to deal with reputable drug suppliers.

Primary responsibility in the case of drug quality ultimately rests with the drug manufacturer. Although the pharmacist has the responsiblity for being aware of gross inperfections in pharmaceutical products, should the product be supotent, superpotent or contaminated, or cause unanticipated injury, it is the manufacturer's responsibility.[24] Thus, even in cases where the pharmaceutical house has not voluntarily agreed to indemnify the pharmacist, the pharmacist can always make the manufacturer a party to any lawsuit arising out of a dispute as to drug quality and therefore avoid liability.

There are also some precautionary measures which pharmacists may take in order to protect themselves from the risk of legal liability. Pharmacists should keep abreast of developments in the pharmaceutical market. A wealth of information is available to pharmacists from drug manufacturers. Pharmaceutical literature can be consulted for a listing of drug products recalled by FDA. This should not represent any new responsiblity for the pharmacist. Furthermore, a pharmacist should know whether or not his or her state has a formulary. If a state formulary exists, and the pharmacist selects a drug product in accordance with the formulary, such action could serve as some evidence of due care in any ensuing legal action.[25]

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22 (Footnote Continued)

> the pharmacist and/or employer, including complete access to all relevant records.
>
> This protection does not apply if the claim results from any negligent, improper or illegal act or failure to act on the part of the pharmacist or employer of if the product had not been properly stored or dispensed.

Fink, supra note 20, at 13.

23 Fink, supra note 21, at 10.

24 Fink, supra note 22, at 5.

25 As one commentator has noted:

> One other area which should be considered
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> (Footnote Continued)

For pharmacists, the repeal of antisubstitution laws means a new rise in status, greater financial returns, and increased responsiblity in the patient's drug therapy regimen. With these added benefits, the pharmacist, as a professional, can be expected to assume greater legal responsiblity for the decisions which he or she makes. A legal representative for the American Pharmaceutical Association aptly summarized this point:

> It is evident that the pharmacist is uniquely qualified to perform this function [drug product selection] and he has performed and is performing it daily in a highly competent manner.
>
> The overriding issue of this whole question, is whether the pharmacist is willing to fully assume his professional role as the expert on prescription medications.
>
> I seriously doubt that any of you would consider dropping delivery service or attempting to keep people out of your pharmacy because of some possible liability situation arising. Why, then should any pharmacist be afraid to assume his professional role and make those judgments which he is professionally qualified to make for fear of possible liability or some other theoretically imagined reason?
>
> There is a certain liablity potential everytime you dispense any prescription. Brand selection does not significantly

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25 (Footnote Continued)

> in the pharmacist's role in product source selection is the increasing trend toward formulary programs which provide lists of acceptable sources of drug products. In such a situation, presumably a group of experts has surveyed available sources of supply and selected those sources deemed to be acceptable from both a quality and price standpoint. The pharmacist who relies on such expert selection likely would not be held liable for a therapeutic misadventure.

Meyers & Fink, supra note 9, at 35.

increase it. If a pharmacist is afraid to make professional decisions, perhaps he should heed the words of Harry Truman, "If you can't stand the heat -- get out of the kitchen."[26]

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26 Kamm, "The Liability of the Pharmacist in the Role of Drug Product Selector," Illinois Pharmacist, January 1971, at 22.

CHAPTER X. THE FEDERAL TRADE COMMISSION'S ROLE

A. Model Drug Product Selection Act

Measurements of the potential benefits from drug product selection (Chapter VIII, supra) demonstrate that antisubstitution laws and regulations cost consumers hundreds of millions of dollars each year by restricting price competition in the multisource prescription drug market. And an analysis of the alleged disadvantages of drug product selection (Chapter IX, supra) demonstrates that consumer benefits can be achieved through enactment of appropriate product selection laws without compromising the quality of health care.

We recommend that the Commission offer states its assistance to facilitate pharmacists' selection of lower-cost generic equivalents whenever appropriate by encouraging states to adopt the FTC-FDA jointly-endorsed Model Drug Product Selection Act, discussed below.

We make this recommendation instead of other possible recommendations for several reasons. The states have been actively replacing their antisubstitution laws with drug product selection laws. The number of state product selection laws has more than doubled during the course of our investigation, leaving only ten states with restrictive antisubstitution laws.[1] In addition, a number of states are amending their product selection laws to make them more effective. In view of this activity, we think the most appropriate use of Commission resources is to assist states in their attempts to make product selection work.

The often-cited comment of Justice Brandeis about the value of the federal system in permitting states to serve as "laboratories" for "social and economic experiments"[2] is applicable here. We have tried in this report to analyze available evidence and identify those provisions of product selection laws that work best. In doing so, we also have tried to identify those areas in which the available evidence is not conclusive. Thus, there still seems to be justification for some experimentation by the states. We do not suggest that any state whose law is working well to produce substantial consumer savings make major modifications merely to conform to the Model Act. We do think, however, that a state law that follows the principles of the Model Act will work to save consumers money and to serve the public interest.

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1 See Table 1. State Laws, Ch. VII.B., supra.

2 New State Ice Co. v. Liebmann, 285 US. 262, 280, 311 (1932) (dissenting opinion).

This section will present the provisions of the Model Act and briefly discuss the basis for each. The Model Act is based on the findings of our investigation, as documented throughout this Report. As noted, the Model Act reflects the thinking of the FDA as well as the FTC. Our attempt throughout has been to make the Model Act as simple and as self-enforcing as possible, and to minimize any regulatory intrusion into the pharmacist's management prerogatives. We believe that laws that do not adhere to those principles and are therefore cumbersome or contrary to the pharmacist's self-interest are unlikely to work well.

MODEL DRUG PRODUCT SELECTION ACT

Section 1. [DEFINITIONS.]

(a) "Established name" has the meaning given in section 502(e)(3) of the federal food, drug and cosmetic act (21 U.S.C. 352(e)(3)).

(b) "Equivalent drug product" means a drug product with the same established name, active ingredient strength, quantity and dosage form as the drug product identified in the prescription, and listed as therapeutically equivalent in the current [name of state] drug formulary.

(c) "Prescriber" means a person licensed by the state to prescribe drug products.

Section 1 adopts standard definitions of "established name" and "prescriber," and defines "equivalent drug products" in terms of chemical equivalents that have been listed in the state formulary as also being therapeutically equivalent.[3]

Section 2. [DRUG PRODUCT SELECTION.]

(a) Unless instructed otherwise by the person receiving the drug pursuant to the prescription, a pharmacist filling a prescription for a drug product prescribed by its trade or brand name may select an equivalent drug product listed in the current [name of state] drug formulary.

Section 2(a) permits rather than requires pharmacists to select lower-cost equivalents. We think that mandatory laws are both unnecessary and unworkable. They are made unnecessary by instead providing pharmacists an economic incentive to select

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3 See discussion of chemical equivalence in Ch. VI.A.4., supra.

lower-cost products (see discussion of Section 2(c) below). They are unworkable because pharmacists' resistance to such government intrusion is likely to thwart the law unless costly enforcement efforts are undertaken.[4] The FTC study, for example, found a significantly lower rate of product selection in Pennsylvania, which has a mandatory law, than in several other states with permissive laws.[5] Similarly, pharmacy surveys by two newspapers in Kentucky indicated a lack of compliance with that state's mandatory law.[6] We therefore think permissive product selection laws will produce a greater savings to consumers without unnecessary government regulation.

Section 2(a) also recognizes the right of the person receiving the drug pursuant to the prescription to insist upon the brand prescribed by the physician (see discussion of Section 2(d) below) and limits product selection to those equivalent drug products listed in the state's positive formulary (see discussion of Section 5 below). The phrase "person receiving the drug pursuant to the prescription" refers to a person (who may or may not be the actual patient) who brings the prescription to the pharmacy and receives the drug after the prescription has been filled, or to a person to whom the drug is delivered (at the pharmacy or elsewhere) after the prescription has been telephoned to the pharmacy by the prescriber.

> (b) The pharmacist shall not select an equivalent drug product if the prescriber handwrites "medically necessary" or words of the same meaning on the written prescription, or when ordering a prescription orally, the prescriber specifies that the prescribed drug product is medically necessary. The designation of medical necessity shall not be preprinted or stamped on the prescription. This subsection does not preclude a reminder of the procedure required to prohibit selection of an equivalent drug product from being preprinted on the prescription.

Section 2(b) recognizes the absolute authority of the prescriber to insist upon a particular drug source he or she judges medically necessary. The term "medically necessary" is suggested for two reasons: it is identical to the phrase required by HEW's

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4 See discussion of pharmacists' opposition to mandatory laws in Ch. VII.B.1., supra.

5 See discussion of FTC Study in Ch. VII.C.3., supra.

6 See discussion of Kentucky newspaper surveys in Ch. VII.B.1., supra.

Maximum Allowable Cost program and thus does not require that prescribers use a different term for Medicaid patients,[7] and it best describes the justification for insisting upon a more expensive product.

Numerous studies show that prescribers rarely (generally less than five percent of the time) find it necessary to use the "medically necessary" designation.[8] The Model Act's use of a positive formulary of FDA-approved drugs to assure the equivalence of substitutable products (as well as its reliance on the pharmacist's professional judgment) should make prescriber concern about the medical need for a particular brand even more infrequent.

This approach--requiring that the prescriber take a couple of seconds to handwrite "medically necessary"--works better than the use of preprinted signature lines on the prescription. Studies show that when prescribers are required (whether they have strong concerns about the medical necessity of a particular brand or not) to sign either a line designated "dispense as written" or one designated "substitution permitted," they prohibit substitution half the time or more.[9] Several studies also indicate that prescribers prohibit substitution with relatively uniform consistency for all drugs, regardless of their therapeutic category, and equally often for single-source drugs (for which no substitution is possible) as for multisource drugs and even for generically-written prescriptions (when the pharmacist must choose some brand to dispense).[10] It seems that prescribers more often exercise their "veto" because they oppose product selection as an intrusion into their professional autonomy than because of possible medical concerns about a particular drug product.[11]

Although the Model Act (and similar statutes) does not prevent the prescriber from writing "medically necessary" on every prescription, it does require an affirmative act indicating the

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7 See discussion of Maxmimum Allowable Cost program in Ch. VII.B., supra.

8 See discussion of state surveys regarding the use of the "medically necessary" designation in Ch. VII.B.3., and C., supra.

9 See discussion of state surveys regarding the use of preprinted prescription forms. Id.

10 See discussion of Delaware and Michigan studies. Id.

11 See discussion of Delaware and Michigan studies and a University of Mississippi survey of physician attitudes in Ch. VII.B.3., supra.

prescriber's conscious decision. The additional cost of an expensive brand-name product should not be imposed on the consumer without ensuring that the decision is made consciously.[12] Preprinted prescription forms are far more likely to be signed by habit on the same line initially chosen, with the initial decision being based on general support or opposition to product selection.

The American Medical Association argues[13] that physicians may fail to make the "medically necessary" designation because they are not in the "habit" of doing so. The Goldberg study in Michigan, however, provides some evidence to refute this explanation: although one might expect the influence of past habit to decrease as prescribers became more familiar with a new product selection law, the percentage of prescriptions designated "dispense as written" decreased from 6.4 percent during the first year of the Michigan law to 4.0 percent during the second year.[14]

Prescribers must be informed, of course, of the law's provision for designating a particular brand as medically necessary. The agency responsible for the state drug formulary could provide this information as part of its functions (see Section 5 below). And the section permits a prescriber concerned about forgetting the provision to preprint a reminder on the prescription. A physician survey prepared for Roche Laboratories indicates that prescriber awareness of the law's provisions may not be a problem: of 200 Florida physicians interviewed in October 1977, 99.5 percent said they knew about the 1976 Florida product selection law, and 97.0 percent also knew that the only way to prevent substitution was "to write 'medically necessary' on a prescription."[15] Although

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12 For this reason, the section prohibits the use of preprinted forms, which otherwise might be supplied to prescribers by brand-name manufacturers in an attempt to limit competition from lower-cost generics.

13 Letter from Dr. James H. Sammons, Executive Vice President, American Medical Association, to Peter Holmes, FTC, Feb. 7, 1978.

14 See discussion of Michigan study, in Ch. VII.B.3. and C.1., supra.

15 Rx/OTC, "Florida Physicians Survey: Substitution," November 1977, at 3-4. Such states as California and Colorado permit but do not require preprinted designations of medical necessity as long as they are initialed personally by the prescriber. This alternative avoids the need to enforce the required use of a particular prescription form (see discussion of the percentage of invalid prescription forms used in New York City, Ch. VII.B.3., supra). California studies show that this provision (Footnote Continued)

this study was imperfect, there is little or no contrary evidence to suggest that prescribers are unaware of the procedure required to prevent substitution. Moreover, brand-name manufacturers have substantial economic incentives to continually remind physicians of the procedure required to limit the prescription to a particular brand.

> (c) The pharmacist shall not select an equivalent drug product unless its price to the purchaser is less than the price of the prescribed drug product.

Section 2(c) requires that a pharmacist who engages in drug product selection provide some cost savings to the purchaser by dispensing a less expensive product than the brand prescribed. We do not recommend a mandatory pass-on of all cost savings to consumers, because that provision diminishes pharmacists' economic incentive to engage in product selection. By denying pharmacists additional profits for costs that may be incurred in searching for, stocking and dispensing lower-cost generics, mandatory pass-ons may even provide an economic disincentive for product selection. Many pharmacists responding to the FTC survey, especially pharmacy owners and managers, said that mandatory pass-ons of all cost savings would deter them from substituting as often as they would otherwise.[16]

The marketplace should work to ensure that pharmacists pass on a large portion of the cost savings to consumers.[17] Moreover, increased pharmacist selection of lower-cost products should eventually produce additional savings by motivating brand-name manufacturers to lower their prices to compete with less expensive generics.

Not only are mandatory pass-ons unnecessary, but they may be unworkable. It is difficult to draft language specifying the savings that must be passed on because pharmacists' pricing sys-

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15 (Footnote Continued)

has not resulted in a large number of prescriptions prohibiting product selection. See California studies cited in Ch. VII.B.3. and C.4., supra.

16 See discussion of mandatory pass-ons and the results of the FTC study in Ch. VII.B.6. and C.3., supra. For a discussion of the potential inventory savings from product selection, see Ch. IV.B., supra.

17 See discussion of retail pharmacy advertising in Ch. IX.D., supra.

tems vary and because an actual event (the sale of the dispensed product) must be compared with a hypothetical event (the sale of the brand prescribed but not dispensed).[18] To enforce and monitor pass-on provisions would require ascertaining the prices of the prescribed and dispensed drug products at the time a particular selection occurred. This determination would certainly be costly and might be impossible.[19] The fact that the FTC study found one-third to one-half of the pharmacists in states with mandatory pass-ons unaware of those provisions indicates that the mandate often may not be complied with.[20]

Although several states have limited the price of the equivalent drug product selected to the pharmacist's usual and customary retail price, we have not included a similar limitation. The purpose of the limitation is to prohibit two-tiered pricing, with one price established for the product when it is used to fill a generic prescription and a higher price charged when it is selected to fill a brand-name prescription. We think it unlikely, however, that competitive pressures will so vary in the two instances that the pharmacist will be able to charge the higher price in the second case but not the first.

> (d) The pharmacist, or the pharmacist's agent, assistant or employee shall inform the person receiving the drug pursuant to the prescription of the selection of a lower-cost equivalent drug product and of the person's right to refuse the product selected.

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18 See discussion of cost savings provisions in Ch. VII.B.6., supra.

19 See, for example, comment of a Michigan State Representative that the Attorney General's office had admitted the unenforceability of such provisions, Ch. VII.B.6., supra. For similar reasons, we do not recommend provisions limiting selection for either a brand-name prescription or a generically-written prescription to the lowest-cost product in stock. The Goldberg study's comparison of savings (14 cents per prescription) from generic prescribing in Wisconsin, which has such a provision, with the savings (74 cents per prescription) in Michigan, which does not, indicates that these provisions may be ineffective. See Ch. VII.B.6., supra. Moreover, a pharmacist can comply with such provisions merely by pricing the least expensive product in stock only a penny below the brand-name item, or by refusing to stock lower-cost products at all.

20 See Ch. VII.C.3., supra.

Section 2(d) makes the purchaser's right to insist upon the brand prescribed (see Section 2(a)) more meaningful by requiring that the person receiving the drug pursuant to the prescription[21] be notified of the selection of a lower-cost generic and of his or her right to insist instead upon receiving the brand prescribed. This notice not only alerts the purchaser to expect to pay a lower charge, but also encourages pharmacists to help educate consumers about the cost benefits of drug product selection. Responses to the FTC study indicate that the increased time spent with patients because of such provisions does not unduly burden pharmacists.[22]

The Model Act does not require that pharmacists inform the purchaser of the differences in prices of the brand prescribed and the generic dispensed because that calculation may be sufficiently burdensome to discourage product selection (the purchaser, of course, may ask the pharmacist the amount of price savings).[23] Similarly, the Model Act does not require that pharmacists notify the purchaser of the availability of a generic equivalent prior to filling the prescription because prior notice is inconvenient, particularly when the prescription is telephoned in by the physician.[24]

Section 3. [PRESCRIPTION LABEL.]

> Unless the prescriber instructs otherwise, the label for every drug product dispensed shall include the product's trade or brand name, if any, or its established name and the name of the manufacturer, packer or distributor, using abbreviations if necessary.

Section 3 requires that prescription labels include the dispensed product's name, or its generic name and the name of the manufacturer, packer or distributor.[25] The requirement applies to all prescriptions because the information is just as useful (in an emergency, for example) for generic prescriptions as for

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21 The term "person presenting the prescription" is used rather than "purchaser" to avoid any questions that might arise involving third party payers.

22 See discussion of FTC study in Ch. VII.B.4. and C.3., supra.

23 See Ch. VII.B.4., supra.

24 See Ch. VII.B.4., supra.

25 The Drug Regulation Reform Act of 1978 also would require that drug labels supplied to pharmacies identify the manufacturer of each product. See Ch. XI., infra.

substituted prescriptions. Further, the extra labeling and recordkeeping requirements imposed on substituted prescriptions should be reduced as much as possible to minimize the difference in administrative requirements between practicing drug product selection and not practicing it.

Section 4. [PRESCRIPTION RECORD.]

The pharmacy file copy of every prescription shall include the trade or brand name, if any, or the name of the manufacturer, packer or distributor of the drug product dispensed.

Section 4 requires that the file copy of all prescriptions identify the product dispensed by including its brand name or the name of its manufacturer, packer, or distributor.[26] As with labeling, the requirement applies to all prescriptions because this information should be equally necessary when a prescription is written generically as when an equivalent product is selected to fill a brand-name prescription. The FTC study indicates that these labeling and recordkeeping requirements will not unduly increase pharmacists' paperwork.[27]

Section 5. [DRUG FORMULARY.]

(a) The [state health department, board of pharmacy or drug formulary commission] shall establish and maintain by regulation a [name of state] drug formulary of equivalent drug products. The formulary shall list all drug products that the commissioner of food and drugs, United States food and drug administration, has approved as safe and effective, and has determined to be therapeutically equivalent. The formulary shall list all drug products that were not subject to premarketing approval for safety and effectiveness under the federal food, drug, and cosmetic act, that are manufactured by firms meeting the requirements of that act, are subject to pharmacopoeial standards adequate to assure product quality, and have been determined by the commissioner of food and drugs to meet any other requirements necessary to assure therapeutic equivalence. The formulary may list additional drug products that are determined by the [department, board or commission]

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26 It is unnecessary to record the generic name of the drug dispensed because its identity is provided by the brand name for which the prescription was written.

27 See Ch. VII.B.5., supra.

to meet requirements adequate to assure product quality and therapeutic equivalence.

Section 5(a) requires that a state agency (whose composition is to be determined by each state) maintain a positive formulary lising those equivalent drug products eligible for selection by pharmacists. The formulary automatically includes all drug products determined therapeutically equivalent and approved as safe and effective by FDA. It further includes all products not subject to FDA approval for safety and efficacy (drugs approved only for safety prior to 1962 and drugs marketed prior to 1938)[28] if they otherwise meet requirements FDA finds necessary to assure therapeutic equivalence.[29] FDA previously has announced that it will be providing states with a list of approved drug products that it has determined are therapeutically equivalent.[30] The section also permits the state agency to list additional drug products it determines to be therapeutically equivalent.

There are two principal reasons for recommending a drug formulary in the Model Act. First, as discussed earlier, some problems with therapeutically significant bioinequivalence have occurred in the past.[31] The number of drugs with any potential for serious bioavailability problems is relatively small (perhaps ten to fifteen percent of all drugs) but still significant. A sound law should rely on the best scientific information available to ensure that products with serious unresolved bioavailability problems are not selected. As discussed below, we think this can be done without undue cost. Second, several studies, including the one conducted for the FTC, have found the greatest degree of product selection in states with a drug formulary.[32] A researcher with the Goldberg study similarly concluded that "provision of lists

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28 See discussion of FDA premarket drug approval in Ch. VI.A.1., supra.

29 This provision avoids the problem presented by the New York formulary, which limits eligible products to those with approved new drug applications. See Ch. VII.B.2., supra.

30 Donald Kennedy, FDA Commissioner, Statement Before the Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, July 27, 1978.

31 See discussion of bioavailability in Ch. VI.A.4. and Ch. IX.C.1., supra.

32 See discussion of surveys in Ch. VII.C., supra.

(formularies) is associated with higher rates of substitution."[33] For example, that study's preliminary analysis of 1977-78 data in Wisconsin, which has a positive formulary, indicates an 18 to 20 percent rate of product selection compared to a 1.5 percent rate in Michigan, which has no formulary.[34] Based on the evidence of this and other studies,[35] it seems that the product information and guidance provided by drug formularies encourages pharmacists to engage in product selection more frequently than they might otherwise.

The recommendation of a positive formulary, listing all substitutable drugs, rather than a negative formulary, listing all nonsubstitutable drugs, is a more difficult decision. However, we think the positive formulary offers several advantages. When asked in the FTC study under which system they would substitute most often, four times as many pharmacists preferred a positive formulary as preferred a negative formulary.[36] This response

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33 Carolee DeVito, Wayne State University, "Drug Product Selection Legislation: Issues and Alternatives," Presented at the Invitational Dissemination Workshop on Drug Product Selection Legislation, Seattle, Washington, Sept. 21-22, 1978, at 11.

34 Id. at 5.

35 See FTC study, Ch. VII.C.3., supra, and Fink study of Delaware, Ch. VII.C.2., supra.

36 See discussion of FTC Study in Ch. VII.C.3., supra. Although an approximately equal number of pharmacists preferred no formulary as preferred a positive formulary, higher rates of product selection generally were reported in states with drug formularies. States without positive formularies could experiment to see if dissemination of the FDA list of equivalent drug products to all pharmacists serves much the same function as establishment of an official statewide positive formulary. States also might consider establishing an advisory formulary, but encourage its use by enacting a legal presumption that a pharmacist would not be considered negligent in substituting an equivalent drug product listed on the formulary (i.e., the pharmacist would be presumed to have exercised due care by selecting from that list). In determining the advantages and disadvantages of an advisory rather than a mandatory formulary, relevant considerations include: the likelihood under either approach of encouraging drug product selection, the likelihood under the two approaches of significant delay in listing or selecting new equivalent products as they enter the market, the likelihood under either approach of selecting inequivalent products, and the degree of the

(Footnote Continued)

indicates that formularies are most useful to pharmacists when they provide guidance in the form of a comprehensive list of substitutable products. In addition, a positive formulary can exclude the substantial number of drug products that have never been approved by FDA but still remain on the market,[37] and thus prevent their use in product selection. Finally, a positive formulary, particularly if combined with price information, potentially could be used as a comparative guide to prescription drugs. By providing a comprehensive list of available sources for each drug, such a guide might facilitate price shopping by consumers or consumer groups.[38]

Administrative costs for the establishment and maintenance of positive formularies, however, generally are greater than those for negative formularies.[39] And delay in adding new products to the positive formulary poses a potential competitive barrier. The Model Act minimizes administrative costs by relying on the FDA to supply a list of drug products that have been determined by the agency to be therapeutically equivalent. By making costly and duplicative efforts by 50 states unnecessary, FDA preparation of a single drug list ensures that the list's benefits outweigh its costs. Further, the Model Act assigns primary responsibility for determination of product equivalence to the agency that is the single best source of drug information and scientific expertise. Most states, faced with limited resources, already rely on FDA for assistance in preparing their formularies.[40] Establishment of an FDA-approved formulary of equivalent products also is consistent with the OTA Panel's recommendation of a federal compilation

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36 (Footnote Continued)

state's intrusion under either approach into matters of professional judgment.

37 See discussion of FDA premarket drug approval in Ch. VI.A.1., supra. FDA is in the process of removing these unapproved products from the market, but is likely to require several years to complete the process. It would be difficult, if not impossible, to identify and list all these products in a negative formulary.

38 The FDA drug list may in the future be combined with drug price information. See Ch. VII.B.2., supra.

39 See Letter from Patrick B. Donoho, Director of State Government Affairs, National Association of Chain Drug Stores, to Peter D. Holmes, FTC, Sept. 18, 1978.

40 See discussion of state formularies in Ch. VII.B.2., supra.

of interchangeable products[41] and with FDA's responsibilities for premarket drug approval,[42] bioequivalence requirements,[43] and Good Manufacturing Practice regulations.[44]

Finally, the Model Act authorizes the state agency to list additional products it determines to be therapeutically equivalent. This should be necessary only if the state feels that significant barriers to competition are resulting from what it perceives to be undue delay by FDA in adding new products to the formulary. To further minimize the possibility of unnecessarily impeding competition, states might wish to consider a "sunset" provision, which would eliminate the formulary after allowing some reasonable period of years for FDA to assure the therapeutic equivalence of all marketed products.

> (b) The [department, board or commission] shall provide for revision of the formulary as necessary but not less than annually.
>
> (c) The [department, board or commission] shall provide for distribution of the formulary and revisions to all pharmacies and prescribers licensed in this state and to other appropriate individuals.

Section 5(b) and (c) requires that the state agency "provide for" revision and distribution of the drug formulary. The term is intended to allow for the possibility that the board or commission might be able to arrange for the actual revision and distribution to be performed by another agency, rather than directly by the board or commission itself.

> (d) The [department, board or commission] shall assess the need and if appropriate provide for public education regarding the provisions of this act and from time to time shall monitor the effects of the

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41 See discussion of the OTA Panel's Report in Ch. IX.C.1., supra. Several scientists also have recommended establishment of a positive formulary by FDA. See Ch. IX.C.2., supra.

42 See Ch. VI.A.1., supra.

43 See Ch. VI.A.4., supra. Although the Model Act establishes a positive formulary of equivalent products, the formulary also could specifically identify those drug products FDA determines to be therapeutically inequivalent.

44 See Ch. VI.A.5., supra.

act.

Section 5(d) requires that the state agency assess the need and where appropriate provide for public education about the product selection law; for example, by examining the extent to which retail pharmacy advertising provides the necessary consumer information.[45] Most consumers are unaware of the availability of generic equivalents and of the ability of pharmacists to select a less expensive equivalent in lieu of the more expensive brand prescribed. The FTC study, for example, found that few consumers ask their pharmacists about the possibility of dispensing a lower-cost generic.[46] Particulary during the first few years of a new product selection law, it is important that consumers be informed about the cost savings provided by generic equivalents, about their right to be informed when product selection occurs, and their right to refuse the product selected. Informed consumers may encourage pharmacists to select lower-cost generic drug products more frequently.[47] Pharmacists and prescribers also need to be informed about their responsibilities under the law.

This section also requires that the state agency periodically monitor the effects of the product selection act. As noted earlier, because of the limited amount of information available there are still some unresolved questions concerning the effectiveness of certain provisions in motivating pharmacists to select generic equivalents and to provide cost savings to consumers. We therefore think it is a useful allocation of resources for each state to examine the effectiveness of whatever law it adopts in this area and to recommend modifications as necessary.

Section 6. [PHARMACIST LIABILITY.] (Optional)

A pharmacist who selects an equivalent drug product pursuant to this act assumes no greater liability for selecting the dispensed drug product than would be incurred in filling a prescription for a drug product prescribed by its established name.

Section 6 is an optional provision assuring pharmacists that their liability for product selection will not exceed the liability incurred when filling a generically-written prescription.

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45 See discussion of pharmacy advertising in Ch. IX.D., supra.

46 See discussion of FTC study in Ch. VII.B.4. and C.3., supra.

47 Two surveys of pharmacists and "pharmacy leaders" found that they expected consumer demand to be an important factor in encouraging more product selection. See Ch. VII.B.4., supra.

The results of the FTC study[48] and other surveys[49] indicates that pharmacists are concerned about the liability risks of product selection and that many therefore are deterred from selecting drug sources as frequently as they otherwise would. Yet our search has failed to identify a single lawsuit or insurance claim filed against a pharmacist for legally substituting a lower-cost generic for the prescribed brand name. Nor are we aware of any pharmacist ever being held liable for selecting the source used to fill a generically-written prescription.[50] It appears that drug product selection poses little or no additional liability for pharmacists.[51]

The FTC survey found that most pharmacists in states with provisions limiting or defining their liability for product selection were unaware of those provisions.[52] We therefore are unable to conclude that such provisions are effective in encouraging pharmacists to engage in product selection. Whether or not a state specifically addresses the liability issue in its law, it must provide objective information about liability to pharmacists, who otherwise may be presented only with misleading and exaggerated statements by some interested party.[53]

Although most liability provisions are more a restatement than a limitation of the legal standard likely to be applied by common law, the mere existence of a liability provision in the state law may serve to reassure pharmacists that they will not be subjected to an unreasonable standard. Joseph Fink, a professor at the Philadelphia College of Pharmacy and Science who has conducted the study of the Delaware product selection law and has written extensively on liability, concludes that a state law should include a liability provision:

> On balance, it is probably better for a legislative body to make a good effort to insulate or indemnify the pharmacist who engages in drug product selection to encourage cost savings

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48 See Ch. VII.C.3., supra.

49 See Ch. VII.B.4. and Ch. IX.E.1., supra.

50 See Ch. IX.E.1., supra.

51 See discussion of potential liability in Ch. IX.E., supra.

52 See Ch. VII.C.3., supra.

53 See, e.g., "Pharmacy and the Law," a Roerig-Pfizer film of a Dade County, Florida symposium on Pharmacy and the Law (final script dated Aug. 11, 1977).

than not to address the issue at all.[54]

If a liability provision is adopted, we recommend limiting the liability from product selection to that incurred in filling a generically-written prescription. Pharmacists have been filling generic prescriptions for years and may be more reassured by a reference to that familiar activity than by a law limiting the evidential impact of drug product selection (for example, a law stating that substitution shall not constitute evidence of negligence if made within the reasonable and prudent practice of pharmacy).[55]

Section 7. [ENFORCEMENT.]

Section 8. [EFFECTIVE DATE.]

Sections 7 and 8 defer to each state the determination of the appropriate enforcement provision and effective date of the Model Act.[56] Violation of pharmacy laws generally are classified as misdemeanors and cause for revocation of the violator's professional license. A private right of action, perhaps with a minimum satutory recovery, might be created to further minimize the need for state enforcement efforts.

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54 Joseph L. Fink, III, Associate Professor of Pharmacy Administration, Philadelphia College of Pharmacy and Science, Statement before the Subcommittee on Consumer Protection and Finance, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, July 27, 1978, at 6.

55 See discussion of liability provisions in Ch. VII.B.7., supra.

56 Although the Model Act is intended to apply only to community pharmacies, a state may wish to consider whether in light of its other health laws it needs to expressly exempt hospitals, nearly all of which have their own controls on source selection, from the drug product selection law.

X.B. Advertising of Generic Drug Products

Most consumers are unaware of the existence and benefits of drug product selection. This is partly because drug product selection laws are so new; however, the dearth of advertising concerning generic drugs aimed at consumers[1] exacerbates the problem. Appropriate advertising could play a significant role in educating consumers about the cost savings of generic drug products. Unfortunately, federal regulatory policy on drug advertising has played a large role in hindering the dissemination of vital information to consumers. We have worked with the Division of Drug Advertising of the Food and Drug Administration to remedy this problem.

Retailers have been presented with a dilemma under federal regulatory policy. To provide consumers with useful information, retailers either must honor certain restrictions that make the advertising cumbersome,[2] or must abandon very useful lines of advertising, such as that describing the nature of generic drug products.

The problem has arisen when retailers have named drug products in advertisements to illustrate the concept of generic drug product selection and have then gone on to make certain "representations"[3] about the named products. For example, a pharmacy advertised its generic drug program by contrasting the brand and generic names of a particular drug, and claiming that certain quality assurance procedures applied generally to its generic drug products.[4] The Division of Drug Advertising initially interpreted its regulations to require elaborate disclosures with such an advertisement on the ground that a specific named product and drug were being promoted.[5]

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1 Discussions with executives of several large pharmacy chains indicate that very little advertising occurs.

2 The Division of Drug Advertising applies to retailers the same requirements designed for "manufacturers, packers and distributors." Unlike retailers, however, these groups commonly work with substantial promotional budgets. See discussion at Ch. II., supra.

3 This term of art signifies a statement or implication about the safety or efficacy of a drug product. Prescription Drug Advertisements, 21 C.F.R. § 202.1(e) (1977).

4 See, e.g., the Giant pharmacy advertisement in The Washington Post, Mar. 16, 1977, at A19.

5 Supra note 2. Meeting between Consumers Safety Officers William V. Purvis, K.R. Feather and Thomas W. Cavanaugh, Federal Faculty Fellow Paul Hugstad of the Division of

(Footnote Continued)

That is, the retailer had to include in the ad a "brief summary"[6] of the product's side effects, contraindications and effectiveness.[7] This "brief summary" would require considerably more advertising space and, therefore, a larger promotional expenditure.

However, after examining the great consumer need for drug information with the FTC, the FDA recently announced a new policy on prescription drug advertising. J. Richard Crout, Director of FDA's Bureau of Drugs, stated[8] that advertising statements about the quality control procedures of drug sellers will not be considered to be "a representation or suggestion" concerning the drug product's safety or effectiveness and thus will not trigger any particular requirement for disclosure. This policy "will be effective until new FDA regulations are finalized."[9]

Another positive development is the proposed Drug Regulation Reform Act of 1978,[10] which if reintroduced in the next session of Congress, might remove the economic disincentive for pharmacists to advertise generic drugs and thus help consumers obtain generic drug information. The bill proposed to exempt from the disclosure requirements advertisements that name drug products in an effort to inform consumers about multisource drugs and facilitate price comparisons.[11] This proposed exemption apparently would permit retail pharmacy advertising that mentions quality control procedures as well as the names of particular drugs or drug products without triggering the full disclosure requirements. If so interpreted, we believe that this proposed exemption would resolve the pharmacist's dilemma and help inform consumers.

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5 (Footnote Continued)

Drug Advertising, and Teresa Hennessy, FTC, on Jan. 9, 1978.

6 Prescription Drugs Advertisements, 21 C.F.R. § 202.1(e) (1977).

7 Federal Food, Drug and Cosmetic Act, § 502(n), 21 U.S.C. § 352(n) (1970 & West Supp. 1977).

8 Letter to Kenneth P. Berkowitz, Counsel, Pharmaceutical Advertising Club, Inc., from J. Richard Crout, M.D., Director, FDA Bureau of Drugs, Sept. 21, 1978.

9 Id.

10 H.R. 11611, 95th Cong., 2d Sess. (1978).

11 Id. § 156(d).

Because both the FDA and the FTC are committed to facilitating drug product selection, we look forward to a resolution of this problem. We support the direction manifested by the FDA's new policy and proposed exemption for ads directed to consumers.[12] We encourage retailers to continue experimenting with advertisements designed to help consumers make informed decisions about generic drug products.

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12 The FDA and the FTC share jurisdiction over prescription drug advertising. Current food and drug law exempts the advertising of safety and efficacy information about particular drug products only from the coverage of §§ 12-17 of the Federal Trade Commission Act, sections which prohibit "false" advertising of prescription drug products. Federal Food, Drug and Cosmetic Act § 502, 21 U.S.C. § 352 (1970 & West Supp. 1977).

In 1971 the two agencies agreed to an allocation of responsibilities in regulating the advertising of food, drugs, devices and cosmetics. This allocation reflected FDA's primary responsibility to regulate the truth or falsity of prescription drug advertising, 3 Trade Reg. Rep. (CCH) ¶ 9851 (1971).

The proposed Drug Regulation Reform Act of 1978 as introduced in the last session of Congress would preserve this jurisdictional relationship. Hence, the Commission's jurisdiction over "deceptive and unfair" acts and practices in the advertising of prescription drugs in general remains intact. Federal Trade Commission Act § 5, 15 U.S.C. § 45 (1970 & Supp. V 1975).

CHAPTER XI. OTHER REMEDIAL APPROACHES

We believe that effective drug product selection laws will work to stimulate price competition in the multisource prescription drug market. A detailed analysis of alternatives to drug product selection is outside the scope of this report; however, in this section we briefly list some of the proposals most frequently suggested.

Critics of the pharmaceutical industry have proposed patent reform, principally compulsory licensing, for years. Proponents maintain that compulsory licensing, by enabling licensees to sell products still on patent, would dilute or erode the market power innovator firms establish through patent protection in conjunction with trademark registration and cross-licensing agreements.[1] At least 25 western countries[2] provide for compulsory licensing on various grounds,[3] including an adverse effect on public health or safety from the failure to license[4] or excessive market concentration from ownership of an entire group of patents.[5]

In this country, compulsory licensing has emerged primarily

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1 See, e.g., Steele, "Patent Restrictions and Price Competition in the Ethical Drugs Industry," 12 J. Indus. Econ. 198 (1967). See also, Jadlow, "Competition and 'Quality' in the Drug Industry: The 1962 Kefauver-Harris Drug Admendments as Barriers to Entry," Antitrust L. & Econ. Rev., Winter 1971-72, at 103, 106. Steele "Monopoly & Competition in the Ethical Drugs Market," 5 J. Law & Econ. 131, 161 (1962).

2 France, for example, has such a provision. Forman, The Economics of Drug Innovation 180 (J. Cooper ed. 1969). According to some commentators, countries with compulsory licensing schemes rarely apply them. Whitney, "Economics of Ethical Drug Industry: A Reply to Critics," 13 Antitrust Bull. 803, 836 (1968).

3 For additional grounds, see Mirabito, "Compulsory Patent Licensing for the United States: A Current Proposal," 57 J. Pat. Off. Soc'y 404, 420 (1975).

4 Canada, France, and the United Kingdom have such a provision. Mirabito, supra note 3, at 424.

5 Forman, supra note 2, at 178. For detailed information about patent systems in other western countries, see Evanson & Wertheimer, "Patent Licensing of Pharmaceuticals," 7 Inquiry 60 (1970); Forman, supra note 2; Steele, 5 J. Law & Econ., supra note 1, at 135 n. 12.

as a remedy in antitrust cases.[6] Congress has considered legislation to require licensing after three years of marketing a patented product and to authorize patent holders to charge royalties no greater than eight percent of the license holders' gross selling price.[7] Other proposals have included the elimination of drug product patents,[8] the denial of patent grants for molecular modifications,[9] and the reduction of the patent monopoly to five years.[10]

Because of the relationship of patent protection and trademark registration,[11] industry critics similarly have proposed trademark reform. Reformers contend that compulsory trademark licensing, for example, would effectively challenge the market power that certain trademarks gain as "first brands,"[12] which are strongly preferred by physicians to equivalent "follow-on" products.[13]

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6 Mirabito, supra note 3, at 406. F.M. Scherer, The Economic Effects of Compulsory Patent Licensing 48 (The Monograph Series in Finance and Economics 1977-2).

7 Note, "The Proposed Drug Industry Antitrust Act - Patents, Pricing, and the Public," 30 Geo. Wash. L. Rev. 875, 877 (1962). Jadlow, supra note 1, at 107.

8 Steele, 12 J. Indus. Econ., supra note 1, at 221.

9 Senator Estes Kefauver advanced this idea in 1962. R.E. McFadyen, Estes Kefauver and the Drug Industry (1973) (unpublished Ph.D. dissertation in Emory University Library).

10 Senators Javits and Williams introduced a bill not only to require licensing, but also to provide that pharmaceutical patents expire 17 years after FDA approval of the patented drugs. S. 2040, 95th Cong., 1st Sess. (1977). This latter provision would serve manufacturers who claim that part of the patent term often expires before FDA approves products for marketing. See the discussion of the role of patents in the prescription drug market at Ch. II., supra.

11 A consideration of the argument that trademark registration extends the monopoly begun by a patent grant appears at Ch. II.B., supra.

12 See Comment, "Compulsory Trademark Licensure as a Remedy for Monopolization," 26 Cath. U. L. Rev. 589 (1977).

13 For a discussion of the proposition that physicians' preferences for "first brands" as opposed to "follow-on brands" offering no therapeutic gain insulate firms from competition more

(Footnote Continued)

Commentators have suggested that the FTC compel licensing whenever trademark promotion impedes the availability of goods of the highest quality at the lowest, competitive prices,[14] or whenever excessive product differentation supplants product innovation.[15]

Trademark dedication, another possible remedy, would mean that the trademark's owner would lose all proprietary rights to its use. The trademark would then be available for use by all.[16] Trademark cancellation, on the other hand, could be initiated by a petition claiming that a mark had become an article's common descriptive name and requesting that the mark's registration be cancelled.[17] Other proposals include: requiring a trademark owner to limit use of the trademark to a fixed percentage of sales,[18] forbidding all use of a registered trademark for a limited period,[19] limiting the amount of money spent to advertise a trademark for a limited period,[20] and denying the renewal of brand-name pharmaceutical trademarks.[21]

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13 (Footnote Continued)

effectively than patents, see R. Bond & D. Lean, Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets (1977).

14 See Comment, "Abuse of Trademarks: A Proposal for Compulsory Licensing," 7 U. Mich. J. L. Reform 644, 663 (1977).

15 Id. at 665.

16 The scope of an order to license, without royalties, could be so broad that the compulsory licensing resembles trademark dedication.

17 Lanham Trademark Act §14, 15 U.S.C. §1064 (1970). The FTC recently filed a petition to cancel or restrict the trademark FORMICA. The petition alleges that this mark has become the common descriptive name for decorative plastic laminates. Trade Reg. Rep. (CCH), No. 336 (June 6, 1978).

18 See "Compulsory Trademark Licensure as a Remedy for Monopolization," supra note 12.

19 McCarthy, "Compulsory Licensing of a Trademark: Remedy or Penalty?," 67 Trademark Rep. 197, 242 (1977).

20 Id.

21 Bond & Lean, supra note 13, at 80.

Many critics have urged the simplification of established or generic drug names, arguing that if generic names were easier to remember, physicians would more likely to use them when writing prescriptions.[22] Current food and drug law[23] empowers the Secretary of HEW to determine a new name for a drug product whose official name is unduly complex or not useful.[24] In practice, HEW (through the FDA) has accepted names selected by the United States Adopted Names Council.[25] The simplification of established names could be a useful adjunct to drug product selection laws as one way to facilitate generic prescribing, and, hence, source selection by pharmacists.

Industry critics have proposed providing physicians with price and performance data. They maintain that physicians would prescribe generically if they knew that branded and generic drug products perform comparably and that generic products generally cost much less. One current attempt to provide this information is the Health Care Financing Administration's Guide to Prescription Drug Prices.[26] Other attempts include proposals to require manufacturers to publicize wholesale prices for advertised drug

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22 See, e.g., letter from Dr. Henry K. Silver to The Honorable Elizabeth Hanford Dole (March 7, 1974).

> Undoubtedly the more easily remembered name would be more likely to be prescribed.
>
> . . . I propose that as much effort be expended in choosing easy-to-remember generic names as the pharmaceutical companies expend in developing brand names. Implementation of this simple recommendation would significantly affect prescribing practice and could result in considerable financial benefit to the American public. . . .

23 Federal Food, Drug, and Cosmetic Act § 508, 21 U.S.C. § 358 (1970 & West Supp. 1977).

24 The Secretary is empowered to review official names and to request the compilers of official compendia to recommend replacements. The Secretary is further empowered to reject these recommendations and to determine replacements.

25 USAN and the USP Dictionary of Drug Names (M.C. Griffiths ed. 1976).

26 Health Care Financing Administration, Dept. of Health, Education and Welfare, Draft Rx Guide to Drug Prices (July 1978).

products;[27] and to urge physicians to learn about local pharmacy fees or markup rates.[28]

Still another proposal has been to prohibit brand-name prescribing by physicians.[29] Physicians could still prescribe the product of a specified manufacturer by, for example, writing "tetracycline hydrochloride (Lederle)" for Lederle Laboratories' "Achromycin." Proponents contend that the reform would improve medical practice:

> On too numerous occasions, we have seen patients simultaneously receiving a similar drug in two preparations of a different brand name. . . . In addition, the increasing knowledge of the effects of drug interactions makes it imperative for the physician to be acutely aware of all drugs the patient is receiving. . . . Although such errors are not frequent, prescribing by generic name would do much to stop these instances of poor therapy.[30]

Finally, reformers have proposed that all labeling and advertising of prescription drug products bear the manufacturers's name.[31] They maintain that this reform is necessary to alert

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27 Friend, "Generic Terminology and the Cost of Drugs," 209 J.A.M.A. 80, 84 (1969).

28 Id.

29 See generally, "Statement of the American Pharmaceutical Association on Drug Product Selection," Dec. 3, 1974, at 3.

In 1970, Massachusetts unsuccessfully tried to change prescribing habits by requiring physicians to include the established name on all branded prescriptions for drugs listed in the state formulary. In a 1975 study of this law's effects, 65% of interviewed pharmacists said that local physicians complied with the law 0% of the time. Krbec & Taubman, "Effect of the Massachusetts Drug Substitution Law on Pharmacists' Dispensing Habits," Med. Marketing & Media 40, 42, July 1976.

30 Azarnoff, Hunninghake & Wortman, "Prescription Writing by Generic Name and Drug Cost," 19 J. Chron. Dis. 1253, 1256 (1966).

31 For example, the Executive Director of the American Pharma-
(Footnote Continued)

professionals to the roles of brand-name and generic firms in the manufacturer and distribution of drug products. Unlike other proposals, this reform has generated little criticism. The proposed Drug Regulation Reform Act of 1978 would have required that labeling on containers and packages of prescription drugs bear the manufacturer's name; presumably this proposal will be reintroduced in the next session of Congress.[32] The PMA has publicly supported this requirement.[33] Additionally, FDA has proposed new regulations to identify the actual manufacturer of each drug product.[34]

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31 (Footnote Continued)

ceutical Association urged this in 1974. Letter from Dr. William S. Apple, Executive Director, American Pharmaceutical Association, to Dr. Alexander M. Schmidt, Commissioner, Food & Drug Administration (Apr. 12, 1974).

32 H.R. 11611, 95th Cong., 2d Sess. § 147 (1978).

33 Hearings on Competitive Problems in The Drug Industry Before the Monopoly Subcomm. of the Senate Small Business Comm., 95th Cong., 1st Sess. (1977) (statement of C. Joseph Stetler).

34 43 Fed. Reg. 45614 (1978). The proposed regulations would revoke FDA's "man in the plant" policy. See discussion of this policy in Ch. II.D.3., supra.

APPENDIX A: MEASURING THE ECONOMIC LOSS FROM MONOPOLY

The traditional approach to measuring the economic loss from monopoly is to presume an industry composed of a single firm, assume that the firm maximizes profits, and contrast the resultant price-output combination with that which would have prevailed under competition.[1] The analysis utilizes the concept of consumer (and producer) surplus, a benefit measured as the dollar amount enjoyed by consumers from purchasing a product at a price lower than that which they would be willing to pay. The smaller output, hence higher price, of monopoly causes a reduction of consumer surplus relative to competition. Conversely, consumer benefit is expanded as monopoly power is eroded. To apply this "monopoly-loss" analysis to individual brand-name drugs, it is necessary to treat each drug as an industry unto itself, along the lines suggested by Bergson.[2] This procedure seems reasonable, for where drug product selection by a pharmacist is prohibited, as in cases where a brand-name drug is prescribed and a state law forbids the substitution of any other item, the manufacturer of a drug enjoys a monopoly position. The impact of brand-name product monopoly is best visualized in Figure 1.

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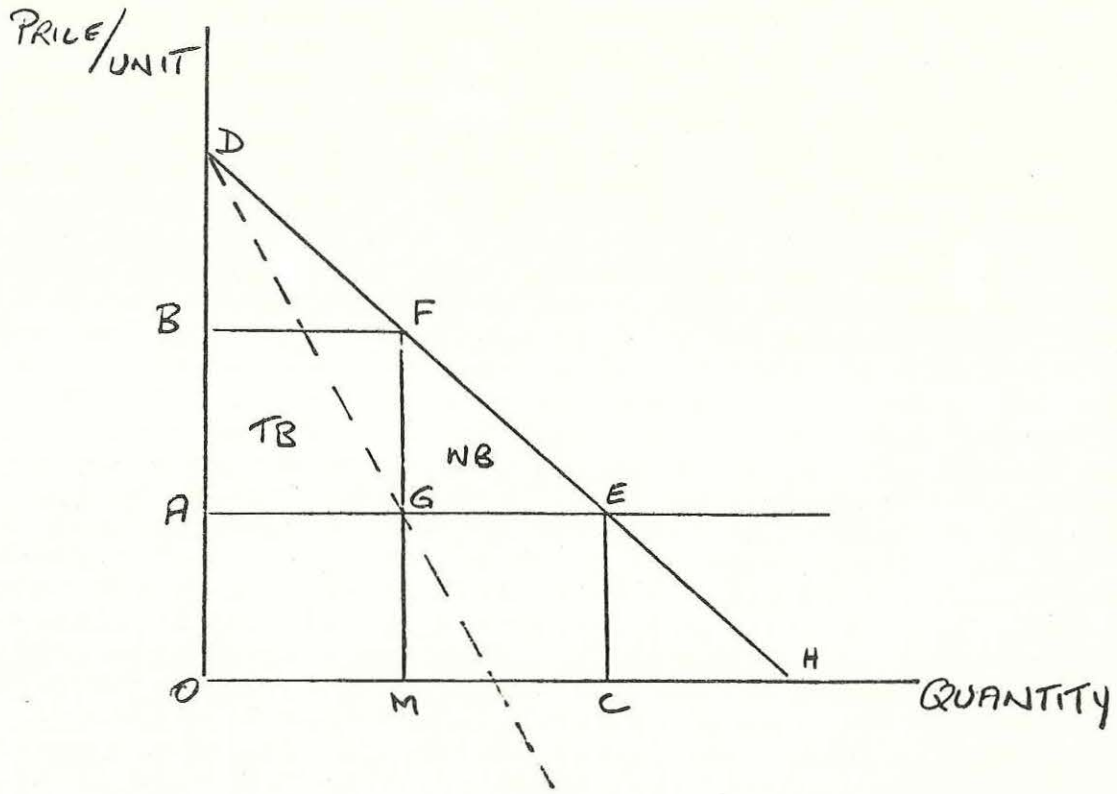
1 A considerable body of literature exists with respect to measuring the economic loss from monopoly (see, e.g., Lerner, "Monopoly and the Measurement of Monopoly Power," 24 Rev. Econ. Studies 11-32 (1956-1957), Harberger, "Monopoly and Resource Allocation," Am. Econ. Rev., XLIV, May 1954, at 77-87; Schwartzman, "The Burden of Monopoly," 68 J. Political Econ., 627-630 (1960); David R. Kamerschen, "An Estimation of the 'Welfare Losses' from Monopoly in the American Economy," unpublished Ph.D. dissertation, Michigan State University, 1964; Bergson, "On Monopoly Welfare Losses," 63 Am. Econ. Rev., 853-870 (1973); Siegfried & Thiemann, "The Welfare Cost of Monopoly: An Interindustry Analysis," J. Econ. Inquiry, Vol. XII, No. 2, June 1974, at 190-202; and Nickell & Metcalf, "Monopolistic Industries and Monopoly Profits or, Are Kellogg's Cornflakes Overpriced?" 88 Econ. J., 254-268 (June 1978). For the most part, these works are couched in a static partial equilibrium framework that takes the distribution of income as given. The erosion of monopoly power would enhance efficiency in resource allocation. Monopolists, however, would lose expected future income (extra-normal profits) to consumers. As some individuals gain and others lose from this redistribution, the net social welfare effect is hard to gauge. Economic theory has not yet resolved the question of the optimal distribution of income.

2 Bergson, id. at 853-870.

Figure 1



In developing this model, several assumptions are made: 1) consumers seek to maximize their utilities by freely choosing among goods that combination which suits their preferences, in accord with their income and the prices they face; 2) producers seek to maximize profits subject to the cost and demand conditions they face; 3) demand is linear and slopes downward to the right; and 4) unit production costs are constant over the relevant range of output.[3] In the above diagram, the demand for a drug, Brand X, is represented by the straight line DH, and indicates that consumers prefer to buy larger quantities of the drug as prices fall. The area under the demand curve, the triangle DOH, represents the total benefit, known also as consumer surplus, to consumers. If the competitive price is OA, the quantity purchased will be OC, and the benefit received by consumers is reduced to the triangle DAE. By contrast, producers receive revenues equal to the retangle OAEC, and capture a portion of the consumer surplus lost to consumers by the price increase. Armed with the concept of consumer surplus, the loss of benefit to consumers from monopoly can be easily derived.

In a competitive environment many producers would offer the drug and competition would force price into equality with marginal cost. If the competitive price equals marginal cost OA, resources are allocated efficiently and optimal economic benefits are obtained, subject to a given income distribution. If the market is monopolized, however, as might be the case for a single drug during, and perhaps for a period after, the period of patent protection, the profit-maximizing price will be OB, at which price OM units are sold. Extra-normal profits, those above that level needed to attract resources to this endeavor, are represented by the rectangle ABFG (unit profit of AB multiplied by the number of units OM = AB). If price equals marginal cost OA, however, the area of consumer benefit would be the triangle DAE, whereas under the monopoly price, the benefit is the smaller triangle DBF. Hence, the loss of benefit to consumers from monopoly is the trapezoid ABFE. Because the monopolist captures a portion of this in the form of extra-normal profits (the area ABFG), the net loss to society as a whole, commonly known as the deadweight

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3 This particular model is examined in a static partial-equilibrium framework, within which events in the market for Brand X are presumed to have no effect on other markets. Models that attempt to include interaction between different markets are general-equilibrium models. While more complete, they are more complex and require knowledge of different degrees of substitutability between the multiplicity of different goods. For purposes of this paper, the partial-equilibrium approach seems more efficient in providing insight. For a good discussion of all assumptions underlying the model, see Kamerschen, supra note 1.

monopoly loss, is the triangle GFE. We refer to these areas ABFG and GFE respectively as transfer benefit (TB) and welfare benefit (WB). If other makers of this drug were permitted access to consumers through, say, a repeal of antisubstitution laws, and if substitute generic items were offered at a competitive price OA, then drug product selection would potentially lead to a transfer of income from drug manufacturers to consumers equal to the profit rectangle TB. It is this area upon which many studies of the potential savings from drug product selection focus. A lower price from enhanced competition also leads to an increase in total drug consumption, which generates benefits manifested in the welfare benefit triangle. This welfare benefit is more difficult to calculate. By using the above model, we can estimate the transfer and welfare benefits.

Changing symbols, let the monopoly price OB = Pm and the monopolist's marginal cost OA = MC. The transfer benefit TB can be calculated by multiplying the difference between the monopoly price Pm and marginal cost MC by the monopoly quantity Qm.

$$TB = Qm\ (Pm - MC)$$

If we assume that generic substitutes are offered at price Pg equal to MC then,

$$TB = Qm\ (Pm - Pg).^{4}$$

To calculate WB requires use of the general expression

$$WB = 1/2\ Pm\ Qm\ nt^{2}$$

where n is the price elasticity of demand, and it is equal to $\frac{Pm - MC}{Pm}$ (the price divergence from marginal cost expressed as a proportion of the monopoly price).

The critical variable for determining the welfare benefit area (WB) is the price elasticity of demand, the value of which is unknown. The classic Lerner formula for the point elasticity of demand, $n = \frac{Pm}{Pm - MC}$ precludes elasticities less than unity under linear demand and profit-maximizing assumptions.[5] In the model depicted in Figure 1, the elasticity at point F (the monopoly price on the demand curve DH) may be shown to be greater than one. But, this causes difficulties with respect to an analysis of the drug market, because collapsing the monopoly price to a

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4 Use of this proxy is required because marginal cost data are unavailable.

5 The demand for Brand X of a particular generic item may be quite elastic given the presence of available substitutes, but the demand for the generic item in general is probably inelastic. The distinction is important and cautions us not to estimate the transfer benefits and then simply halve that figure to attain the deadweight loss.

competitive price would theoretically double the quantity of drugs being sold.[6]

This result does not seem realistic. Most scholars suggest that the demand for prescription drugs in general is inelastic (takes values between zero and one).

An alternative technique to estimate potential WB is to use the general formulation for WB, presume nonprofit-maximizing behavior, relax the linear demand assumption, and insert various values for n greater than zero but less than one. Clearly, the model contains a potential for error in estimating WB. The linear demand assumption is likely to result in an overestimate of the actual deadweight loss, but it is not possible to project the degree of error caused by this assumption.

Various refinements to the above model are possible. To obtain long-run estimates, an assumed time stream of annual potential benefits could be discounted in order to find the present value of that stream. Also, as applied to drugs, the attainment of maximum benefits requires that drug product selection always occurs where possible. Because pharmacists may opt to select lower-cost products in only a proportion of all possible cases, maximum benefits may not be achieved. In this event, different drug product selection rates may be used as weights to determine the sensitivity of benefits to the assumed values.

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6 Under the linear demand and profit maximization assumptions, it can be shown that

$$WB = 1/2\ (TB)$$

or alternatively

$$WB = 1/2\ (R)\ 1/n$$

where R is the monopolistic revenue. This formulation is only satisfactory for values of n greater than 1.

APPENDIX B: MISCELLANEOUS STUDIES OF ECONOMIC BENEFITS

A number of studies deserve mention. Rather than discussing in detail the methods, product scope and geographic focus, only the findings are briefly reported.

Curran[1] noted an increasing trend toward generic prescribing and suggested that the consumer savings from drug product selection were considerable. He estimated that savings ranged on the average from 20 to 40 percent of a leading brand's retail price.[2] His calculations for 45 multisource brands are reproduced in Table 1. Curran surmised an increased prospect of greater product selection over time and with it downward pressures on retail prices with resultant savings generated for consumers.

Horvitz, et al.[3] examined prescription prices of 12 drugs surveyed in 33 pharmacies in Rochester, New York. Kemp and Moyer[4] examined manufacturer catalog prices of various antibiotic drugs. The conclusions of these two papers were similar: savings may exist, but realization of these savings by consumers is not guaranteed by generic prescription writing alone. Horvitz noted that in only 35 percent of the sample comparisons did a generic prescription cost less than a brand-name prescription in the same pharmacy.[5] Kemp and Moyer observed a similar problem in examining the wide array of catalog prices on oral penicillin products: some unbranded products had list prices higher than branded products. Hence, on generically-written prescriptions where the drug dispensed could be selected from the full range of products, no guarantee existed that low-priced products would be dispensed.

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1 Curran, "Multisource Drugs: An Acceleration in the use of Lower-Costing Substitutes," Reynolds Securities Information Report, May 13, 1977.

2 Id. at 12.

3 Horvitz, Morgan, & Fleckenstein, "Savings from Generic Prescriptions: A Study of 33 Pharmacies in Rochester, New York," 82 Annals Internal Med. 601-607 (May 1975).

4 Kemp & Moyer, "Equivalent Therapy at Lower Cost," 28 J.A.M.A., May 20, 1974, at 1009-1014.

5 Horvitz, et al., supra note 3, at 604.

Table 1: POTENTIAL PERCENTAGE REDUCTION IN PATIENT COST FROM SUBSTITUTION OF SELECTED MULTISOURCE BRAND-NAME PRODUCTS

Brand Name	S.M.	S.K.L.	LED	Other	Company
Hydrodiuril 50mg (MRK)	47%	*	*		
Premarin 1.25mg (AHP)	37%	22%	*		
Librium 10mg	49%	35%	44%		
Dimetapp tab (RAH)	45%	*	*		
Lanoxin 0.25mg	M.S.	M.S.	M.S.		
Tylenol Cod 30mg (JNJ)	M.S.	M.S.	M.S.		
Empirin Cod 30 mg (JNJ)	M.S.	M.S.	M.S.		
Actifed tab	29%	*	*		
Darvon Cmpd 65 (LLY)	36%	29%	28%		
V-Cillin K 250mg	30%	21%	36%	26%	Squibb, Pfizer
Donnatal tab (RAH)	30%	*	*		
Elavil 25mg (MRK)	26%	*	*		
Benadryl 50mg (WLA)	27%	22%	25%		
Fiorinal tab	33%	*	*		
Lomotil tab (SRL)	44%	*	*		
Dilantin Na 100mg (WLA)	30%	*	*		
Duiril 500mg (MRK)	13%	*	4%		
Antivert 12.5mg (PFE)	42%	*	38%		
Ser-Ap-Es	50%	*	*		
Achromycin V 250mg	4%	M.S.	A	5%	Upjohn
Mycolog Cr (SQB)	23%	*	*		
Erythrocin (ABT)	14%	M.S.	M.S.	13%	Squibb
Isordil 10mg (AHP)	70%	*	23%		

Phenaphen Cod 30mg (RAH)	M.S.	*	*		
Pavabid 150mg (MKC)	51%	*	45%		
Synthroid 1mg	35%	*	*		
Thorazine 25mg (SKL)	32%	A	27%		
Chlor-Trimeton 12mg (SGP)	42%	A	36%		
Hydropres 50mg (MRK)	54%	*	*		
Phenergan Exp/Cod (RAH)	20%	*	18%		
Vibramycin 100mg (PFE)	21%	*	*		
Butisol Na 30mg (JNJ)	32%	*	*		
Gantrisin .5Gm	20%	17%	17%		
Darvon 65mg (LLY)	39%	29%	28%		
Sinequan 25mg (PFE)	*	*	*	15%	Pennwalt
Esidrix 50mg	57%	*	*		
Naldecon (BMY)	38%	*	*		
Phenergan VC Exp/C (AHP)	22%	*	20%		
Tofranil 25mg	45%	32%	38%		
Vasodilan (BMY)	33%	*	*		
Actifed C Exp	28%	*	*		
Benadryl Exp (WLA)	16%	*	13%		
Phenergan Exp (AHP)	24%	*	22%		
Teldrin 12mg (SKL)	46%	A	36%		
Diupres 250 (MRK)	26%	*	*		

S.M. - Spencer Mead, Div. of Barth-Spencer (AMAX-BTH)
SKL - Smith Kline Corp.
LED - Lederle Div. American Cyanamid (NYSE-ACY)
M.S. - Minimal savings
* - Not available
A - Company's own product. SKL sells Chlor-Trimeton as Teldrin.

These studies should not be construed as arguments against product

selection. The removal of impediments to product selection does create the potential for large consumer savings to be realized.

Strom, et al.[6] followed HEW's 1968 Task Force on Prescription Drugs study and estimated potential acquisition-cost savings for drugs among the leading 100 drugs of 1971. They estimated that consumers might save $224 million if these cost savings were passed on. Because the study is not reported in great detail, further evaluation is difficult. The authors claimed, however, more restrictiveness with respect to choice of substitutable products, and more rigor with respect to arithmetic calculations, than the earlier HEW study.

Swift and Ryan,[7] in studying the potential savings in one hospital from brand standardization (stocking the brand with lowest bid cost of a given chemical entity), found savings of about $35,000, or 40 percent, for 50 drugs in 1974. In addition, cost savings of about $9,300, or 70 percent would be possible from efficiencies in inventory control. Rosenberg, et al.[8] using 1970-1971 data examined the potential price effect upon the New York City Medicaid Program from generic prescribing, and concluded that savings would be $416,000, 23 percent of dollar outlays.

Savings are also revealed in data gathered and recently reported by the FTC.[9] In examining promotion and product differentiation in two prescription drug markets, orally-effective diuretics and antianginal preparations, sales and quantity data were gathered by brand, dosage form, and dosage strength. From these data, manufacturers' transaction prices were derived and compared for like generic drugs. The reproduced Tables 2 and 3

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6 Strom, Stolley & Brown, "Drug Antisubstitution Studies I: Estimation of Possible Savings by Repeal of Antisubstitution Laws," 1 Drugs in Health Care 99-103 (1974).

7 Swift & Ryan, "Potential Economic Effects of a Brand Standardization Policy in a 1000-bed Hospital," 32 Am. J. Hospital Pharmacy 1242-1250 (December 1975).

8 Rosenberg, et al., "Prescribing Patterns in the New York City Medicaid Program," 12 Medical Care 138-151 (February 1974).

9 R. S. Bond & D. F. Lean, "Sales, Promotion and Product Differentiation in Two Prescription Drug Markets," Report to the Federal Trade Commission (February 1977).

Table 2: Quantity Sold, Sales, and Average Prices of Generically Identical Brands--Oral Diuretic Drugs

	Quantity sold (000) 1968-1970	Sales (000) 1968-1970	Average price per thousand
Hydrochlorothiazide 50 mg			
Oretic (Abbott)	182,161	$ 2,143	$11.76
Esidrix (Ciba)	295,018	12,117	41.07
Hydrodiuril (Merck)	835,856	40,187	48.08
Hydrochlorothiazide 50 mg Reserpine .1 mg			
Oreticyl (Abbott)*	3,949	241	60.95
Serpasil Esidrix (Ciba)	29,577	2,079	70.28
Hydropres (Merck)	325,823	23,732	72.84
Trichlormethiazide 4 mg			
Metahydrin (Lakeside)	121,764	3,163	25.98
Naqua (Schering)	114,158	4,854	42.52
Trichlormethiazide 4 mg Reserpine .1 mg			
Metatensin (Lakeside)	15,541	692	44.54
Naquival (Schering)	26,625	1,448	54.37
Benzthiazide 50 mg			
Aquatag (Tutag)	28,956	637	22.00
Exna (Robins)	44,912	1,992	44.36

*Note: Oreticyl contains .125 mg. of deserpidine rather than .1 mg. of reserpine

Source: Federal Trade Commission, Bureau of Economics. Prescription Drug Survey

Table 3: Comparative Prices: Peritrate versus Other PETN Products, 1968-71*

	Peritrate	Others	Total number of sellers
PETN 10 mg.			50
Mean price per thousand	$18.98	$2.76	
Sales	$6,466,360	$244,817	
Quantity (thousands)	340,624	88,829	
PETN 20 mg.			61

Mean price per thousand	$27.54	$3.87
Sales	$14,340,225	$582,351
Quantity (thousands)	520,621	150,340
PETN 80 mg. S.A.		
Mean price per thousand	$56.03	$53.67
Sales	$41,828,098	$1,169,616
Quantity (thousands)	746,544	23,653

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*Dollar sales of these forms combined accounted for 31.2 percent of the sales of long-term prophylactics and 29.8 percent of all antianginal sales.

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

illustrate that great differences in average prices were visible over the 1968-1971 period. As the report noted:

> . . . the survey data do provide some insight into the magnitude of income transferred from drug buyers to drug sellers. For example, after nearly 20 years on the market, over $15 million worth of single-entity PETN was sold under the Peritrate trademark in 1971. Because the same quantity of drugs could have been purchased generically for less than $4 million, the income transferred from drug buyers to drug sellers was as much as $11.5 million for just three dosage forms of one drug in one year.[10]

The PMA provided the FTC with yet another study. In this case, the repeal of antisubstitution laws in four states, California, Michigan, Florida, and Delaware was considered.[11] Unfortunately, the PMA committee that reported this study was disbanded in 1977 and the committee's files were destroyed.

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10 The income transfer was calculated from Prescription Drug Survey data using manufacturers' transaction prices. The figures were derived for three dosage strengths of PETN: 10 mg., 20 mg., and 80 mg.-SA. Together these three dosage strengths accounted for 24.9 percent of total antianginal sales in 1971.

11 PMA Committee on the Effects of Amendments to State Antisubstitution Laws, "Preliminary Report on the Effect of the Repeal of Antisubstitution Laws in California, Michigan, Florida, and Delaware," Apr. 25, 1977.

Only an incomplete copy of the report was provided and evaluation is not possible. Apparently, retail price data were gathered for a few unidentified brands from pharmacies during monthly periods in 1975 and 1976. The report indicated that savings from drug product selection in California averaged three percent of the prescribed brand's price in 1976: the savings ranged up to 36 percent on some products, but in a couple of instances a more expensive substitute was selected. Michigan data for May 1975 showed average savings of 2 percent, ranging on individual drugs from 13 percent to a minus 6.5 percent, when a more expensive product was selected. Florida's figures were difficult to interpret, although savings amount to 52 percent on one product.[12] No results were provided for Delaware. These PMA surveys do not appear to be scientifically designed and the results must be viewed cautiously. A tentative conclusion, however, is that the selection of substitutes generally results in lower consumer drug costs.

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12 With respect to Florida, the Jack Eckerd drug store chain established that their consumers saved over $1 million from the state's drug product selection law. F-D-C Reports, June 26, 1978, at 29-30.

APPENDIX C: FTC STUDY QUESTIONNAIRE AND RESPONSES

PHARMACIST QUESTIONNAIRE

(ASK TO SPEAK TO PHARMACIST).

Hello, I'm _____ from IMS a healthcare research firm. We're conducting a national study among pharmacists concerning their attitudes toward generic substitution.

1. In what type of pharmacy do you work? (READ LIST)

AN INDEPENDENT PHARMACY	
A SMALL CHAIN PHARMACY, THAT IS NO MORE THAN 11 STORES	
A LARGE CHAIN PHARMACY THAT IS MORE THAN 11 STORES	

2. What is the average daily prescription volume in your store? That is, about how many prescriptions per day are filled by your store?

# SCRIPTS/DAILY	_____
DON'T KNOW	
NO RESPONSE	

3. Are you familiar with the generic drug substitution law, sometimes referred to as brand interchange or product selection, in _____(NAME OF STATE) which allows the retail pharmacist to substitute a generic equivalent on certain prescriptions written by brand name?

(ASK Q. #4)	YES	
(SKIP TO DEMOGRAPHICS Q. #27)	NO	

4. What, if any, is the standard policy in your store concerning generic substitution? Is it store policy to substitute...(READ LIST).

	WHENEVER POSSIBLE,	
	SOMETIMES,	
	NEVER, OR	
	IS THERE NO STANDARD POLICY?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

Now I'd like to ask you a few questions about the effects of the substitution law as you see it.

5. In about what percentage of the new prescriptions for which substitution is now possible, are you currently making substitutions?

IF "NONE" SKIP TO Q. #7	%	___
	DON'T KNOW	
	NO RESPONSE	

6. When you substitute, do you dispense the least expensive drug in stock...(READ LIST)

	ALL OF THE TIME,	
	MOST OF THE TIME,	
	SOME OF THE TIME, OR	
	NEVER	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

Now I'd like to ask some questions about the attitudes of physicians and patients toward substitution.

7. On what percentage of new prescriptions for multisource drugs would you say physicians prohibit substitution in writing?

%	___
DON'T KNOW	
NO RESPONSE	

8. Does the frequency with which physicians prohibit substitution vary by type of drug?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

9. About what percentage of patients ask you if substitution is possible?

%	___
DON'T KNOW	
NO RESPONSE	

10. About what percentage of patients refuse substitution of a less expensive drug?

%	___
DON'T KNOW	
NO RESPONSE	

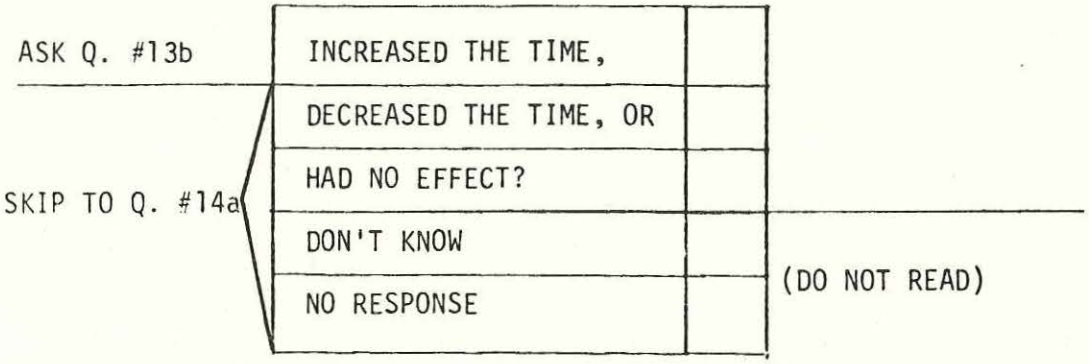
11. What effect has the law had on your relationship with physicians? Has it had...(READ LIST)

	A POSITIVE EFFECT,	
	A NEGATIVE EFFECT,	
	BOTH POSITIVE AND NEGATIVE EFFECT, OR	
	NO EFFECT?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

12. What effect has the law had on your relationship with patients? Has it had...(READ LIST)

	A POSITIVE EFFECT,	
	A NEGATIVE EFFECT,	
	BOTH POSITIVE AND NEGATIVE EFFECT, OR	
	NO EFFECT?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

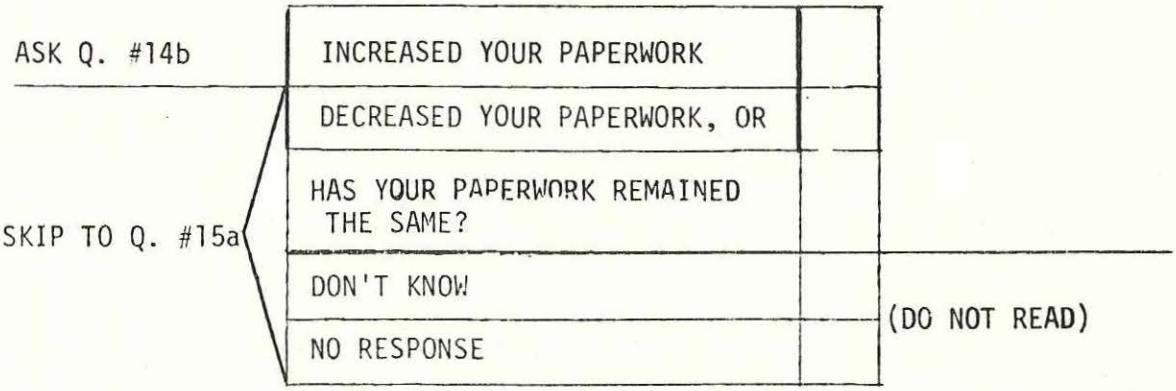
13a. What effect has the law had on the time you spend with patients? Has it...(READ LIST)



13b. Does this increase in time cause you to substitute less often than you would otherwise?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

14a. What about the effect of the law on paperwork? Has it...(READ LIST)



14b. Does this increase in paperwork cause you to substitute less often than you would otherwise?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

15a. Now, concerning your risk of being subject to liability lawsuits. Do you think the law has...(READ LIST)

ASK Q. #15b

SKIP TO Q. #16

INCREASED YOUR RISK,	
DECREASED YOUR RISK, OR	
HAD NO EFFECT?	
DON'T KNOW	
NO RESPONSE	

(DO NOT READ)

15b. Does this increased risk cause you to substitute less often than you would otherwise?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

16. What effect has the law had on your prescription inventory costs? Do you think it has...(READ LIST)

(DO NOT READ)

INCREASED YOUR COSTS,	
DECREASED YOUR COSTS, OR	
HAD NO EFFECT?	
DON'T KNOW	
NO RESPONSE	

17. What about the effect of the law on your net profit margin on prescription drugs. Has the law...(READ LIST)

	INCREASED YOUR PROFIT MARGIN,	
	DECREASED YOUR PROFIT MARGIN, OR	
	HAS YOUR PROFIT MARGIN REMAINED THE SAME?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

18a. In your opinion, what effect has the law had on the retail price paid by the patient? Has it...(READ LIST)

SKIP TO Q.#19	INCREASED THE PRICE,	
ASK Q. #18b	DECREASED THE PRICE, OR	
SKIP TO Q.#19	HAD NO EFFECT?	
	DON'T KNOW	
	NO RESPONSE	

18b. On the average, what percentage of the prescribed brand's retail price would you guess is saved by patients when substitution occurs?

%	_____
DON'T KNOW	
NO RESPONSE	

19. Since enactment of the generic substitution law would you say that the quality of information directed to you by the pharmaceutical industry about their products has...(READ LIST)

	GOTTEN BETTER,	
	GOTTEN WORSE, OR	
	REMAINED THE SAME?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

Now I'd like to ask your opinions about substitution.

20. Do you generally have sufficient information about drug products to exercise your authority to substitute?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

21a. If your state law specified that substitution would not increase the pharmacist's legal liability, would it make you...(READ LIST)

	MORE WILLING TO SUBSTITUTE,	
	LESS WILLING TO SUBSTITUTE, OR	
	WOULD IT HAVE NO EFFECT ON YOUR WILLINGNESS TO SUBSTITUTE?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

21b. Does your state law already include this kind of provision?

ASK Q. #21c	YES	
	NO	
SKIP TO Q. #22	DON'T KNOW	
	NO RESPONSE	(DO NOT READ)

21c. How would you change your substitution practices if your state law did not include this provision? Would you...(READ LIST)

	SUBSTITUTE MORE OFTEN,	
	SUBSTITUTE LESS OFTEN, OR	
	SUBSTITUTE ABOUT AS OFTEN AS YOU DO NOW?	
	DON'T KNOW	
(DO NOT READ)	NO RESPONSE	

22. Would you substitute most often if your state had...(READ LIST)

	A LISTING OF ALL PRODUCTS DEEMED SUITABLE FOR SUBSTITUTION,	
	A LISTING OF ALL PRODUCTS DEEMED NOT SUITABLE FOR SUBSTITUTION, OR	
	NO LIST, BUT LEFT EACH PHARMACIST TO DETERMINE WHICH DRUGS WERE SUITABLE FOR SUBSTITUTION?	
	DON'T KNOW	
(DO NOT READ)	NO RESPONSE	

23. (ASK IN ARKANSAS, DELAWARE, PENNSYLVANIA, WISCONSIN)
Do you think the formulary developed in your state provides adequate guarantees of product equivalence?

YES	
NO	
DON'T KNOW	
NO RESPONSE	

24a. If your state law required you to pass on to patients all savings in wholesale or acquisition costs, would it make you...(READ LIST)

	MORE WILLING TO SUBSTITUTE,	
	LESS WILLING TO SUBSTITUTE, OR	
	WOULD IT HAVE NO EFFECT ON YOUR WILLINGNESS TO SUBSTITUTE?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

24b. Does your state law already include this kind of provision?

ASK Q. #24c	YES	
	NO	
SKIP TO Q. #25	DON'T KNOW	
	NO RESPONSE	

24c. How would you change your substitution practices if your state law did not include this provision? Would you...(READ LIST)

	SUBSTITUTE MORE OFTEN,	
	SUBSTITUTE LESS OFTEN, OR	
	SUBSTITUTE ABOUT AS OFTEN AS YOU DO NOW?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

25. What is your opinion of your state's law on substitution? Do you prefer... (READ LIST)

	THE LAW AS WRITTEN,	
	A DIFFERENT SUBSTITUTION LAW, OR	
	AN ANTISUBSTITUTION LAW?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

26. In the next two years, do you feel your level of substitution will... (READ LIST)

	INCREASE GREATLY,	
	INCREASE SOMEWHAT,	
	STAY AT ITS CURRENT LEVEL,	
	DECREASE SOMEWHAT, OR	
	DECREASE GREATLY?	
(DO NOT READ)	DON'T KNOW	
	NO RESPONSE	

Finally, I'd like to ask a few questions about your pharmacy.

27. In what type of location is your pharmacy...(READ LIST)

AN URBAN LOCATION,	
A SUBURBAN LOCATION, OR	
A RURAL LOCATION?	

28. How many pharmacists are employed in your store?

# PHARMACISTS	___
DON'T KNOW	
NO RESPONSE	

29. What is your position in the store? Are you...(READ LIST)

	THE OWNER,	
	THE MANAGER, OR	
	A STAFF PHARMACIST	
(DO NOT READ)	OTHER, (SPECIFY)_____	

30. How many years have you been in pharmacy practice? (READ LIST)

# YEARS	___
DON'T KNOW	
NO RESPONSE	

Table 1

NUMBER OF PHARMACISTS (SAMPLE SIZE)
INTERVIEWED (BY STATE)

State	Total Number of Pharmacies	Sample Number of Pharmacies	Proportion of Total Pharmacies Sampled (%)
Arkansas	622	92	14.8
California	4,241	135	3.2
Delaware	150	41	27.3
Minnesota	822	121	14.7
Oregon	460	78	17.0
Pennsylvania	2,577	132	5.1
Wisconsin	960	124	12.9

Table 2

TYPE OF PHARMACY (BY STATE)

State	Independent Chain	Small Chain	Large Chain	Total
Arkansas	75 81.5%	8 8.7%	9 9.8%	92
California	99 73.3%	13 9.6%	23 17.0%	135
Delaware	29 70.7%	6 14.6%	6 14.6%	41
Minnesota	88 72.7%	14 11.6%	19 15.7%	121
Oregon	53 67.9%	6 7.7%	19 24.4%	78
Pennsylvania	92 69.7%	11 8.3%	29 22.0%	132
Wisconsin	90 72.6%	21 16.9%	13 10.5%	124
TOTAL RESPONSE	526 72.8%	79 10.9%	118 16.3%	723 100%

x^2 = 19.07 with 26 DF (sig. = 0.09)

Cramer's V = .11

Table 3

LOCATION OF PHARMACY

(BY STATE)

State	Urban	Suburban	Rural	Total
Arkansas	48 52.7%	28 30.8%	15 16.5%	91
California	77 57.0%	46 34.1%	12 8.9%	135
Delaware	16 39.0%	17 41.5%	8 19.5%	41
Minnesota	64 52.9%	24 19.8%	33 27.3%	121
Oregon	39 50.0%	30 38.5%	9 11.5%	78
Pennsylvania	63 48.1%	58 44.3%	10 7.6%	131
Wisconsin	74 59.7%	38 30.6%	12 9.7%	124
TOTAL RESPONSE	381 52.8%	241 33.4%	99 13.7%	721* 100%

x^2 = 32.29 with 18 DF (sig. = 0.01)

Cramer's V = .22

*Number of Missing Observations = 2

Table 4

NUMBER OF PHARMACISTS EMPLOYED

(BY STATE)

State	One	Two	Three or More	Total
Arkansas	20 22.0%	50 54.9%	21 23.1%	91
California	43 31.9%	52 38.5%	40 29.6%	135
Delaware	12 30.8%	21 53.8%	6 15.4%	39
Minnesota	20 16.5%	68 56.2%	33 27.3%	121
Oregon	15 19.2%	29 37.2%	34 43.6%	78
Pennsylvania	16 12.2%	76 58.0%	39 29.8%	131
Wisconsin	14 11.3%	61 49.2%	49 39.5%	124
TOTAL RESPONSE	140 19.5%	357 49.7%	222 30.9%	719* 100%

x^2 = 43.72 with 12 DF (sig. = 0.01)

Cramer's V = 0.17

Number of Missing Observations = 4

Table 5
POSITION OF RESPONDENT IN STORE
(BY STATE)

State	Owner	Manager	Staff Pharmacist	Total
Arkansas	37 40.7%	27 29.7%	27 29.7%	91
California	58 43.3%	32 23.9%	44 32.8%	134
Delaware	18 46.2%	6 15.4%	15 38.5%	39
Minnesota	43 35.8%	28 23.3%	49 40.8%	120
Oregon	33 42.9%	14 18.2%	30 39.0%	77
Pennsylvania	44 33.6%	48 36.6%	39 29.8%	131
Wisconsin	53 42.7%	22 17.7%	49 39.5%	124
TOTAL RESPONSE	286 39.9%	177 24.7%	253 35.3%	716* 100%

x^2 = 20.96 with 12 DF (sig. = 0.05)

Cramer's V = 0.06

*Number of Missing Observations = 7

Table 6

RESPONSE OF PHARMACISTS-

YEARS IN PRACTICE

(BY STATE)

	1 or 2 Years	3 to 5 Years	6 to 10 Years	11 to 15 Years	16 to 20 Years	21 to 25 Years	26 to 30 Years	Over 30 Years	Total	Mean	Median
Arkansas	6 6.7%	28 20.0%	17 18.9%	13 14.4%	6 6.7%	9 10.0%	14 15.6%	7 7.8%	90	15.178	11.750
California	16 11.9%	14 10.4%	23 17.0%	24 17.8%	19 14.1%	16 11.9%	14 10.4%	9 6.7%	135	15.750	14.550
Delaware	3 7.7%	1 2.6%	5 12.8%	2 5.1%	12 30.8%	10 25.6%	2 5.1%	4 10.3%	39	18.872	19.917
Minneasota	10 8.3%	14 11.6%	19 15.7%	18 14.9%	11 9.1%	21 17.4%	16 13.2%	12 9.9%	121	16.942	15.333
Oregon	4 5.1%	10 12.8%	10 12.8%	12 15.4%	15 19.2%	12 15.4%	7 9.0%	8 10.3%	78	17.244	17.786
Pennsylvania	12 9.2%	14 10.7%	15 11.5%	14 10.7%	21 16.0%	14 10.7%	22 16.8%	19 14.5%	131	19.237	18.333
Wisconsin	10 8.1%	25 20.2%	31 25.0%	11 8.9%	13 10.5%	8 6.5%	14 11.3%	12 9.7%	124	14.855	19.929
TOTAL RESPONSE	61 8.5%	96 13.4%	120 16.7%	94 13.1%	97 13.5%	90 12.5%	89 12.4%	71 9.9%	718* 100%	15.659	15.100

X^2 = 71.64 with 42 DF (sig. = 0.01)

Cramer's V = 0.13

*Number of Missing Observations = 5

Table 7

RESPONSE OF PHARMACISTS -

SEX (BY STATE)

State	Male	Female	Total
Arkansas	87 94.6%	5 5.4%	92
California	126 93.3%	9 6.7%	135
Delaware	39 95.1%	2 4.9%	41
Minnesota	115 95.0%	6 5.0%	121
Oregon	72 92.3%	6 7.7%	78
Pennsylvania	121 91.7%	11 8.3%	132
Wisconsin	118 95.2%	6 4.8%	124
TOTAL RESPONSE	678 93.8%	45 6.2%	723 100%

x^2 = 2.30 with 6 DF (sig. = 0.89)

Cramer's V = 0.06

Table 8

AVERAGE DAILY PRESCRIPTION

RATE OF PHARMACIES

(BY STATE)

State	10-50 Per Day	51-75 Per Day	76-100 Per Day	101-750 Per Day	Total	Mean	Median
Arkansas	15 17.2%	21 24.1%	26 29.9%	25 28.7%	87	98.805	89.500
California	34 28.3%	25 20.8%	28 23.3%	33 27.5%	120	101.508	79.643
Delaware	7 28.0%	5 20.0%	9 36.0%	4 16.0%	25	83.880	85.000
Minnesota	28 27.7%	28 27.7%	23 22.8%	22 21.8%	101	86.871	74.583
Oregon	15 21.7%	22 31.9%	10 14.5%	22 31.9%	69	110.333	74.750
Pennsylvania	21 20.4%	16 15.5%	24 23.3%	42 40.8%	103	117.068	99.944
Wisconsin	24 20.5%	42 35.9%	23 19.7%	28 23.9%	117	91.120	74.333
TOTAL RESPONSE	144 23.2%	159 25.6%	143 23.0%	176 28.3%	622* 100.0%	99.646	79.889

x^2 = 32.29 with 18 DF (sig. = 0.02)

Cramer's V = 0.13

*Number of Missing Observations = 101

Table 9

FAMILIARITY WITH GENERIC SUBSTITUTION LAW

(BY STATE)

State	Number In Sample	Number Claiming Familiarity
Arkansas	92	92
California	135	135
Delaware	41	41
Minnesota	121	121
Oregon	78	78
Pennsylvania	132	132
Wisconsin	124	124
TOTAL RESPONSE	723	723 (100%)

Table 10

RESPONSE OF PHARMACISTS -
STANDARD STORE POLICY ON GENERIC
SUBSTITUTION (BY STATE)

State	Substitute Whenever Possible	Substitute Sometimes	Never Substitute	No Standard Policy	Total
Arkansas	9 10.2%	41 46.6%	11 12.5%	27 30.7%	88
California	38 28.4%	67 50.0%	6 4.5%	23 17.2%	134
Delaware	24 60.0%	12 30.0%	0 0.0%	4 10.0%	40
Minnesota	11 9.2%	62 51.7%	19 15.8%	28 23.3%	120
Oregon	13 16.9%	46 59.7%	2 2.6%	16 20.8%	77
Pennsylvania*	30 24.0%	51 40.8%	17 13.6%	27 21.6%	125
Wisconsin	74 59.7%	33 26.6%	6 4.8%	11 8.9%	124
TOTAL RESPONSE	199 28.1%	312 44.1%	61 8.6%	136 19.2%	708** 100%

*State law mandates that substitution be made "whenever possible."

X^2 = 126.21 with 12 DF (sig.= 0.01)

**Number of Missing Observations = 15

Cramer's V = 0.30

Note: For statistical reasons, the categories of "substitute sometimes" and "never substitute" were combined in calculating the chi-square and phi statistics.

Table 11

RESPONSE BY PHARMACISTS -

NEW PRESCRIPTIONS NOW INVOLVING

SUBSTITUTION (BY STATE)

State	Less than 5%	6-10%	11-25%	26-50%	50-100%	Total	Mean	Median
Arkansas	45 54.9%	17 20.7%	10 12.2%	7 8.5%	3 3.7%	82	11.768	5.233
California	27 22.1%	24 19.7%	30 24.6%	16 13.1%	25 20.5%	122	29.074	19.800
Delaware	3 8.1%	5 13.5%	9 24.3%	10 27.0%	10 27.0%	37	42.649	39.500
Minnesota	58 50.4%	22 19.1%	16 13.9%	9 7.8%	10 8.7%	115	16.078	5.476
Oregon	24 32.9%	20 27.4%	12 16.4%	13 17.8%	4 5.5%	73	19.014	10.083
Pennsylvania	57 46.0%	18 14.5%	21 16.9%	14 11.3%	14 11.3%	124	20.121	9.500
Wisconsin	14 12.1%	19 16.4%	17 14.7%	21 18.1%	45 38.8%	116	44.147	45.500
TOTAL RESPONSE	228 34.1%	125 18.7%	115 17.2%	90 13.5%	111 16.6%	669* 100.0%	25.326	10.336

x^2 = 136.83 with 24 DF (sig. = 0.01)

Cramer's V = 0.23

*Number of Missing Observations = 54

Table 12

RESPONSE OF PHARMACISTS -

AMOUNT OF TIME LEAST EXPENSIVE DRUG

IS DISPENSED (BY STATE)

State	Dispense Least Expensive Drug: All of the Time	Most of the Time	Some of the Time	Never	Total
Arkansas	19 24.1%	31 39.2%	23 29.1%	6 7.6%	79
California	59 45.4%	35 26.9%	31 23.8%	5 3.8%	130
Delaware	13 34.2%	14 36.8%	9 23.7%	2 5.3%	38
Minnesota	34 32.7%	32 30.8%	34 32.7%	4 3.8%	104
Oregon	39 51.3%	14 18.4%	16 21.1%	7 9.2%	76
Pennsylvania	42 36.8%	21 18.4%	32 28.1%	19 16.7%	114
Wisconsin	48 41.7%	25 21.7%	33 28.7%	9 7.8%	115
TOTAL RESPONSE	254 38.7%	172 26.2%	178 27.1%	52 7.9%	656* 100%

x^2 = 43.00 with 18 DF (sig. = 0.01)

Cramer's V = 0.15

*Number of Missing Observations = 67

Table 13

RESPONSE OF PHARMACISTS -

PRESCRIPTIONS FOR WHICH PHYSICIANS

PROHIBIT SUBSTITUTION IN WRITING

(BY STATE)

State	Less than 5%	6-10%	11-25%	26-50%	50-100%	Total	Mean	Median
Arkansas	46 54.8%	11 13.1%	11 13.1%	5 6.0%	11 13.1%	84	18.536	5.136
California	96 75.0%	19 14.8%	8 6.3%	5 3.9%	0 0.0%	128	5.758	1.411
Delaware	1 2.8%	5 13.9%	8 22.2%	15 41.7%	7 19.4%	36	38.972	31.000
Minnesota	78 67.8%	17 14.8%	8 7.0%	6 5.2%	6 5.2%	115	10.783	2.292
Oregon	57 79.2%	8 11.1%	5 6.9%	0 0.0%	2 2.8%	72	6.167	1.470
Pennsylvania	11 9.2%	11 9.2%	12 10.0%	26 21.7%	60 50.0%	120	55.567	50.500
Wisconsin	85 72.0%	14 11.9%	11 9.3%	7 5.9%	1 0.8%	118	8.136	4.571
TOTAL RESPONSE	374 55.6%	85 12.6%	63 9.4%	64 9.5%	87 12.9%	673* 100.0%	19.330	5.079

x^2 = 308.10 with 18 DF (sig. = 0.01)

Cramer's V = 0.39

*Number of Missing Observations = 50

Note: For statistical reasons, the categories of "26-50%" and "50-100%" were combined in calculating the chi-square and phi statistics.

Table 14

RESPONSE OF PHARMACISTS -
VARIATION OF PROHIBITION FREQUENCY
BY DRUG TYPE (BY STATE)

State	Varies by Drug	Does Not Vary by Drug	Total
Arkansas	39 45.3%	47 54.7%	86
California	52 42.6%	70 57.4%	122
Delaware	23 56.1%	18 43.9%	41
Minnesota	55 50.5%	54 49.5%	109
Oregon	32 42.1%	44 57.9%	76
Pennsylvania	81 64.8%	44 35.2%	125
Wisconsin	58 52.7%	52 47.3%	110
TOTAL RESPONSE	340 50.8%	329 49.2%	669* 100%

x^2 = 17.02 with 6 DF (sig. = 0.01)

Cramer's V = 0.16

*Number of Missing Observations = 54

Table 15

RESPONSE OF PHARMACISTS -

PATIENTS WHO ASK IF

SUBSTITUTION IS POSSIBLE

(BY STATE)

State	Less than 5%	6-10%	11-25%	26-50%	50-100%	Total	Mean	Median
Arkansas	68 73.9%	13 14.1%	6 6.5%	3 3.3%	2 2.2%	92	6.326	1.157
California	64 48.5%	38 28.8%	14 10.6%	13 9.8%	3 2.3%	132	11.879	9.553
Delaware	13 33.3%	9 23.1%	10 25.6%	6 15.4%	1 2.6%	39	17.303	10.222
Minnesota	87 73.1%	20 16.8%	9 7.6%	2 1.7%	1 0.8%	119	5.924	3.667
Oregon	45 57.7%	16 20.5%	14 17.9%	3 3.8%	0 0.0%	78	8.769	5.071
Pennsylvania	76 58.5%	19 14.6%	21 16.2%	10 7.7%	4 3.1%	130	11.577	5.000
Wisconsin	62 50.4%	30 24.4%	19 15.4%	11 8.9%	1 0.8%	123	11.715	5.481
TOTAL RESPONSE	415 58.2%	145 20.3%	93 13.0%	48 6.7%	12 1.7%	713* 100.0%	10.042	5.063

x^2 = 49.02 with 12 DF (sig. = 0.00)

Cramer's V = 0.19

*Number of Missing Observations = 10

Note: For statistical reasons, the categories of "26-50% and "50-100%" were combined in calculating the chi square and Cramer's V statistics.

Table 16

RESPONSE OF PHARMACISTS -

PATIENTS WHO REFUSE

SUBSTITUTION

(BY STATE)

State	Less than 5%	6-10%	11-25%	26-50%	50-100%	Total	Mean	Median
Arkansas	65 77.4%	8 9.5%	5 6.0%	5 6.0%	1 1.2%	84	6.583	0.500
California	87 66.9%	19 14.6%	9 6.9%	11 8.5%	4 3.1%	130	10.054	2.214
Delaware	28 73.7%	5 13.2%	2 5.3%	2 5.3%	1 2.6%	38	8.421	2.500
Minnesota	91 78.4%	8 6.9%	6 5.2%	8 6.9%	3 2.6%	116	7.819	0.714
Oregon	58 80.6%	5 6.9%	5 6.9%	1 1.4%	3 4.2%	72	7.250	1.200
Pennsylvania	86 72.3%	7 5.9%	5 4.2%	10 8.4%	11 9.2%	119	13.824	1.208
Wisconsin	68 56.7%	20 16.7%	15 12.5%	12 10.0%	5 4.2%	120	12.858	4.833
TOTAL RESPONSE	483 71.1%	72 10.6%	47 6.9%	49 7.2%	28 4.1%	679* 100.0%	10.010	1.397

x^2 = 26.90 with 12 DF (sig. = 0.01)

Cramer's V = 0.14

*Number of Missing Observations = 44

Note: For statistical reasons, the categories of "26-50%" and "50-100%" were combined in calculating the chi square and Cramer's V statistics.

Table 17

RESPONSE OF PHARMACISTS -

EFFECT OF LAW ON PHYSICIAN-PHARMACIST RELATIONS

(BY STATE)

State	Positive Effect	No effect/Both Positive & Negative Effect	Negative Effect	Total
Arkansas	17 18.7%	66 72.5%	8 8.8%	91
California	37 27.4%	97 71.9%	1 0.7%	135
Delaware	11 27.5%	28 70.0%	1 2.5%	40
Minnesota	22 18.2%	96 79.3%	3 2.5%	121
Oregon	10 12.8%	65 83.3%	3 3.8%	78
Pennsylvania	16 12.1%	108 81.8%	8 6.1%	132
Wisconsin	22 17.7%	98 79.0%	4 3.2%	124
TOTAL RESPONSE	135 18.7%	558 77.4%	28 3.9%	721* 100%

X^2 = 14.38 with 6 DF (sig. = 0.03)

Cramer's V = 0.14

*Number of Missing Observations = 2

Note: For statistical reasons, the categories of "No effect/Both Positive & Negative Effect" and "Negative Effect" were combined in calculating the chi square and Cramer's V statistics.

Table 18

RESPONSE OF PHARMACISTS -

EFFECT OF LAW ON PATIENT-PHARMACIST RELATIONS

(BY STATE)

State	Positive Effect	No Effect/ Both Positive Negative Effect	Negative Effect	Total
Arkansas	35 39.3%	51 57.3%	3 3.4%	89
California	98 72.6%	35 25.9%	2 1.5%	135
Delaware	24 60.0%	14 35.0%	2 5.0%	40
Minnesota	60 50.0%	54 45.0%	6 5.0%	120
Oregon	47 60.3%	28 35.9%	3 3.8%	78
Pennsylvania	41 31.3%	85 64.9%	5 3.8%	131
Wisconsin	75 60.5%	44 35.5%	5 4.0%	124
TOTAL RESPONSE	380 53.0%	311 43.4%	26 3.6%	717* 100%

X^2 = 57.91 with 12 DF (sig. = 0.01)

Cramer's V = 0.28

* Number of Missing Observations = 6

Note: For statistical reasons, the categories of "No Effect/Both Positive & Negative Effect" and "Negative Effect" were combined in calculating the chi square and Cramer's V statistics.

Table 19

RESPONSE OF PHARMACISTS -
EFFECT OF LAW ON TIME SPENT
WITH PATIENTS (BY STATE)

State	Increased Time	No Effect	Decreased Time	Total
Arkansas	34 37.0%	57 62.0%	1 1.1%	92
California	74 54.8%	60 44.4%	1 0.7%	135
Delaware	28 68.3%	13 31.7%	0 0.0%	41
Minnesota	65 53.7%	55 45.5%	1 0.8%	121
Oregon	38 48.7%	40 51.3%	0 0.0%	78
Pennsylvania	68 52.3%	61 46.9%	1 0.8%	130
Wisconsin	84 67.7%	40 32.3%	0 0.0%	124
TOTAL RESPONSE	391 54.2%	326 45.2%	4 0.6%	721* 100%

X^2 = 24.63 with 12 DF (sig. = 0.01)

Cramer's V = 0.18

*Number of Missing Observations = 2

Note: For statistical reasons, the categories of "No Effect" and "Decreased Time" were combined in calculating the chi square and Cramer's V statistics.

Table 20

DOES INCREASED TIME WITH PATIENTS CAUSE LESS SUBSTITUTION?

(BY STATE)

State	Yes	No	Total
Arkansas	4 12.5%	28 87.5%	32
California	18 24.3%	56 75.7%	74
Delaware	4 14.3%	24 85.7%	28
Minnesota	11 16.9%	54 83.1%	65
Oregon	5 13.2%	33 86.8%	38
Pennsylvania	15 22.7%	51 77.3%	66
Wisconsin	20 23.8%	64 76.2%	84
TOTAL RESPONSE	77 19.9%	310 80.1%	387* 100%

$x^2 = 5.14$ with 6 DF (sig. = 0.53)

Cramer's V = 0.12

*Number of Missing Observations = 336

Table 21

RESPONSE OF PHARMACISTS -

EFFECT OF GENERIC SUBSTITUTION LAW

ON PAPERWORK (BY STATE)

State	Increased Paperwork	Same Paperwork	Decreased Paperwork	Total
Arkansas	24 26.4%	65 71.4%	2 2.2%	91
California	38 28.1%	97 71.9%	0 0.0%	135
Delaware	14 34.1%	27 65.9%	0 0.0%	41
Minnesota	25 20.8%	94 78.3%	1 0.8%	120
Oregon	21 26.9%	56 71.8%	1 1.3%	78
Pennsylvania	27 20.8%	103 79.2%	0 0.0%	130
Wisconsin	50 40.3%	73 58.9%	1 0.8%	124
TOTAL RESPONSE	199 27.7%	515 71.6%	5 0.7%	719* 100%

χ^2 = 16.78 with 6 DF (sig. = 0.01)

Cramer's V = 0.15

*Number of Missing Observations = 4

Note: For statistical reasons, the categories of "Same Paperwork" and "Decreased Paperwork" were combined in calculating the chi square and Cramer's V statistics.

Table 22
DOES INCREASED PAPERWORK
CAUSE LESS SUBSTITUTION?
(BY STATE)

State	Yes	No	Total
Arkansas	4 17.4%	19 82.6%	23
California	9 23.7%	29 76.3%	38
Delaware	2 14.3%	12 85.7%	14
Minnesota	5 20.0%	20 80.0%	25
Oregon	1 4.8%	20 95.2%	21
Pennsylvania	10 37.0%	17 63.0%	27
Wisconsin	7 14.3%	42 85.7%	49
TOTAL RESPONSE	38 19.3%	159 80.7%	197* 100%

x^2 = 9.86 with 6 DF (sig. = 0.13)

Cramer's V = 0.22

*Number of Missing Observations = 526

Table 23

RESPONSE OF PHARMACISTS -

EFFECT OF LAW ON LIABILITY LAWSUIT

RISK (BY STATE)

State	Increased Risk	No Effect	Decreased Risk	Total
Arkansas	57 62.0%	35 38.0%	0 0.0%	92
California*	89 67.4%	43 32.6%	0 0.0%	132
Delaware	25 64.1%	13 33.3%	1 2.6%	39
Minnesota	81 68.6%	37 31.4%	0 0.0%	118
Oregon*	57 74.0%	20 26.0%	0 0.0%	77
Pennsylvania*	79 62.7%	47 37.3%	0 0.0%	126
Wisconsin	75 62.5%	45 37.5%	0 0.0%	120
TOTAL RESPONSE	463 65.8%	240 34.1%	1 0.1%	704** 100%

X^2 = 4.66 with 6 DF (sig. 0.59)

Cramer's V = 0.12

*Law limits liability in these states.

**Number of Missing Observations = 19

Note: For statistical reasons, the categories of "No Effect" and "Decreased Risk" were combined in calculating the chi square and Cramer's V statistics.

Table 24

DOES INCREASED LIABILITY RISK
CAUSE LESS SUBSTITUTION?
(BY STATE)

State	Yes	No	Total
Arkansas	32 57.1%	24 42.9%	56
California	27 30.7%	61 69.3%	88
Delaware	11 44.0%	14 56.0%	25
Minnesota	37 46.3%	43 53.8%	80
Oregon	28 50.0%	28 50.0%	56
Pennsylvania	34 44.7%	42 55.3%	76
Wisconsin	20 27.0%	54 73.0%	74
TOTAL RESPONSE	189 41.5%	266 58.8%	455* 100%

x^2 = 19.07 with 6 DF (sig. = 0.01)

Cramer's V = 0.20

*Number of Missing Observations = 268

Table 25

RESPONSE OF PHARMACISTS -

EFFECT OF LAW ON INVENTORY COSTS

(BY STATE)

State	Increased Costs	No Effect	Decreased Costs	Total
Arkansas	44 48.9%	28 31.1%	18 20.0%	90
California	60 45.1%	27 20.3%	46 34.6%	133
Delaware	27 69.2%	5 12.8%	7 17.9%	39
Minnesota	51 42.9%	35 29.4%	33 27.7%	119
Oregon	45 58.4%	23 29.9%	9 11.7%	77
Pennsylvania	74 58.7%	35 27.8%	17 13.5%	126
Wisconsin	80 65.0%	16 13.0%	27 22.0%	123
TOTAL RESPONSE	381 53.9%	169 23.9%	157 22.2%	707* 100%

x^2 = 44.11 with 12 DF (sig. = 0.01)

Cramer's V = 0.18

*Number of Missing Observations = 16

Table 26

RESPONSE OF PHARMACISTS -

EFFECT OF LAW ON NET PROFIT MARGIN

(BY STATE)

State	Increased Profit	Same Profit	Decreased Profit	Total
Arkansas	28 32.2%	47 54.0%	12 13.8%	87
California	43 34.1%	77 61.1%	6 4.8%	126
Delaware	12 35.3%	18 52.9%	4 11.8%	34
Minnesota	20 17.4%	74 64.3%	21 18.3%	115
Oregon	18 26.5%	42 61.8%	8 11.8%	68
Pennsylvania	23 20.4%	75 66.4%	15 13.3%	113
Wisconsin	35 30.7%	69 60.5%	10 8.8%	114
TOTAL RESPONSE	179 27.2%	402 61.2%	76 11.6%	657* 100%

x^2 = 23.09 with 12 DF (sig. = 0.03)

Cramer's V = 0.13

*Number of Missing Observations = 66

Table 27

EFFECT OF LAW ON RETAIL PRICE PAID
(BY STATE)

State	Increased Price	No Effect	Decreased Price	Total
Arkansas	6 6.5%	38 41.3%	48 52.2%	92
California	8 6.0%	19 14.3%	106 79.7%	133
Delaware	3 7.5%	4 10.0%	33 82.5%	40
Minnesota	4 3.4%	30 25.2%	85 71.4%	119
Oregon	5 6.5%	12 15.6%	60 77.9%	77
Pennsylvania	8 6.2%	38 29.5%	83 64.3%	129
Wisconsin	3 2.5%	9 7.5%	108 90.0%	120
TOTAL RESPONSE	37 5.2%	150 21.1%	523 73.7%	710* 100%

x^2 = 49.32 with 6 DF (sig. = 0.01)

Cramer's V = 0.26

*Number of Missing Observations = 13

Note: For statistical reasons, the categories of "No Effect" and "Decreased Price" were combined in calculating the chi square and Cramer's V statistics.

Table 28
RETAIL PRICE
SAVING WHEN SUBSTITUTION OCCURS
(BY STATE)

State	Less than 5%	6-10%	11-25%	26-50%	50-100%	Total	Mean	Median
Arkansas	44 53.7%	11 13.4%	16 19.5%	10 12.2%	1 1.2%	82	11.585	2.159
California	32 25.6%	9 7.2%	44 35.2%	38 30.4%	2 1.6%	125	20.752	20.306
Delaware	8 22.9%	0 0.0%	5 14.3%	21 60.0%	1 2.9%	35	30.857	36.250
Minnesota	37 31.9%	12 10.3%	27 23.3%	40 34.5%	0 0.0%	116	18.233	19.864
Oregon	19 25.7%	5 6.8%	21 28.4%	29 39.2%	0 0.0%	74	20.865	20.500
Pennsylvania	54 43.2%	7 5.6%	18 14.4%	43 34.4%	3 2.4%	125	19.112	14.667
Wisconsin	19 17.1%	6 5.4%	35 31.5%	46 41.4%	5 4.5%	111	26.126	25.179
TOTAL RESPONSE	213 31.9%	50 7.5%	166 24.9%	227 34.0%	12 1.8%	688* 100%	20.317	20.172

x^2 = 65.11 with 12 DF (sig. = 0.00)

Cramer's V = 0.22

*Number of Missing Observations = 55

Note: For statistical reasons, the categories of "6-10%" and 11-25%"; "26-50%" and "50-100%" were combined in calculating the chi squares and Cramer's V statistics.

Table 29

SINCE ENACTMENT, HOW HAS QUALITY OF INFORMATION CHANGED?

(BY STATE)

State	Better	Same	Worse	Total
Arkansas	52 56.5%	34 37.0%	6 6.5%	92
California	60 44.8%	66 49.3%	8 6.0%	134
Delaware	18 47.4%	19 50.0%	1 2.6%	38
Minnesota	57 47.9%	58 48.7%	4 3.4%	119
Oregon	38 48.7%	37 47.4%	3 3.8%	78
Pennsylvania	74 57.8%	51 39.8%	3 2.3%	128
Wisconsin	43 34.7%	72 58.1%	9 7.3%	124
TOTAL RESPONSE	342 48.0%	337 47.3%	34 4.8%	713* 100%

x^2 = 17.01 with 6 DF (sig. = 0.01)

Cramer's V = 0.15

*Number of Missing Observations = 10

Note: For statistical reasons, the categories of "Same" and "Worse" were combined in calculating the chi square and Cramer's V statistics.

Table 30

PHARMACIST HAS SUFFICIENT INFORMATION TO SUBSTITUTE (BY STATE)

State	Yes	No	Total
Arkansas	68 74.7%	23 25.3%	91
California	102 76.7%	31 23.3%	133
Delaware	28 73.7%	10 26.3%	38
Minnesota	92 77.3%	27 22.7%	119
Oregon	49 62.8%	29 37.2%	78
Pennsylvania	95 73.6%	34 26.4%	129
Wisconsin	79 63.7%	45 36.3%	124
TOTAL RESPONSE	513 72.1%	199 27.9%	712* 100%

x^2 = 11.18 with 6 DF (sig. = 0.08)

Cramer's V = 0.13

*Number of Missing Observations = 11

Table 31

IF STATE LAW LIMITED LIABILITY, HOW WOULD WILLINGNESS TO SUBSTITUTE CHANGE? (BY STATE)

State	More Willing	No Effect	Less Willing	Total
Arkansas	31 33.7%	58 63.0%	3 3.3%	92
California*	47 34.8%	85 63.0%	3 2.2%	135
Delaware	11 27.5%	28 70.0%	1 2.5%	40
Minnesota	38 31.7%	79 65.8%	3 2.5%	120
Oregon*	27 35.1%	48 62.3%	2 2.6%	77
Pennsylvania*	40 30.8%	85 65.4%	5 3.8%	130
Wisconsin	46 37.4%	73 59.3%	4 3.3%	123
TOTAL RESPONSE	240 33.5%	456 63.6%	21 2.9%	717** 100%

x^2 = 2.29 with 6 DF (sig. = 0.89)

Cramer's V = 0.06

*State has limited liability provision.

**Number of Missing Observations = 6

Note: For statistical reasons, the categories of "No Effect" and "Less Willing" were combined in calculating the chi square and Carmer's V statistics.

Table 32

RESPONSE OF PHARMACISTS -
AWARENESS OF EXISTENCE OF STATE PROVISION
LIMITING LEGAL LIABILITY (BY STATE)

State	Yes	No	Total
Arkansas	18 22.8%	61 77.2%	79
California*	33 28.7%	82 71.3%	115
Delaware	8 22.2%	28 77.8%	36
Minnesota	39 37.1%	66 62.9%	105
Oregon*	20 28.2%	51 71.8%	71
Pennsylvania*	41 40.6%	60 59.4%	101
Wisconsin	31 29.2%	75 70.8%	106
TOTAL RESPONSE	190 31.0%	423 69.0%	613** 100%

x^2 = 10.69 with 6 DF (sig. = 0.10)

Cramer's V = 0.13

*State has limited liability provision.

**Number of Missing Observations = 110

Table 33

IF NO LIMIT ON LIABILITY,
HOW WOULD PRACTICE CHANGE?
(BY STATE)

State	More Often	Same As Now	Less Often	Total
Arkansas	1 5.6%	10 55.6%	7 38.9%	18
California *	4 12.5%	22 68.8%	6 18.8%	32
Delaware	1 12.5%	5 62.5%	2 25.0%	8
Minnesota	2 5.1%	30 76.9%	7 17.9%	39
Oregon*	1 5.3%	14 73.7%	4 21.1%	19
Pennsylvania*	1 2.5%	28 70.0%	11 27.5%	40
Wisconsin	1 3.2%	13 41.9%	17 54.8%	31
TOTAL RESPONSE	11 5.9%	122 65.2%	54 28.9%	187** 100%

*State has limited liability provision.

**Number of Missing Observations = 536

Note: Due to cell frequencies of insufficient size to allow for meaningful statistical calculations, no statistics are presented.

Table 34

RESPONSE OF PHARMACISTS -

MOST DESIRABLE TYPE OF FORMULARY

(BY STATE)

State		Positive Formulary	Negative Formulary	No Listing	Total
Arkansas	(N)	39 47.6%	13 15.9%	30 36.6%	82
California	(NF)*	50 39.4%	15 11.8%	62 48.8%	127
Delaware	(N)	6 15.8%	6 15.8%	26 68.4%	38
Minnesota	(NF)	44 37.6%	14 12.0%	59 50.4%	117
Oregon	(NF)	29 40.8%	7 9.9%	35 49.3%	71
Pennsylvania	(P)	46 39.7%	10 8.6%	60 51.7%	116
Wisconsin	(P)	79 65.3%	7 5.8%	35 28.9%	121
TOTAL RESPONSE		293 43.6%	72 10.7%	307 45.7%	672** 100%

(N) State has negative formulary.

(P) State has positive formulary.

(NF) State has no formulary list.

$X^2 = 43.83$ with 12 DF (sig. = 0.01)

Cramer's V = 0.18

*California has no formulary list, despite provisions in the state law authorizing development of a negative formulary.

**Number of Missing Observations = 51

Table 35

FORMULARY PROVIDES ADEQUATE GUARANTEES
OF PRODUCT EQUIVALENCE
(BY STATE)*

State		Yes	No	Total
Arkansas	(N)	35 41.2%	50 58.8%	85
Delaware	(N)	16 47.1%	18 52.9%	34
Pennsylvania	(P)	43 36.8%	74 63.2%	117
Wisconsin	(P)	58 49.2%	60 50.8%	118
TOTAL RESPONSE		152 42.9%	202 57.1%	354** 100%

x^2 = 4.03 with 3 DF (sig. = 0.26)

Cramer's V = 0.11

*Asked only in four states.

**Number of Missing Observations = 369

(N) State has negative formulary.

(P) State has positive formulary.

Table 36

RESPONSE OF PHARMACISTS -
EFFECT ON WILLINGNESS TO SUBSTITUTE IF LAW
REQUIRES PASS-ON OF COST SAVINGS TO PATIENTS
(BY STATE)

State	More Willing	No Effect	Less Willing	Total
Arkansas	8 9.2%	51 58.6%	28 32.2%	87
California*	11 8.2%	88 65.7%	35 26.1%	134
Delaware*	1 2.5%	25 62.5%	14 35.0%	40
Minnesota*	6 5.0%	79 66.4%	34 28.6%	119
Oregon	0 0.0%	44 58.7%	31 41.3%	75
Pennsylvania	9 7.2%	86 68.8%	30 24.0%	125
Wisconsin*	12 9.8%	77 62.6%	34 27.6%	123
TOTAL RESPONSE	47 6.7%	450 64.0%	206 29.3%	703** 100%

X^2 = 8.76 with 6 DF (sig. = 0.18)

Cramer's V = 0.11

*State law has a mandatory cost-savings (wholesale or acquisition) provision.

**Number of Missing Observations = 20

Note: For statistical reasons, the categories "More Willing" and "No Effect" were combined in calculating the chi square and Cramer's V statistics.

Table 37

DOES STATE LAW REQUIRE
COST-SAVINGS PASS-ON?
(BY STATE)

State	Yes	No	Total
Arkansas	17 20.2%	67 79.8%	84
California*	80 65.6%	42 34.4%	122
Delaware*	17 43.6%	22 56.4%	39
Minnesota*	51 49.5%	52 50.5%	103
Oregon	20 27.4%	53 72.6%	73
Pennsylvania	37 35.6%	67 64.4%	104
Wisconsin*	77 65.8%	40 34.2%	117
TOTAL RESPONSE	299 46.6%	343 53.4%	642** 100%

x^2 = 74.86 with 6 DF (sig. = 0.01)

Cramer's V = 0.34

*State law has a mandatory cost-savings (wholesale or acquisition) provision.

**Number of Missing Observations = 81

Table 38

EFFECT ON SUBSTITUTION IF LAW
HAD NO MANDATORY PASS-ON PROVISION
(BY STATE)

State	More Often	Same As Now	Less Often	Total
Arkansas	1 6.3%	8 50.0%	7 43.8%	16
California*	13 16.9%	56 72.7%	8 10.4%	77
Delaware*	4 25.0%	10 62.5%	2 12.5%	16
Minnesota*	5 10.2%	38 77.6%	6 12.2%	49
Oregon	3 15.0%	16 80.0%	1 5.0%	20
Pennsylvania	2 5.6%	31 86.1%	3 8.3%	36
Wisconsin*	14 18.2%	54 70.1%	9 11.7%	77
TOTAL RESPONSE	42 14.4%	213 73.2%	36 12.4%	291 100%

*State law has a mandatory cost-savings (wholesale or acquisition) provision.

**Number of Missing Observations = 432

Note: Due to cell frequencies of insufficient size to allow for meaningful statistical calculations, no statistics are presented.

Table 39

RESPONSE OF PHARMACISTS -

OPINION OF STATE'S SUBSTITUTION LAW

(BY STATE)

State	Prefer Law as Written	Prefer Different Subst. Law	Prefer Anti-Substitution	Total
Arkansas	55 64.7%	11 12.9%	19 22.4%	85
California	85 65.4%	32 24.6%	13 10.0%	130
Delaware	22 59.5%	12 32.4%	3 8.1%	37
Minnesota	80 68.4%	19 16.2%	18 15.4%	117
Oregon	53 69.7%	15 19.7%	8 10.5%	76
Pennsylvania	48 39.0%	37 30.1%	38 30.9%	123
Wisconsin	56 46.3%	44 36.4%	21 17.4%	121
TOTAL RESPONSE	399 57.9%	170 24.7%	120 17.4%	689* 100%

x^2 = 56.64 with 12 DF (sig. = 0.01)

Cramer's V = 0.20

*Number of Missing Observations = 34

Table 40

RESPONSE OF PHARMACISTS
EXPECTED CHANGES IN SUBSTITUTION OVER
THE NEXT TWO YEARS (BY STATE)

State	Increase Greatly	Increase Somewhat	Stay at Current	Decrease Somewhat	Decrease Greatly	Total
Arkansas	18 20.2%	50 56.2%	21 23.6%	0 0.0%	0 0.0%	89
California	31 23.3%	76 57.1%	24 18.0%	1 0.8%	1 0.8%	133
Delaware	10 24.4%	26 63.4%	4 9.8%	1 2.4%	0 0.0%	41
Minnesota	18 15.1%	78 65.5%	21 17.6%	1 0.8%	1 0.8%	119
Oregon	10 12.8%	43 55.1%	24 30.8%	0 0.0%	1 1.3%	78
Pennsylvania	30 23.4%	64 50.0%	28 21.9%	5 3.9%	1 0.8%	128
Wisconsin	46 37.1%	69 55.6%	8 6.5%	1 0.8%	0 0.0%	124
TOTAL RESPONSE	163 22.9%	406 57.0%	130 18.3%	9 1.3%	4 0.6%	712 * 100%

X^2 = 41.15 with 12 DF (sig. = 0.01)

Cramer's V = 0.17

*Number of Missing Observations = 11

Note: For statistical reasons, the categories of "Stay at Current," "Decrease Somewhat" and "Decrease Greatly" were combined in calculating the chi square and Cramer's V statistics.

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