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Staff Report on SALES, PROMOTION, and PRODUCT DIFFERENTIATION in TWO PRESCRIPTION DRUG MARKETS

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SALES, PROMOTION, and PRODUCT DIFFERENTIATION in TWO PRESCRIPTION DRUG MARKETS

by
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and
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Staff Report to the FEDERAL TRADE COMMISSION

Federal Trade Commission

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PROLOGUE

ORIGIN AND SCOPE OF STUDY

When the Bureau of Economics first undertook a preliminary analysis of the prescription drug industry, a decision was made to focus upon aspects of the industry that had received little investigation. That firms in the industry generally experienced high accounting rates of return, that product prices were often substantially above production costs, and that industrywide promotion was very high has been widely documented in existing literature. Among the most interesting and seemingly important questions that the preliminary analysis raised were those related to the brand-name prescribing habits of physicians. Accordingly, the Bureau chose to focus the Prescription Drug Study upon the concept of product differentiation and its relationship to promotion and sales.

Because a careful analysis of product differentiation requires a thorough understanding of potential therapeutic substitutability among brands, a decision was made to limit the study to three well defined markets having different structural characteristics: the market for metronidazole, a patent protected vaginal anti-infective for which therapeutic substitutes were relatively poor; the market for orally effective diuretics, a market in which patent protection allowed only a few firms to compete; and the market for antianginal drugs, a market with no important patents and a large number of firms.

Collecting data from the participants in each market, the Bureau set out first to confirm a hypothesis frequently found in the economic literature: that markets with only a few sellers of differentiated products will exhibit unusually high, possibly wasteful levels of promotional expenditures (Scherer 1970, pp. 334–337). Thus it was expected that total expenditures for promotion in oral diuretics would account for a higher percentage of total sales than would expenditures for promotion in either the metronidazole or antianginal markets.

Data collected via the Prescription Drug Survey did indeed reveal that sellers of oral diuretics spent a higher percentage of their sales on promotion than did the seller of metronidazole. But the data also revealed some other very interesting and unanticipated phenomena. First, although many more firms competed in the market for antianginal agents than in the

market for oral diuretics, concentration was higher in antianginals than in oral diuretics throughout most of the time period under study.[1] Second, sellers of antianginal drugs on average devoted a higher, rather than lower, percentage of their sales dollar to promotion than did sellers of oral diuretic drugs. Finally, the disaggregated data revealed that the leading firms in both antianginals and oral diuretics had promotion-to-sales ratios substantially lower than those of the nonleading firms: the high market ratios reflected primarily the promotion of nonleading firms.

Subsequent analysis of the antianginal and oral diuretic markets led to what the Bureau believes are important and significant findings. This Economic Report focuses solely upon those two markets.

[1] Four-firm sales concentration in 1971 was 82 percent in the antianginal market and 67 percent in the oral diuretic market: eight-firm concentration was 91 and 82 percent, respectively.

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Special written contributions were made by Michael Lynch, who developed the dominant firm model presented in Appendix A, and by Ira Whitten, who authored Appendix B, as well as the oral diuretic section of Appendix C.

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SUMMARY

This report presents new evidence on the concept of product differentiation and upon its relationship to brand promotion and brand sales. Focusing upon two therapeutic markets for prescription drugs, the analysis presents a complex picture, part of which supports and part of which refutes the widely-held notion that leading brands gain and retain market dominance primarily as a result of promotional activity.

In each of the markets here under study, the first firm to offer and promote a new type of product received a substantial and enduring sales advantage. Moreover, although the promotional dollars spent by the first firms were absolutely large, the first firms nonetheless devoted a smaller percentage of their sales dollars to promotion than did their competitors. In each market the success of the first brand did stimulate other firms to enter with therapeutically substitutable products. Yet such follow-on brands failed to dislodge the early entrant from a dominant position. Neither heavy promotion nor low price appears to have been sufficient to persuade prescribing physicians to select in great volume the substitute brands of late entrants.

But late entrants were not universally unsuccessful. Follow-on firms that were first to offer and promote brands having some therapeutic novelty useful to at least a subset of patients did achieve substantial sales volumes. The large sales of novel brands were associated with heavy promotional expenditures.

In general, then, the data appear to reveal that sales and promotional dominance do go hand-in-hand. Nonetheless, the data also show that the opportunities for gaining sales via promotion are decidedly limited. Qualitative characteristics such as the timing of entry and therapeutic novelty appear to determine both the profit-maximizing level of promotion and the sales associated with that promotion. Large-scale promotion of brands that offer nothing new is likely to go unrewarded. When other things are equal, physicians appear to prefer the brands of existing sellers to those of new sellers.

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CHAPTER I

INTRODUCTION

Prior to World War II, drugs were sold primarily under generic names. The physician's prescription told the pharmacist which basic chemicals were to be used, and the pharmacist would combine those chemicals into dosage forms for the patient's consumption. The introduction of penicillin and other antibiotics, however, signaled the end of traditional practices. The phenomenal growth in demand for antibiotic drugs demonstrated the dramatic sales and profit potential from the development and introduction of new drugs. At the same time the rapid entry of firms into antibiotic production resulted in substantial price declines that also demonstrated how quickly prices and profits might be eroded by the entry of competition. Seeking to enhance and protect the market positions of their products, firms began to adopt strategies now institutionalized in the industry. Large sums of money were expended to develop patentable drugs. New drugs were assigned easy-to-remember trademarked brand names to supplement the generic or established names. Furthermore, firms devoted additional dollars to promote their trademarked brands, learning quickly of the willingness of physicians to prescribe by brand rather than by generic name.

The substantial investment by pharmaceutical firms in promotion is by now a well-known phenomenon. In 1970, thirty of the largest marketers of prescription drugs spent $682 million on promotion of these drugs. That amount represented 21 percent of the firms' total sales in the United States and amounted to an outlay of more than $2,400 per employed physician.[1] Whether such intensive promotional activity enhances the welfare of consumers by better informing physicians or lessens the welfare of consumers by wasting scarce resources, the promotional activity of drug firms has been the subject of considerable public criticism. During hearings conducted by the late Senator Estes Kefauver, drug promotion was alleged not only to be wasteful, but also to be deficient in informational content, to perpetuate inflated prices, and to limit the ability of small firms to compete. More recently, testimony before a committee chaired by Senator Gaylord Nelson reiterated the concern of consumers,

[1] Dollar figures are based upon data submitted to the Federal Trade Commission via the Prescription Drug Survey. Physician employment data were taken from the *U.S. Factbook* (1975).

politicians, social scientists, and physicians themselves. In its summary the Subcommittee on Monopoly noted (U.S. Senate 1972, p. 39):

> ... there seems little doubt that the current promotional practices contribute substantially to minimizing more intensive price competition in many retail prescription drug markets. The consumer is not only adversely affected by the absence of such competition, he is also asked to finance—in the form of the prices he pays for drugs—the very barriers which may deny him lower drug costs.

On the informational content of prescription drug promotion, the report adds (U.S. Senate 1972, p. 63):

> ... the record suggests that drug advertising and detailing rarely provide prescribers with complete and balanced comparisons of the benefits and risks of competing drugs... . Manufacturers do not readily help physicians objectively reevaluate the proper uses of older agents in the light of new developments.

Despite continued public criticism, there have been no economic analyses of prescription drug promotion at narrowly defined market levels where promotion might be related to the success or failure of individual brands. Accordingly, the Bureau of Economics has used the data gathering powers of the Federal Trade Commission to obtain the information needed to analyze, on a level more detailed than has heretofore been possible, promotion, product differentiation, and sales in two markets for prescription drugs.

The Markets

Oral diuretics are drugs used in the treatment of edema and hypertension. For purposes of this study, the market for diuretic drugs dates back to the introduction of the benzothiadiazine chemicals (thiazides) in 1957. Combining highly effective therapy with the ease of oral administration, introduction of these thiazide chemicals marked a turning point in diuretic and antihypertensive therapy, and drugs formerly used in the above indications were virtually abandoned in favor of the thiazides. New (nonthiazide) chemicals appeared in later years and within classes of oral diuretics a high degree of therapeutic substitutability existed. Oral diuretics were offered by between 15 and 20 firms in the 1960's, a period of rapidly growing demand. The drugs have been sold primarily under brand rather than generic names. Furthermore, virtually all the agents were sold under patent or patent licenses. Hence, oral diuretic drugs were selected as an example of patented drugs marketed by only a few sellers.

Drugs classified as antianginal agents are indicated for the relief and prevention of angina pectoris, a severe pain in the vicinity of the heart. No important patents have protected antianginal products, and these drugs have been offered by over 100 sellers in the past 20 years. Since medical literature suggested that, within classes, antianginal brands were therapeutically highly substitutable, antianginals were selected as an example of a class of unpatented drugs marketed by many sellers.

The Data

Annual sales, quantity sold, and dollar promotional data by type were requested from each firm that could be identified as having marketed a drug in one or more of the selected markets during the period 1956–71. In addition, the firms were asked to supply copies of patents, patent-license agreements, and marketing reports, as well as information on sources of supply. Sales and quantity sold data are available for each dosage strength of each relevant brand, and promotional data are available for each brand.

The data and materials obtained via the Survey are unusually detailed and provide a unique opportunity for testing certain hypotheses regarding economic behavior. Nevertheless, the data do have limitations.

First, some observations are missing from the data. Since the study covers a time period extending back to 1956, it is inevitable that some drug products that should be in the markets were not identified. The extent of such exclusionary errors is unknown but is thought to be limited. Furthermore, among those drug products that were identified, data were frequently not retrieved. The reasons underlying the unavailability of data range from firm bankruptcies to the inadequacy of firm records. Such missing observations are typically for firms the sales of which are small relative to the market as a whole.

Second, the data supplied by the firms are subject to variation in accuracy. Estimates, particularly of promotional data, were common among smaller firms, and the bases on which such estimates were made may vary substantially. Similarly, some large firms employed different estimating techniques with the potential for variation in accuracy probably less than that of the smaller firms, since the large firms are more likely to be estimating from some recorded data set.

Finally, when the study was first being formulated, a decision was made to focus upon only a few carefully delineated markets rather than upon a larger number of markets each of which would necessarily have been less carefully defined. While the decision to limit the number of markets under study has enabled the staff to become quite familiar with the individual drug products involved, multivariate analysis *across* markets is obviously not possible.

Organization of the Report

Chapter II presents an introductory theoretical discussion of product differentiation and its relationship to sales and promotion. Chapters III and IV then document with detailed data the nature and meaning of product differentiation in the markets for oral diuretic and antianginal drugs. Chapter V integrates the observations in Chapters III and IV with a more generalized discussion of product differentiation theory. Chapter V also introduces multivariate analysis to identify systematically the determinants of brand sales and promotion in both markets. Finally, Chapter VI offers conclusions and discusses policy implications of the findings.

CHAPTER II

PRODUCT DIFFERENTIATION AND ADVERTISING

Economists have long speculated that firms considering entry into an existing market may face a disadvantage relative to firms already established in that market. Joe Bain wrote:

> ... a general tendency of buyers to prefer established to new products may place potential entrants to a differentiated product industry at a disadvantage as compared to firms already established in the industry (Bain 1956, p. 116)

Bain noted that newly entering firms might have to accept a lower selling price and/or incur higher selling costs than existing firms to persuade buyers to accept their products. The total disadvantage due to product differentiation would depend upon the sum of the price and selling-cost disadvantages and upon the length of time that the entrant might expect the disadvantages to persist.

In case studies of several manufacturing industries, Bain identified numerous product differentiation characteristics that would probably disadvantage prospective entrants. The characteristics included product reputation, established dealer systems, brand allegiances, customer service, and advertising (Bain 1956, pp. 128–129). Hence, Bain's definition of product differentiation was multi-faceted and decidedly qualitative.

While subsequent students of the effects of product differentiation did not fail to recognize the complex nature of the subject, the search for an easily quantifiable measure of product differentiation inevitably led to advertising. As Mann recently noted:

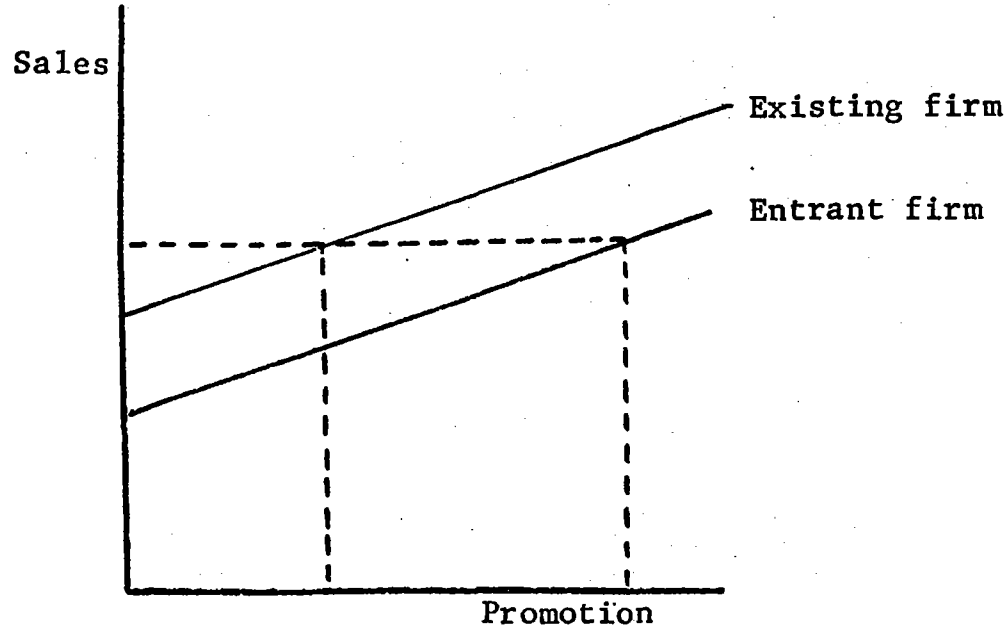
> ... product differentiation is not a well-specified concept ... and ... a more manageable inquiry is to single out one way sellers try to exploit the differentiability of a product ... (Since) sufficient data are available on advertising ... the cross-sectional empirical investigations to date have been limited to the role of advertising (Mann 1974, pp. 138–139).

But advertising has been identified as more than a proxy for the broader concept of product differentiation. Advertising by itself has been characterized as a barrier to the entry of new competition. Comanor and Wilson state:

> . . . high prevailing levels of advertising create additional costs for new entrants which exist at all levels of output. . . . In addition, the effect of advertising on firm revenues is subject to economies of scale which result from increasing effectiveness of advertising messages per unit of output as well as from decreasing costs for each advertising message purchased (Comanor and Wilson 1967, pp. 425–426).

The Comanor and Wilson thesis has two parts. First, Comanor and Wilson assume asymmetry over time in the effectiveness of a given level of advertising expenditure. To achieve a given sales volume in a given period of time while selling at a given price, a new entrant would have to advertise his product more than did an existing firm. Abstracting for the moment from the economies of scale argument, Comanor and Wilson's first point may be shown diagrammatically as depicted in Figure II.1. Holding all other factors constant every level of sales requires more advertising dollars for entering firms than for existing firms.

Figure II.1



Strictly speaking, the assumption of asymmetry over time in the sales effectiveness of advertising does not identify advertising as a barrier to entry. Instead, the assumption implies that consumers themselves create a barrier by responding to the promotion of early-to-enter brands more favorably than to the promotion of later-to-enter brands. In their recent book, Comanor and Wilson [1974] provide an explanation for such consumer behavior. The authors suggest that consumer's experiences with existing brands create a reservoir of consumer information about the qualities if those brands. Consumers have little or no information about

newly entering brands, and entrant firms must advertise intensively to create a stock of such information. Comanor and Wilson further argue that firms entering an existing market may have to advertise more intensively than established firms did when they entered the market:

> ... the effectiveness of advertising in a new product area may be greater than where products are well established and consumers have to come to rely on specific brands. Consumer attachments are often originally weak or absent, so that adveritising messages encounter relatively little resistance. [For firms entering an already established market] consumer resistance may be encountered that requires a proportionately larger volume of advertising if a substantial market share is to be gained (Comanor and Wilson 1974, p. 46).

Comanor and Wilson's analysis implies that the stock of consumer information created through experience with existing brands creates a disadvantage for newly entering brands. The disadvantage would exist even if established trademarked brands had never been advertised in the media at all. Hence, Comanor and Wilson's first proposition does not really identify advertising as the cause of the barrier to entry. Instead, Comanor and Wilson have merely restated Bain's proposition that product differentiation implies that, when other things are equal, including advertising, consumers prefer existing brands to newly entering brands.

The second part of the Comanor and Wilson thesis is the assumption of economies of scale to advertising. Comanor and Wilson assert that, up to some point, additional dollars spent on advertising yield increasing dollars of sales. They are not alone in believing that advertising is subject to economies of large scale. Numerous writers have argued that quantity discounts and increased message effectiveness may give large-scale advertisers a cost advantage over their smaller competitors (Simon 1970, pp. 3–8). Whatever the merit of the various arguments, however, direct empirical tests of the proposition have been few and have provided ambiguous results (Simon 1970, pp. 8–22). The assumption of economies to large-scale advertising changes the shape of the advertising-sales relationship. Figure II.2 depicts an advertising-sales relationship that is S-shaped. The lower part of the S shows the area of increasing returns, and the upper part of the S illustrates the area of decreasing returns to increased advertising.

Combined, the two Comanor and Wilson assumptions imply that the advertising-sales relationships faced by entrant and existing firms appear as shown in Figure II.3 on the following page.

Empirical tests of the proposition that product differentiation and/or advertising create barriers to entry have been rather indirect. Because sales, price and promotional data have seldom been available at the product or brand level, most studies have not been able to focus directly

upon consumer preferences for new *vis-a-vis* existing products, nor upon the relationship, if any, of qualitative characteristics and advertising to

Figure II.2

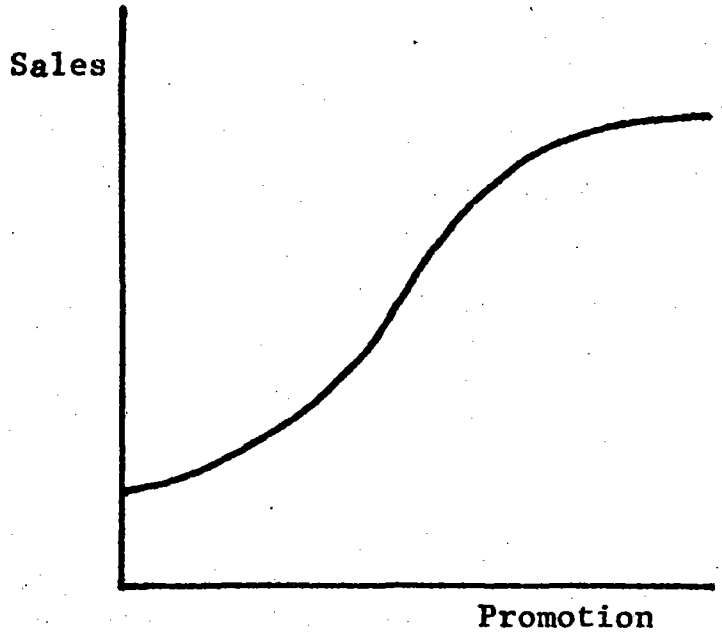
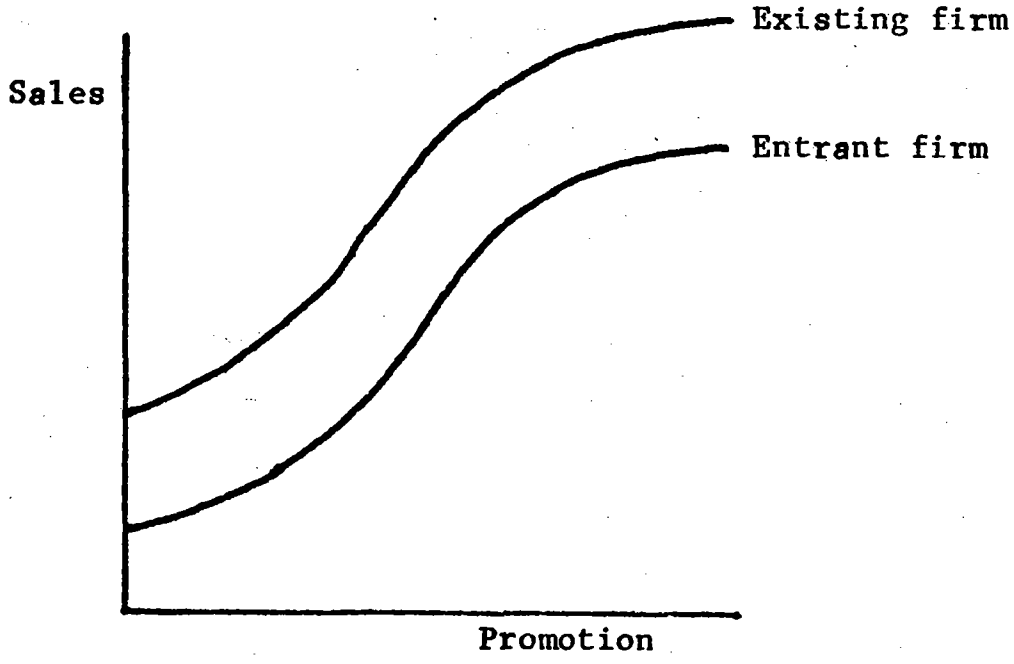


Figure II.3



those preferences. Although numerous variations exist, most empirical tests have followed a similar methodology. A sample of consumers goods

markets has been selected, and advertising as a percentage of sales has then been related either to the size distribution of firms in the markets (concentration) or to a weighted average of the profitability of the firms in the markets. Where empirical analyses have revealed that markets with higher than average advertising-to-sales ratios also exhibited higher than average concentration or firm profitability, the evidence has often been interpreted as confirming the hypothesis that product differentiation and/or advertising creates a barrier to entry.[1]

But because the empirical tests have been indirect, the meaning of the empirical results has been subject to considerable dispute.[2] Critics have noted that the direction of causality in any observed relationships between advertising and concentration or profitability is unclear. That is, high concentration or high profitability may cause high advertising rather than the high advertising causing high concentration or profitability (Schmalensee, 1972). If firms could increase their profitability merely by advertising, one might logically wonder why all firms do not promote their way to riches. The road to high profits undoubtedly involves more than the advertising budget.

Other critics have noted that where industries with high advertising also have high profits, the relationship may merely reflect accounting inadequacies. Firms treat advertising as a current expense, and all advertising expenditures made in any given year are deducted from income for that year. Yet, the effects of some advertising expenditures certainly must linger beyond the year in which they were made. Thus, some portion of advertising expenditures should be treated as a capital expenditure much as expenditures for plant and equipment are treated. At least one study of a small sample of industries has indicated that when profitability data are adjusted to eliminate the accounting bias, the positive relationship between advertising and profitability disappears (Bloch, 1974). But also see, Comanor and Wilson (1974, 169–195) for a contrary view.

The problem with existing work is that it does not test directly the Bain hypothesis of asymmetry of consumer acceptance between existing and newly entering brands. The purpose of this study is to focus directly upon that hypothesis as it applies to two therapeutic markets in-prescription drugs.

The following chapters document with detailed data the advantage to being early to enter and the advantage to entering with a "different" product in two therapeutic drug markets. Chapter III focuses upon the experience in orally-effective diuretic drugs, while Chapter IV focuses upon antianginal drugs. Chapter V introduces multivariate analysis and attempts to provide a more generalized theoretical discussion of the meaning of the observed relationships.

[1] See Mann (1974) for a review of this empirical work.

[2] See Ferguson (1974) for a critical appraisal of existing empirical work.

CHAPTER III

ORALLY EFFECTIVE DIURETICS

The volume and composition of extra-cellular body fluids are regulated by a number of interacting mechanisms. When one or more of the mechanisms allows the volume of such fluids to increase beyond normal levels, the condition is known as edema. Edema may be associated with any number of diagnoses, including congestive heart failure, kidney disease, cirrhosis of the liver, premenstrual syndrome, and pregnancy. Although the different diagnoses may require different therapies. the condition of edema may be treated by diuretic agents. Diuretics cause the kidneys to increase the urinary excretion of sodium and water, usually by inhibiting the reabsorption of sodium by the kidneys (American Medical Association 1971, p. 43).

Prior to 1958, diuretic therapy was administered by using any of a number of agents, each of which had important limitations. So-called xanthine and osmotic drugs did induce diuresis, but were of limited potency.[1] More important were the mercurial compounds and the carbonic anhydrase inhibitor, Diamox. The mercurial compounds had long been recognized as potent, safe, and relatively inexpensive diuretic agents (Burack 1970, p. 118). But to be effective, mercurials had to be injected. Thus, therapy with the mercurials usually involved the inconvenience and expense of office or hospital visits.[2] The first carbonic anhydrase inhibitor, acetazolamide (brand-name Diamox), briefly gained widespread

[1] The xanthine drugs, which include caffeine, theobromine, and theophylline, have long been known for their ability to increase diuresis. Prior to the development of modern diuretic agents, aminophylline, a soluble salt of theophylline, was relatively important in diuretic therapy, and a remotely related compound, amisometradine, was introduced as an oral diuretic as recently as 1954. Nonetheless, the American Medical Association (AMA) Council on Drugs notes that although the xanthine drugs may occasionally be used for edema, they have generally been replaced by more potent drugs and are now used primarily in other types of therapy (American Medical Association 1971, p. 43; Modell 1970, p. 90; Goodman and Gilman 1965, p. 850).

As with the xanthine drugs, the use of so-called osmotic drugs as diuretic agents has declined steadily as more potent agents have become available. Urea, one of the osmotic diuretics, was prescribed as an oral diuretic in cases of edema associated with cardiac failure. Because large doses are required, because it is unpleasant tasting, and because newer drugs are more effective, urea is seldom used as an oral diuretic today. Mannitol, the other of the osmotic diuretics also has limited use as a diuretic. Administered intravenously, mannitol is impractical as a treatment for chronic edema. Current uses of both urea and mannitol are confined primarily to treatment of patients hospitalized for surgery, trauma, burns, and other special conditions (American Medical Association 1971, p. 43; Modell 1970, p. 90; Goodman and Gilman 1965, p. 829).

[2] The AMA notes that the one oral mercurial, Neohydrin, was therapeutically much inferior to the injectable mercurials (American Medical Association 1971, p. 46).

use of an oral diuretic after its introduction in 1953. Experience with the drug, however, revealed that patients rapidly developed a tolerance for it.[3]

Thus, prior to 1958 there was clear need for a drug that combined therapeutic effectiveness with the ease of oral administration. The thiazide and thiazide-like drugs were the first agents to offer both such advantages, and it should hardly have been surprising that their introduction significantly altered the market for diuretics. The thiazides were not merely good substitutes for previously existing diuretics; they virtually replaced them. Table III.1 reveals that even in 1958 thiazide sales were more than three times greater than the sales of most other diuretics combined.

TABLE III.1.—Diuretic Sales by Class: The Early Years, 1956–62

(Millions of dollars)

	1956	1957	1958	1959	1960	1961	1962
Injectable mercurials	2,325	2,420	1,867	1,453	1,558	1,719	1,662
Oral mercurials	1,936	2,019	1,121	514	321	245	213
Carbonic anhydrase inhibitors	6,152	7,584	4,951	3,892	3,211	3,218	3,619
Amisometradines	1,173	1,811	650	233	117	75	42
Thiazide & Thiazide-like drugs	0	108	26,841	47,169	60,888	71,490	85,709
Total	11,586	13,942	35,430	53,261	66,095	76,747	91,245
Thiazides as a percentage of total	0	.8	75.8	88.6	92.1	93.2	93.9

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

But the rapid market acceptance of the thiazide drugs was not due solely to their efficacy in treating edema. The thiazides were also effective in reducing the blood pressure of hypertensive patients. Although many drugs available prior to 1958 did tend to lower blood pressure, most had side-effects which made their long-term use undesirable in many patients. As recently as 1955, Goodman and Gilman (1955, p. 741) stated that: "results of attempts to lower blood pressure by drugs are generally unsatisfactory." The thiazide drugs provided physicians with an orally effective antihypertensive drug relatively free from unwanted side-effects. Accordingly, the thiazides quickly became the backbone of antihypertensive therapy.

Historical Context

In late 1957, Merck and Co., Inc. (Merck) began marketing Diuril chlorothiazide, the first thiazide diuretic, an event that had a dramatic

[3] Current use of Diamox is probably primarily by ophthalmologists who use the drug in the treatment of glaucoma (see Burack 1970, p. 118).

impact upon diuretic therapy and upon the pharmaceutical industry. A 1958 marketing memorandum written for a potential competitor noted:

> Even prior to its introduction, many pharmaceutical organizations sensed the possibility that Diuril (MSD) might constitute a major medical breakthrough and an outstanding marketing success. This was based upon the initial clinical studies enthusiastically reported in the literature in 1957.
>
> By the second week in February 1958 (approximately 6 weeks after introduction), the speed and unprecedented acceptance of Diuril confirmed these pre-introductory considerations (Through ... market research, for example, we were able to determine that approximately 90% of all physicians had already used Diuril clinically by the end of April 1958—just four months after introduction.)
>
> The potential (in terms of dollars and profits) for products with the same type of effect and safety, coupled with the comparative chemical simplicity of chlorothiazide, triggered immediate research activities in ... just about the entire industry.

Much of the research was directed toward manipulation of the chlorothiazide molecule, and within a period of eight months during 1958, six firms, including Merck, Abbott, Ciba, Schering, Chinoin, and Loevens, had filed independent patent applications on hydrochlorothiazide and other analogues of chlorothiazide (U.S. vs. Ciba 1975, p. 15). Although the patent office declared an interference (a process for determining priority of invention), it was Ciba that expected to receive the ultimate patent, legal entanglement notwithstanding. Ciba began developing a strategy for marketing Esidrix hydrochlorothiazide to compete with Diuril (U.S. vs. Ciba 1975, p. 15).

Marketing memoranda reveal that Ciba's marketing strategy was developed in light of two constraints. First, Merck's Diuril had already proven to be a tremendous marketing success, and, while Ciba's Esidrix was more potent than Diuril (a 50 milligram tablet of Esidrix was therapeutically equivalent to a 500 milligram tablet of Diuril), there appeared to be no obvious therapeutic differences between the products. Second, Ciba was aware that Merck also inteded to introduce hydrochlorothiazide, using the brand name Hydrodiuril. A marketing memorandum dated November 24, 1958, reveals that Ciba expected to have a short lead-time on Merck:

> If present estimates are validated, and Ciba does enter the market with a two-month competitive lead, it must "cast the die" for this product within those two months of exclusivity ... To accomplish this feat requires a combination of careful planning, and the ability to remain extremely flexible at any stage of promotional planning, as well as the ability to use these next 90 days before introduction to compensate for the rather short exclusivity period after introduction.

Accordingly, the memorandum recommended spending $100,000 on direct mail and journal advertising prior to the introduction of Esidrix and to follow that promotion with more than $1 million in promotion during

the remainder of 1959. (Ciba actually spent nearly $3 million promoting Esidrix in 1959.)

Although Ciba was able to beat Merck to the market with hydrochlorothiazide, Ciba's lead-time was considerably less than it had hoped. Merck introduced Hydrodiuril on February 26, 1959, exactly two weeks after Ciba introduced Esidrix. The sales of Hydrodiuril, the trademark for which was HydroDIURIL emphasizing the Diuril name, very quickly out distance those of Esidrix.[4]

When it became apparent that the sales of Esidrix were not going to achieve the original goals, Ciba developed a strategy to enhance its profits by licensing other firms to sell hydrochlorothiazide and other chlorothiazide analogues under certain conditions (U.S. vs. Ciba 1975, p. 13). Thus, Merck's sales advantage may explain much of the post-1959 entry into the market. Had Ciba been able to overcome Merck's advantage, Ciba might not have been willing to license so liberally.[5]

Merck's Sales Advantage

Orally effective diuretics may be classified into four classes or submarkets: single-entity thiazides, combination thiazide-antihypertensives, potassium-sparing, and loop diuretics. Merck's sales advantage is explained by examining its performance in each of these sub-sets.

Single-Entity Thiazides

Subsequent to the entry of competitive products in 1959, the sales of Diuril declined from $27 million to $17 million, remaining relatively steady thereafter. The sales decline in Diuril, however, was more than offset by the success of Diuril's sister products, Hydrodiuril and Hydrodiuril-KA.[6] Through 1971, Diuril and Hydrodiuril remained the two largest-selling single-entity thiazide drugs capturing in 1971, 24 and 28 percent, respectively, of the single-entity thiazide submarket in 1971.

Notwithstanding the long-lived success of Merck's single-entity thiazide products, the broader market for oral diuretics did change substantially over time. The first and perhaps the most important change was the introduction and rapid success of products that combined a thiazide with one or more other antihypertensive drugs.

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[4] The product introduction dates for Esidrix and Hydrodiuril were February 12 and February 26, 1959, respectively.

[5] See appendix for a detailed description of the patent and license arrangements in the market for oral diuretics.

[6] Hydrodiuril-KA was hydrochlorothiazide with a potassium supplement encased in an enteric-coated core. Because of reports of small bowel ulcerations associated with the enteric-coated potassium, Hydrodiuril-KA and similar products declined in popularity during the latter 1960's.

Combination Thiazide-Antihypertensive Drugs

The treatment of hypertension often involves a coordinated therapeutic program using several drugs. The thiazides provide the backbone of most such programs. Used alone, the thiazides are effective in treating mild to moderate hypertension. Used in combination with other drugs—most notably reserpine, hydralazine, methyldopa, and guanethidine—the thiazides are effective in treating moderate to severe hypertension (AMA 1973, p. 46).

Although medical literature recommends that antihypertensive therapy never be initiated with combination drugs, it does suggest that fixed combination drugs may be substituted for certain (but not all) separately prescribed ingredients. Such substitution is medically advisable only when the fixed combination includes drugs in nearly the same proportions as determined optimal by experimental therapy (AMA 1973, p. 61). Thus, physicians may often substitute a prescription for a drug combining a thiazide and another antihypertensive agent for separate prescriptions for each drug individually. In fact, combination thiazide-antihypertensive drugs began appearing in 1959, and their sales ultimately became substantially larger than the sales of single-entity thiazide drugs (see Table III.2).

TABLE III.2.—Share of Oral Diuretic Sales Accounted for by Market Segments

(percent)

Submarkets	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Orally Effective Diuretics	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Thiazide and Thiazide-like Drugs	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	99.3	94.8	92.3	89.9	87.0	84.9
Single entity	100.0	100.0	72.2	63.4	60.0	58.2	57.1	54.0	51.0	46.8	41.5	37.4	33.8	30.2	28.3
Combination	0	0	27.1	34.4	37.1	39.3	39.5	41.6	44.6	45.2	45.0	45.5	45.2	44.6	43.0
Potassium Sparing	0	0	.7	2.2	3.0	2.5	3.4	4.4	4.5	7.3	8.3	9.4	11.0	12.2	13.6
Loop Diuretics	0	0	0	0	0	0	0	0	0	.7	5.2	7.7	10.1	13.0	15.1

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Eight combination thiazide-antihypertensive drugs appeared on the market in 1959 capturing $12.8 million in sales, somewhat less than 40 percent of single-entity sales in that year. Merck's marketing advantage clearly extended to the combination products. Diupres and Hydropres (combinations of reserpine with chlorothiazide and hydrochlorothiazide, respectively) captured nearly two-thirds of the total combination sales in 1959. Nonetheless, Merck's dominance in the combination submarket was less pronounced than in the single-entity submarket, where in 1959 Merck captured nearly 90 percent of the sales.

As Merck continued to introduce new combination products, its dominance in the combination submarket persisted throughout the period under study. Merck's most important combination product became Aldoril, a combination of methyldopa and hydrochlorothiazide, first introduced in 1963. Yet, competitor's brands were able to capture substantial portions of the combination sub-market. Ciba's Ser-Ap-Es (a triple combination of hydrochlorothiazide, hydralazine, and reserpine) and Bristol's Salutensin (a triple combination of hydroflumethiazide, protoveratrine A, and reserpine) accounted for 17 and 8 percent, respectively, of 1971 combination sales. Because the market for combination thiazide-antihypertensive drugs ultimately grew to be so important, Merck's dominance in the broader market for thiazide and thiazide-like drugs was less pronounced than in the single-entity submarket.

Two other developments in the market for oral diuretic drugs served to reduce Merck's dominant position.

Potassium-Sparing Diuretics

First, two single-entity diuretics unrelated to the thiazides were developed and marketed. G.D. Searle (Searle) offered Aldactone spriono-lactone, and Smith Kline & French (SKF) offered Dyrenium triamterine, both promoted for their abilities to induce diuresis without also causing the body to lose potassium—a characteristic shared by all thiazide and thiazide-like drugs. More successful than the single-entity products were Searle's and SKF's combination products which combined the potassium-sparing drugs with hydrochlorothiazide purchased under license from Ciba. Sales of Searle's Aldactazide and SKF'S Dyazide grew to $13 million and $11 million, respectively, by 1971. The combined sales of the single-entity and combination potassium-sparing drugs reached $32 million in

1971 and accounted for nearly 14 percent of total oral diuretic sales (see table III.2).[7]

Loop Diuretics

Second, two diuretics much more potent than the thiazides were developed and marketed during the latter half of the 1960's. Known for technical reasons as loop diuretics, medical literature suggests that the two drugs, Lasix furosemide and Edecrin ethacrynic acid, are practically identical in their pharmacologic action and further notes that, because of their potency, the drugs should be used only in patients who do not respond to the less potent, but safer, thiazide drugs (AMA 1973, p. 73).

In the submarket for the loop diuretics it was Merck that lost the battle to be first in the market with a new therapeutic agent. Although a 1965 marketing memorandum reveals that Merck originally believed that the two extra-potent products would reach the market at about the same time in 1966, Merck's forecast was wrong. American Hoechst introduced Lasix in 1966, but Merck was unable to market Edecrin until 1967. Merck's advantage in the thiazide segment of the market was not sufficient to overcome Hoechst's lead in the loop diuretic submarket. By 1971, Lasix had demonstrated phenomenal growth, becoming the largest selling oral diuretic with 14 percent of the market. Merck's Edecrin never captured even 2 percent of the market and in 1971 accounted for less then 1 percent of total oral diuretic sales. Whereas Merck had expected Edecrin to achieve a sales volume of $10 million as early as 1970, Edecrin's 1970 sales were less than $2.5 million (Merck Marketing Document).

A Closer Look at Merck's Advantage

Table III.3 details by year Merck's share of sales in the market for orally effictive diuretic drugs and in the various market segments. While Merck's market share declined rather steadily between 1958 and 1971, the absolute level, even in 1971, remained high. Moreover, because of the rapid growth of oral diuretic sales (from $27 million in 1958 to $238 million in 1971), Merck's sales increased in every year.

[7] Sales of the potassium-sparing drugs were given a substantial boost when small-bowel lesions were associated with the thiazide drugs supplemented with enteric-coated potassium. Until the lesions were discovered, a number of firms offered thiazides with the potassium supplement as a solution to the potassium depletion caused by the thiazides. Since patients using thiazide drugs could readily supplement their diets with potassium-rich foods such as orange juice, potassium depletion was never a serious drawback to using the thiazides in any case (see Modell 1970, p. 93).

TABLE III.3.—Market Share of Merck and Co., by Submarket

Submarkets	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Thiazide and Thiazide-like drugs	100	81	65	60	54	50	48	46	44	43	42	40	40	38
Single entity	100	88	74	68	62	56	54	54	55	55	55	55	56	53
Combination	—	66	54	53	47	44	45	42	41	40	40	39	40	40
Potassium sparing	—	0	0	0	0	0	0	0	0	0	0	0	0	0
Loop Diuretics	—	—	—	—	—	—	—	—	0	31	21	15	8	5
General Market:														
Oral diuretics	100	81	65	60	54	50	48	46	44	42	40	38	36	33

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

The continued dominance of a single firm such as Merck might be explained by any of a number of factors other than Bain's hypothesized product-differentiation advantage. Before looking more closely at the existence and nature of any such advantage, it is necessary to consider alternative explanations for Merck's favored market position.

Economics literature is replete with hypotheses that might rationalize the persistent supremacy of a leading firm. First, patents may limit the number of entrants into a market, or they may prevent entry altogether. Second, patented or secret technology may allow a firm to market a product superior to that of its competitors. Third, patented or secret technology may allow a firm to enjoy production or distribution efficiencies that enable it to sell its product at a price lower than the prices of its competitors. Finally, it has been argued that a firm or brand may be dominant because of the sheer volume of dollars it spends on promotion. It is instructive to consider each of the possible explanations individually.

Patent Barriers to Entry

Entry into orally effective diuretics has been limited by patent protection. Yet, patent protection has not been ironclad. As noted above, the success of Merck's Diuril quickly stimulated other firms to enter the market by inventing around the basic patent. Thanks in part to the success of such inventive activity and in part to the licensing policy of Ciba, sales of oral diuretics were distributed among 15 to 20 firms throughout most of the 1960's. Hence, although only a limited number of firms were able to enter the market, Merck's continued dominance among those firms cannot by explained by the patent barriers. Table III.4 reveals that the distribution of oral diuretic sales was highly skewed. In no year were there more than two firms other than Merck that managed to capture more than 19 percent of the market. Among the 25 firms in the oral diuretic market in 1971, only 5 firms other than Merck captured more than 5 percent and only 11 firms other than Merck captured more than 1 percent of the market.

TABLE III.4.—Size Distribution of Firms—Oral Diuretics

	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Market Share														
Greater than 20%	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10–20%			2	2	2	2	2	2	1	1	1	1	2	2
5–10%		2		1	1	1	1	3	3	3	5	4	3	3
1– 5%		1	5	4	7	6	7	10	8	9	5	6	6	5
Less than 1%		1	3	5	5	7	6	2	6	5	7	7	9	14
Total number of firms	1	5	11	13	16	17	17	18	19	19	19	19	21	25
Concentration Levels														
CR_4	100	99	93	90	84	80	78	75	72	68	66	66	67	68
CR_8	100	100	99	98	94	92	92	90	89	86	87	88	88	88
Herfindahl index	1.000	.6717	.4612	.3974	.3293	.2823	.2695	.2523	.2312	.2151	.2000	.1860	.1752	.1654

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

TABLE III.5.—Sales of Generically Identical Brands

	Average annual sales (millions of dollars)	Time period
Hydrochlorothiazide		
Oretic	0.5	1959–1971
Esidrix	3.9	1959–1971
Hydrodiuril	12.6	1959–1971
Trichlormethiazide		
Naqua	1.6	1959–1971
Metahydrin	0.8	1960–1971
Benzthiazide		
Exna	0.8	1960–1971
Aquatag	0.2	1965–1971

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Product Superiority

Substitutability among products within the market segments should be high. The AMA notes that differences among the single-entity thiazide drugs involve dosage and duration of action and that in other respects the drugs are almost identical (AMA 1971, p. 47). The AMA is not the sole source for inferring therapeutic substitutability. In his book, *The New Handbook of Prescription Drugs,* Richard Burack states: "With respect to action the only major differences ... concern duration." (Burack 1970, p. 318). But perhaps the most convincing evidence on the subject is from the firms themselves. As one firm noted in a marketing Memorandum:

> There are no clinically significant differences between the thiazide-type products—they all work with about equal significance in the treatment of edema and hypertension

Nor can physicians' brand preferences be explained by a preference for one generic ingredient over another. Table III.5 reveals that even among brands having identical generic ingredients, sales remain highly skewed. Merck's dominance cannot be explained by the therapeutic superiority of its products.

Efficiency and Price Advantage

The ability of a dominant firm to operate at lower cost and sell at a lower price could lead to a distribution of sales skewed in that firm's favor. Although the Prescription Drug Survey did not collect data on costs of production, cost advantages could lead to sales advantages only if the lower costs were translated into lower prices. Thus, a comparison of Merck's prices with those of its competitors' is sufficient to determine whether an efficiency-price advantage could explain Merck's dominance.

Although the medical and marketing literature suggests that within market segments oral diuretic drugs should be highly substitutable, differences in potency and duration of action do exist. Thus, recommended dosages vary from one generic ingredient to another, and price comparisons across generic ingredients are difficult to make. Accordingly, the price comparisons given in Table III.6 are confined to comparisons among generically identical drugs.

The price data for hydrochlorothiazide and hydrochlorothiazide with reserpine reveal emphatically that an efficiency-induced price advantage does not explain the dominance of Merck's brands. Between 1968 and 1970 Merck received for 50 mg. Hydrodiuril an average price 17 percent higher than Ciba received for 50 mg. Esidrix and 309 percent higher than Abbott received for 50 mg. Oretic. Yet the dollar sales of Hydrodiuril were 232 percent higher than the sales of Esidrix and 1,775 percent higher than the sales of Oretic.

The data for the other generic ingredients in Table III.6 reveal that larger-selling brands have higher, not lower, average prices than their competitors. Not only are prices positively correlated with market shares, the price differences are sometimes substantial. The presence of such price differences casts doubt upon the widely held proposition that drug firms fail to compete on the basis of price. The data in Table III.6 clearly show that nonleading firms do engage in price competition, at least to some classes of buyers. That lower-priced brands fail either to achieve leading market shares or to force down prices in general suggests that prescribing physicians simply fail to respond significantly to competition on the basis of price.

TABLE III.6.—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 III.7.—Dollars of Promotion as a Percentage of Sales

	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Promotion/Sales, Oral Diuretics, less Merck	0	58.7	35.4	33.6	33.6	33.5	37.1	33.5	35.7	31.7	27.5	27.3	24.3	20.9
Promotion/Sales, Merck	11.2	13.5	11.4	7.9	5.8	6.7	7.8	7.1	7.5	10.2	11.6	10.0	9.1	7.8

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Promotion

Not only has Merck been able to maintain a dominant, if declining, market share, it has been able to do so while spending significantly less of the sales dollar for promotion than its competition. Table III.7 reveals that competitors have been able to erode Merck's dominant share only by devoting a substantial portion of their receipts to promoting their products. The advantage was especially dramatic between 1962 and 1966, when on average Merck accounted for 48 percent of market sales but only 16 percent of market promotion.

Of course the absolute dollars spent by Merck have been substantial. Yet, even in absolute dollars, Merck was outspent by Ciba. Between 1958 and 1971, Merck invested $70.2 million promoting its oral diuretics while Ciba spent $72.9 million. Nonetheless, over the years between 1959 and 1971 when both firms were in the market, Ciba accumulated only $209 million in sales versus Merck's $780 million.

The data are even more revealing when one focuses upon individual brands. Table III.8 lists the 20 most promoted oral diuretic brands. Column A presents the rank of each brand based upon its total promotion. Column B presents the rank of each brand based upon its total sales. Both promotion and sales include all dollars spent or received over the entire market life of a brand through 1971. Comparison of promotion with sales rank for each brand reveals that relatively high promotion is no guarantee of relatively high sales. Indeed, close examination of the table will reveal that the four largest selling brands—Diuril, Hydrodiuril, Hydropres, and Diupres (all Merck brands)—were not among the four most-promoted brands. In fact, Hydropres, the brand ranked third in total sales, ranked fifteenth in total promotion.

The two identical hydrochlorothiazide products introduced by Merck and Ciba in February 1959 provide further evidence that Merck's advantage is not based upon sheer volume of promotion. Between 1959 and 1971, Ciba outspent Merck on promotion by more than 50 percent. Whereas Merck's total promotion of Hydrodiuril was $14.3 million, Ciba's total promotion of Esidrix was $22.5 million.[8] Yet by 1971 Hydrodiuril had totaled $186 million in sales while Esidrix had totaled only $112 million. Merck had devoted less than 8 percent of its Hydrodiuril sales to promotion; for Esidrix, Ciba had devoted 20 percent.

Exploring the Product Differentiation Advantage

A simple process of elimination, then, suggests that further consideration should be given to Bain's hypothesis that, other things equal,

[8] Sales and promotion dollars include Hydrodiuril and Hydrodiuril-KA and Esidrix and Esidrix-K.

consumers prefer the brands of existing firms to those of newly entering firms. Pharmaceutical firms themselves appear to have accepted the Bain

TABLE III.8.—Promotional and Sales Rankings of Orally Effective Diuretic Drugs: 1958–71*

Drug	(A) Rank Promotion	(B) Rank Sales
Ser-Ap-Es	1	5
Lasix	2	6
Hygroton	3	8
Esidrix	4	12
Diuril	5	1
Dyazide	6	13
Regroton	7	19
Esimil	8	22
Salutensin	9	11
Renese	10	15
Hydrodiuril	11	2
Aldactazide	12	10
Aldoril	13	7
Diupres	14	4
Hydropres	15	3
Enduronyl	16	14
Enduron	17	17
Aldactone	18	16
Edecrin	19	26
Hydromox	20	28

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

*With sales ranks scaled 1 to 20, the Spearman rank-correlation coefficient is equal to .4256. The coefficient is significant at the five percent but insignificant at the one percent level.

hypothesis. Perhaps because they had a very substantial profit motive for doing so, drug firms seem to have learned long ago that the prescribing behavior of physicians creates a substantial advantage to being first or early to enter a market with a new and different product:

> During October personal interviews were conducted, by experienced resident physicians, with 102 general practitioners and 51 specialists in internal medicine—all in private practice. . . . When asked to specify the thiazide diuretic most frequently prescribed, MSD [Merck] products accounted for the majority of mentions. . . . Nearly 50 percent gave as their reason for using their product of choice—"habit familiarity, first available." . . . MSD has accrued a distinct advantage in this competitive field as the original producer of a "breakthrough" product (Merck Marketing Report).

> Pfizer's experience also illustrates that extremely heavy investments to earn good market share with a relatively late market entry makes short-run profits relatively lean . . . The recent experience of Schering . . . is an example of a late market entrant which has been unsuccessful . . . Even considerable marketing investments do not assure success . . . if the reasonably good product does not satisfy some important market needs better than competitive products. In short, some product differentiation, however

> small, must accompany a strong marketing program ... It is concluded that market performance will be guided by the principles discussed above until such time as a strongly differentiated product is introduced, coupled with a strong marketing program (Abbott Marketing Report).

> Our task of establishing "Edecrin" in the market will be unusually difficult since LASIX, a clinically similar competitive product, is already released and will have been on the market about six months by the time "Edecrin" is marketed. This will necessitate an unusually high ratio of promotion to sales on "Edecrin" (118%) (Merck Marketing Report).

> Within two weeks of one another in February of 1959, the second and third products hit the market, and they were identical thiazide derivatives. The drug was hydrochlorothiazide ... and it was marketed under the brand names of ESIDRIX (Ciba) and HydroDIURIL (MS&D). CIBA worked feverishly to get its products on the market before HydroDIURIL: and although we succeeded in "beating MS&D to the punch" by two weeks, it wasn't enough of a lead to offset the advantage they had of being known in the diuretic market already. Consequently, from the start, HydroDIURIL has had a larger sales volume than ESIDRIX... (Ciba Marketing Memorandum).

Although Bain enunciated his hypothesis primarily to explain the higher average profitability of firms in product differentiated markets, the foregoing statements suggest that pharmaceutical firms believe that the hypothesis may also explain the relative success and failure of individual brands and firms within the market. The statements imply that, because prescribing physicians do prefer existing to newly entering brands, the order in which brands enter a market may explain differences in market share when other things are held constant. Of course, the statements also suggest that drug firms may react to such prescriber behavior by varing one or more of the "other things," most notably the therapeutic characteristics of the product. Hence, a more general statement of the hypothesis might be that brands that are first to offer some therapeutic advantage should fare better in the marketplace than brands that merely duplicate existing therapy.

Merck's persistent dominance in the face of competition from cheaper, more highly-promoted substitute drugs would suggest that the product-differentiation advantage from being first with a "breakthrough" product is very substantial indeed. But, while Diuril was clearly a novel product at the time it was first introduced, Diuril was not the only brand to offer some therapeutic novelty. In testimony before a Senate Subcommittee Commissioner Schmidt of the Food and Drug Administration (FDA) presented a tentative identification of drugs which offered important and modest therapeutic advances when they were first introduced.

Table III.9 lists the oral diuretic and antihypertensive drugs rated by the FDA as offering important or modest therapeutic gains at the time the drugs were approved for marketing. The table also includes the year of

FDA approval and the name of the firm that first marketed the drug. All other orally effective diuretic drugs, including those in the various submarkets, were rated by FDA as offering little or no therapeutic gain.

TABLE III.9.—Orally Effective Diuretic and Antihypertensive Drugs Receiving Important or Modest Gain Classification From FDA

ORAL DIURETICS

IMPORTANT GAIN			MODEST GAIN		
Chlorothiazide	1957	(Merck)	Chlorthalidone	1960	(Geigy)
Spironolactone	1960	(Searle)	Triamterine	1964	(Smith, Kline, & French)
Furosemide	1966	(American Hoechst)			

ANTIHYPERTENSIVES

IMPORTANT GAIN			MODEST GAIN
Hydralazine	1952	(Ciba)	
Reserpine	1953	(Ciba)	none
Guanethidine	1960	(Ciba)	
Methyldopa	1962	(Merck)	

Note: Because their uses as diuretics were rendered obsolete by the introduction of chlorothiazide, acetazolamide, which received an important gain classification, and aminometradine and amisometradine, which received modest gain classifications, have been excluded from the table.

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

The FDA classification scheme can, then, provide a basis for distinguishing brands that were first to offer some new therapeutic advantage from brands that merely duplicated already existing therapy. Table III.10 lists diuretic and combination diuretic-antihypertensive brands that incorporate chemicals rated by the FDA as offering some therapeutic gain.[9] As the market share data also given in Table III.10 reveal, brands that were first to offer some therapeutic gain did substantially better on average than did brands that offered nothing new. Brands offering important or modest therapeutic gains on average each accounted for about five percent of 1971 oral diuretic sales while brands that offered little or no gain on average each accounted for less than one percent of 1971 oral-diuretic sales.

Still another avenue for exploring the advantage to being first is to focus upon the disadvantage to being late. Eli Lilly, one of the largest pharmaceutical firms, did not enter the oral diuretic market until late in 1963—nearly six years after the introduction of Diuril. Lilly entered with a product line including Anhydron, a single-entity thiazide, Anhydron-K, a potassium-supplemented thiazide, and Anhydron-KR, a potassium-supplemented combination thiazide-antihypertensive. All three products were

[9] Ciba's brands incorporating reserpine and hydralazine are not listed as important gain brands since both chemicals had been marketed as single-entity drugs for many years prior to their introduction in the combination diuretic-antihypertensive dosage forms. Similarly, Merck's Aldoclor combination of chlorothiazide and methyldopa is not listed since its sister product, the Aldoril combination of hydrochlorothiazide and methyldopa had been on the market for five years prior to the introduction of Aldoclor.

based upon cyclothiazide, another of the molecular analogues of chlorothiazide.

TABLE III.10—Brands of Oral Diuretic and Combination Diuretic-Antihypertensive Drugs First to Offer New Therapeutic Advantages

Brands Incorporating Chemicals Rated as Important Gains

Chemical	Brand	Year of Introduction	1971 Market Share (Percent)
Chlorothiazide	Diuril	1958	6.79
	Diupres	1959	3.41
	Aldactone	1959	2.91
Spironolactone	Aldactazide	1961	5.49
Methyldopa	Aldoril	1963	7.68
Guanethidine	Esimil	1965	1.90
Furosemide	Lasix	1966	14.25
		Total market shares	42.43
		Average market share	6.06

Brands Incorporating Chemicals Rated as Modest Gains

Chemical	Brand	Year of Introduction	1971 Market Share (Percent)
Chlorthalidone	Hygroton	1960	4.74
	Regroton	1964	2.95
Triamterine	Dyrenium	1964	0.46
	Dyazide	1965	4.76
		Total market shares	12.91
		Average market share	3.23

Brands Incorporating Chemicals Rated as Little or No Gain

Total market shares	44.66
Average market share	0.91

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Lilly invested heavily in promoting its new Anhydron product line. Between October 1963 and December 1964, Lilly spent $4.8 million on promotion—a rate of $320,000 per month. (By contrast Merck and Ciba had spent respectively $177,000 and $259,000 per month when Hydrodiuril and Esidrix were introduced in 1959.) Despite the heavy promotion, sales of the Anhydron product line did not respond. By the end of 1964, sales of the new product line had totaled less than $2.7 million. Apparently recognizing the futility of further promotion, Lilly cut its promotional effort substantially. Nonetheless, it was not until 1967 that the total dollars received in Anhydron sales exceeded the total dollars spent on Anhydron promotion. Even as late as 1971, total dollars of promotion accounted for 71 percent of Anhydron's total sales.

TABLE III.11.—Brands of Oral Diuretic Drugs

Firm	Diuretic Chemical Entity	Brands Including the Chemical Entity	Additional Ingredients	Years Marketed From	Years Marketed To	Peak Market Share[1]	1971 Market Share[1]
Abbott	(Hydrochlorothiazide	(Oretic	None	1959	1971	1.2	0.2
		(Oreticyl	Deserpidine	1959	1971	0.6	*
		(Oreticyl Forte	Deserpidine	1959	1971	0.5	*
	(Methyclothiazide	(Enduron	None	1960	1971	2.7	1.2
		(Enduronyl	Deserpidine	1961	1971	1.7	0.7
		(Enduronyl Forte	Deserpidine	1961	1971	1.0	0.7
		(Eutron	Pargyline	1965	1971	0.9	0.6
American Hoechst	Furosemide	Lasix	None	1966	1971	14.2	14.2
Bristol	(Hydroflumethiazide	(Saluron	None	1960	1971	0.8	*
		(Salutensin	Reserpine, protoveratrine A	1960	1971	3.9	3.6
	(Bendroflumethiazide	Benuron	None	1965	1969	0.1	—
Central	Benzthiazide	Diucin	None	1971	1971	*	*
Ciba	Hydrochlorothiazide	(Esidrix	None	1959	1971	6.1	2.5
		(Esidrix K	Potassium chloride	1960	1970	3.8	—
		(Singoserp-Esidrix	Syrosingopine	1959	1971	1.1	0.2
		(Apresoline-Esidrix	Hydralazine	1959	1971	0.3	*
		(Serpasil-Esidrix	Reserpine	1959	1971	2.7	0.6
		(Esimil	Quanethidine	1965	1971	1.9	1.9
		(Ser-Ap-Es	Reserpine, hydralazine	1960	1971	7.3	7.3
Geigy	Chlorthalidone	(Hygroton	None	1960	1971	4.5	4.2
		(Regroton	Reserpine	1964	1971	2.7	2.7

Table continued on following page. See footnotes at end of table.

TABLE III.11.—Brands of Oral Diuretic Drugs—Continued

Firm	Diuretic Chemical Entity	Brands Including the Chemical Entity	Additional Ingredients	Years Marketed From	Years Marketed To	Peak Market Share[1]	1971 Market Share[1]
Lakeside	Trichlormethiazide	(Metahydrin	None	1960	1971	0.8	0.5
		(Metatensin	Reserpine	1962	1971	0.3	*
Lederle	Quinethazone	(Hydromox	None	1962	1971	1.4	0.5
		(Hydromox-R	Reserpine	1965	1971	0.2	0.2
Lemmon	Benzthiazide	Lemazide	None	1970	1971	*	*
Lilly	Cyclothiazide	(Anhydron	None	1963	1971	0.4	*
		(Anhydron K	Potassium chloride	1963	1971	0.5	*
		(Anhydron K R	Potassium chloride, reserpine	1963	1971	0.6	*
McNeil	Hydrochlorothiazide	(Butizide	Butabarbital	1962	1971	0.3	0.2
		(Butiserpazide	Reserpine, butabarbital	1962	1971	0.9	0.7
Mallard	Benzthiazide	(Aquex	None	1971	1971	*	*
		(Urazide	None	1971	1971	*	*
Mallinckrodt Neisler	Methyclothiazide	(Aquatensin	None	1971	1971	*	*
		(Diutensin	Cryptenamine	1962	1971	0.4	0.4
		(Diutensin-R	Cryptenamine, reserpine	1962	1971	0.7	0.6

		(Diuril	None	1957	1971	100.0	6.8
	(Chlorothiazide	(Diupres	Reserpine	1959	1971	3.7	3.4
	(	(Aldoclor	Methyldopa	1968	1971	0.9	0.9
	(						
	(	(Hydrodiuril	None	1959	1971	15.3	7.9
	(	(Hydrodiuril-KA	Potassium chloride	1960	1970	4.1	—
Merck, Sharpe and Dome	(Hydrochlorothiazide	(Hydropres	Reserpine	1959	1971	9.2	5.3
	(	(Hydropres-KA	Reserpine, potassium chloride	1960	1970	1.9	—
	(	(Aldoril	Methyldopa	1963	1971	7.7	7.7
	(	(Cyclex	Meprobamate	1960	1971	1.0	0.2
	(						
	(Ethacrynic Acid	Edecrin	None	1967	1971	1.6	0.8
No. American Pharmacal	Benzthiazide	Marazide	None	1971	1971	*	*
Pasadena Research	Benzthiazide	Aquasec	None	1970	1971	n.a.	n.a.
Pfizer	Polythiazide	(Renese	None	1961	1971	3.3	1.2
		(Renese-R	Reserpine	1963	1971	1.1	0.9
Reid Provident	Benzthiazide	Proaqua	None	1971	1971	*	*
Robins	Benzthiazide	(Exna	None	1960	1971	1.0	0.2
		(Exna-R	Reserpine	1965	1971	0.3	*
Schering	Trichlormethiazide	(Naqua	None	1960	1971	1.6	0.7
		(Naquival	Reserpine	1962	1971	0.3	0.2

Table continued on following page. See footnotes at end of table.

TABLE III.11.—Brands of Oral Diuretic Drugs—Continued

Firm	Diuretic Chemical Entity	Brand Including the Chemical Entity	Additional Ingredients	Years Marketed From	To	Peak Market Share[1]	1971 Market Share[1]
		(Aldactone	None	1959	1971	2.9	2.9
C.D. Searle	Spironolactone	(Aldactazide	Hydrochlorothiazide	1961	1971	5.5	5.5
Smith Kline & French	Triamterine	(Dyrenium	None	1964	1971	1.6	0.5
		(Dyazide	Hydrochlorothiazide	1965	1971	4.8	4.8
		(Naturetin	None	1959	1971	0.8	0.6
	(Bendroflumethiazide	(Naturetin CK	Potassium chloride	1960	1971	4.0	0.3
	(	(Rautrax-N	Rauwolfia serpentina, potassium chloride	1960	1971	5.4	1.4
	(	(					
	(	(Rautrax N-Modified	Rauwolfia serpentina, potassium chloride	1960	1971	0.4	*
	(	(					
Squibb	(	(Rauzide	Rauwolfia serpentina	1967	1971	1.7	1.7
	(						
	(Flumethiazide	(Rautrax	Rauwolfia serpentina, potassium chloride	1959	1971	6.7	0.3
	(	(					
S.J. Tutag	Benzthiazide	Aquatag	None	1965	1971	0.2	*
		(Miluretic	Meprobamate	1960	1964	0.2	—
Wallace	Hydrochlorothiazide	(Caplaril	Mebutamate	1963	1970	0.2	—
	(Hydrochlorothiazide	EK 25	None	1961	1963	*	*
Western Research	(						
	(Benzthiazide	Diretic	None	1971	1971	*	*

[1] Market shares are based upon U.S. domestic sales only. Export sales are not included.
* 0.1 percent or less
n.a. Not Available

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

CHAPTER IV

ANTIANGINALS

Introduction

The use of drugs for the relief and prevention of anginal pain dates back to the late 1800's. Prior to 1952 antianginal drugs were sold primarily under generic (or established) names, but with the 1952 introduction of Peritrate, the first brand of pentaerythritol tetranitrate (PETN), the use and promotion of brand names increased substantially. Introduced by Warner-Chilcott (a Division of Warner-Lambert), Peritrate was the first antianginal drug to be heavily promoted, and its acceptance rate by physicians was so high that by 1956 Peritrate accounted for about 70 percent of market sales. Although its share gradually declined over time, Peritrate remained the largest selling antianginal drug even in 1971 when it accounted for about 30 percent of market sales (see Table IV.5). The success of Peritrate did not fail to attract entry. By 1971, 97 firms were in the market offering 229 brands as shown in Table IV.1. The participation of many firms of small size was encouraged by the absence of patents and by the expansion of demand: sales rose at an annual rate of 14 percent from almost $8 million in 1956 to about $62 million in 1971. Despite entry, sales remained concentrated in the hands of Warner-Lambert and a few other firms, the four-firm sales concentration remaining stable at about 80 percent over the last ten years of the period. What explains the long-term marketing advantages held by the drug Peritrate? What effect has this drug's dominance had on the conduct of rival firms in the market? This chapter attempts to answer those questions.

The Treatment of Angina Pectoris

Angina pectoris is characterized by severe pain from the heart to the shoulder, including the left arm. Less frequently the pain is felt in the area from the heart to the abdomen (Taber 1970, p. A–59). Although the cause of the pain—and hence the mechanism for its relief—is not fully understood, the condition appears to afflict a substantial number of

TABLE IV.1.—Antianginal Sales, Number of Firms and Brands, Sales Concentration, and Ratio of Promotion to Sales

Year	Antianginal Sales (dollars)	No. of firms	No. of brands	Four-firm concentration (percent)	Eight-firm concentration (percent)	Herfindahl index	No. of firms with less than 1% of Sales	Market promotion to sales ratio (percent)	Market promotion to sales ratio excl. Peritrate (percent)
1956	7,698,396	46	93	96.3	98.5	0.52	42	—	17.9
1957	10,104,972	51	96	90.2	97.5	0.51	44	—	10.1
1958	11,909,191	57	115	84.4	94.9	0.46	48	—	23.7
1959	14,394,100	59	123	84.6	95.7	0.43	51	—	25.1
1960	16,423,180	64	134	84.0	93.5	0.44	55	—	21.9
1961	19,728,190	67	142	81.9	91.5	0.44	56	—	27.6
1962	23,261,638	70	163	81.5	92.3	0.42	59	30.3	49.0
1963	26,202,431	72	167	82.5	92.8	0.41	62	28.1	46.7
1964	30,567,563	79	182	81.0	91.7	0.37	69	25.9	38.2
1965	35,398,004	80	192	79.1	91.1	0.34	70	25.0	32.3
1966	38,138,910	89	204	79.8	91.4	0.31	79	22.0	28.5
1967	40,030,689	88	208	79.8	91.2	0.28	78	24.8	30.3
1968	48,094,515	92	221	80.7	90.1	0.27	80	28.2	35.6
1969	50,870,274	92	219	80.6	90.3	0.26	80	24.4	28.6
1970	56,437,925	96	229	80.5	91.0	0.25	78	23.6	26.9
1971	62,108,424	97	229	82.4	92.4	0.26	86	20.6	22.9

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey

individuals: about 26 million prescriptions were filled for drugs promoted to relieve or prevent anginal pain in 1970.[1]

Drugs used for the relief and prevention of anginal pain are often referred to as coronary vasodilators. To a large extent this designation is historical stemming from the early belief that the cause of angina pectoris was a diminished blood flow through the coronary arteries to the cardiac muscle (myocardium) of the heart. Hence, vasodilatation, or expansion of small blood vessels, was considered the appropriate therapy. Initially, it was felt that the pain was a result of an increase in blood pressure which vasodilatation would alleviate.[2] Current evidence suggests that the pain may result from an inadequate supply of oxygen to the heart (myocardial hypoxia).[3] However, it has not been clinically established that vasodilatation is the required drug action for an enhanced delivery of oxygen (Goodman and Gilman 1965, p. 736).

For many years now the basic drug weaponry in the treatment of angina has been the nitrite-nitrate family of chemicals, and a summary of their appearance dates is presented in Table IV.2. Amyl nitrite (the inhalant) and nitroglycerin were first used clinically in 1867 and 1879, respectively, and were the pioneer drugs in this field. Effective in alleviating pain, these two drugs along with a sublingual form of isosorbide dinitrate (Krantz 1974, p. 35) remain to this day the bulwarks of drug therapy to alleviate the pain of angina.

TABLE IV.2—Drug Appearances: The Nitrites

Drug	Initial investigation date	Date first marketed in U.S.
Amyl nitrite	1867	Unknown
Nitroglycerin	1879	Unknown
Erythrityl tetranitrate	1895	Unknown
Mannitol hexanitrate	1895	1942
Sodium nitrite	1897	Unknown
Octyl nitrite	1938	Unknown
Trolnitrate phosphate	1940	1953
Isosorbide dinitrate	1939	1959
Pentaerythritol tetranitrate	1943	1952

Sources: See text.

As experimentation continued, other "nitrates" appeared. Erythritol (erythrityl) tetranitrate and mannitol hexanitrate were investigated in 1895,

[1] About 6.5 million new prescriptions were filled in 1970, and information in marketing reports indicates that for every new prescription written another three prescriptions were refilled (19.5 million).

[2] Mark Nickerson notes that " . . . all drugs that lower blood pressure must do so by vasodilation. . ." (Goodman and Gilman, 1965, p. 73.)

[3] The AMA Drug Evaluations (1973) reports "current evidence indicates that a reduction in the oxygen requirements of the myocardium accounts for the therapeutic action of the drugs"; see also Goodman and Gilman (1955, p. 730) and (1965, p. 736).

and sodium nitrite was studied initially in 1897. Later, in 1941, Goodman and Gilman (1941, p. 561) would note that these three preparations were "... to be preferred for the purpose of relieving the severity and decreasing the frequency of attacks of pain." Mannitol hexanitrate was first marketed in the U.S. in 1942 (AMA 1960, p. 317), but the market introductory dates of erythrityl tetranitrate and sodium nitrite are uncertain. Octyl nitrite was first investigated clinically in 1938 (Melville 1954, p. 31/1), and trolnitrate phosphate (known also as triethanolomine trinitrate biphosphate and triethanol trinitrate) was first examined in 1940 in Germany (Melville 1954, p. 31/1). Trolnitrate phosphate was first marketed in the U.S. under the trade name Metamine by Leeming in 1953. Aviado (1972, p. 496) reports that pentaerythritol tetranitrate (PETN) was first used as an antianginal agent in 1943, and Melville (1954, p. 31/1) dates the first investigation of the pharmacolgic and toxic properties of PETN in the U.S. to 1944. Eight years then elapsed before Peritrate was introduced in 1952. Finally, isosorbide dinitrate, investigated as early as 1939 (Charlier 1961, p. 76) and first marketed in 1959 under the brand name Isordil, became the last of the "nitrites" to appear.

Because the pain of angina and its relief are subjective sensations experienced by the patient, the effectiveness of alternative therapeutic regimens has been difficult to determine. Certain drugs have been established as effective in *alleviating* pain through years of use. However, the effectiveness of long-term agents indicated for use in the *prevention* of anginal pain (a regimen described as long-term prophylaxis) has been more difficult to determine, and solid scientific proof of the efficacy of these agents has yet to be established. Whatever their efficacy, a myriad of drugs have been promoted and prescribed for long-term angina therapy.

The Rapid-Acting Agents: Drugs to Relieve Acute Anginal Pain

In 1867 a British physician discovered that the pain of angina pectoris might be relieved by inhaling the fumes of amyl nitrite (Burack) 1970, pp. 190–191). Since that time amyl nitrite and other rapid-acting nitrites have been widely recognized for their ability to relieve anginal pain. Although the mechanism by which the nitrite drugs bring about relief has remained obscure, the ability of these drugs to relieve anginal pain is so consistent that they are used for diagnostic purposes. Modell (1970, p. 371) notes that failure of nitroglycerin (one of the rapid-acting sub-linguals) to relieve pain casts doubt on the diagnosis of angina pectoris.

The Inhalants:

Amyl nitrite produces its effects more rapidly than other nitrites; but the drug must be administered by inhalation, its odor is conspicuous and

unpleasant, and it may produce headaches even among bystanders. Further, because it is an inhalant, the dosage is difficult to control (Modell 1970, p. 374). Given the limitations of amyl nitrite, use of the drug is largely restricted to patients who cannot take other forms of medication or who require therapy while at the hospital or in the presence of a physician (p. 375).

Octyl nitrite is another rapid-acting nitrite administered by inhalation. Although the fumes of octyl nitrite are not as unpleasant as those from amyl nitrite, the potential for serious overdosage is a problem. According to Modell (1970), the agent is not widely used (p. 375) and data submitted to the FTC suggest that the drug has not been marketed since 1957.

Sales of inhalants amounted to only $405,000 in 1971, or less than 1 percent of the sales of all other antianginal preparations. The use of these drugs is indeed limited, and because they serve only specialized purposes they will be excluded from the group of drugs that will comprise the antianginal market for purposes of this study.

The Sublinguals:

Except under unusual circumstances, nitroglycerin is the recognized drug of choice for relieving anginal pain. [4] Nitroglycerin is administered by placing a pill under the patient's tongue and usually provides relief in one to three minutes. Since the sublingual dosage form is fixed, nitroglycerin is much safer for self-administration than are the inhalants (Modell 1970, p. 375). Further, the use of nitroglycerin is not objectionable to bystanders as is the odiferous amyl nitrite.

More recently a second sublingually effective drug has become available. Introduced in 1959, isosorbide dinitrate may also be prescribed to relieve anginal pain. When administered sublingually it provides relief within two to three minutes (AMA 1971, p. 17), thus being somewhat slower than nitroglycerin.

Sales of sublinguals are not large, amounting to only $3.5 million in 1971. As a proporation of all antianginal sales, sublinguals (in essence the rapid-acting agents) have ranged from 3 percent to 6 percent over the 1956 to 1971 period, accentuating the relatively greater importance of drugs designed to prevent angina pain.

Long-Term Prophylactics: Drugs to Prevent Anginal Pain

Once an attack of angina pectoris occurs, the patient's immediate concern is for a drug to relieve his pain. Nitroglycerin and, to a lesser extent, isosorbide dinitrate may satisfy that demand. Perhaps of greater

[4] See AMA (1971, p. 16); Modell (1970, p. 376); and Burack (1970, p. 191).

utility to the angina patient, however, would be a drug that could prevent or at least reduce the frequency and severity of anginal attacks.

The angina patient may undertake to prevent an anginal attack under two distinguishable circumstances. First, on the basis of prior experience, the patient may know that certain kinds of physical activity or mental stress are likely to produce anginal pain. By taking certain drugs immediately before he undertakes such activity, the patient may reduce the probability and severity of an anginal attack. Second, by taking drugs at regularly scheduled intervals, the anginal patient might hope to reduce the probability and severity of unpredictable anginal attacks. Drugs intended to provide one or both kinds of therapy are widely available, the largest chemical class of which is the "nitrate" preparations. Certainly the prevention of pain should be more desirable than alleviating pain once it occurs, and this desire is reflected by the fact that sales of long-term prophylactics grew from $7,237,369 to $58,617,669 between 1956 and 1971—levels that account for 94 percent of all antianginal sales in both years. The proportion has been relatively constant over the whole period, as shown in Table IV.3.

TABLE IV.3—Shares Held by Antianginal Chemicals, 1956–71.
(Figures are percentages).

Antianginal drugs	Date of FDA Approval	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Sub-linguals:		5.99	5.17	4.58	4.00	4.04	3.85	3.42	3.24	3.35	2.94	3.16	3.62	3.83	4.18	4.62	5.62
nitroglycerin (glyceril trinitrate)		5.99	5.17	4.58	4.00	4.04	3.66	3.21	2.93	3.01	2.38	2.31	2.36	2.02	2.18	2.14	2.70
isosorbide dinitrate	1959	0	0	0	0	0	.19	.21	.31	.34	.56	.85	1.26	1.81	2.00	2.48	2.92
Long-Acting Prophylactics:		94.01	94.83	95.42	96.00	95.96	96.15	96.58	96.76	96.65	97.06	96.84	96.38	96.17	95.82	95.38	94.38
pentaerythritol tetranitrate		75.45	79.13	79.90	81.51	83.84	83.65	80.32	78.36	75.94	73.10	69.35	63.15	57.34	50.01	44.26	39.58
Peritrate	1951	69.56	69.81	66.48	63.61	64.53	62.44	62.57	61.36	58.63	54.97	51.99	47.29	43.60	38.27	33.81	30.43
dioxyline phosphate	1951	9.00	5.99	4.17	3.18	2.47	1.99	1.65	1.45	1.20	.98	.88	.83	.68	.57	.48	.40
nitroglycerin (glyceril trinitrate)	1954	.20	2.88	4.68	4.38	3.01	2.84	2.12	2.21	2.13	2.09	3.06	5.26	6.52	7.39	8.75	8.82
mannitol hexanitrate		8.13	5.97	4.74	3.30	2.36	1.64	1.22	.98	.82	.65	.52	.46	.38	.36	.29	.22
sodium nitrite		1.09	.70	.53	.46	.48	.35	.23	.23	.22	.16	.13	.11	.08	.06	.06	.04
tronitrate phosphate		*	*	*	*	.57	.38	.26	.21	.85	2.26	1.85	1.41	1.09	.93	.69	.55
erythritol tetranitrate		.14	.16	1.40	.75	1.25	1.27	1.90	1.63	2.16	2.24	2.57	3.06	2.41	2.90	2.29	2.13
isosorbide dinitrate	1959	0	0	0	2.42	1.98	1.72	2.36	3.08	4.12	7.24	11.11	15.34	18.42	22.06	24.66	26.23
dipyridamole	1961	0	0	0	0	0	2.31	6.52	8.61	9.21	8.34	7.37	6.76	4.94	4.23	3.70	3.63
propranolol hydrochloride	1967[1]	0	0	0	0	0	0	0	0	0	0	0	0	4.31	7.31	10.20	12.78

[1] On the question of FDA approval for use in the treatment of angina, see footnote 12 of this chapter

* Data not available

0 = Not marketed

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Early Entry and the Dominance of Peritrate

Following the introduction of the first single-entity Peritrate in 1952, new dosage forms of the chemical including combinations with other drugs were put on the market by Warner-Lambert. By 1956 Peritrate was available in combination with aminophylline and phenobarbital. In 1957, a new sustained-action dosage form, Peritrate-SA, was offered—a dosage form that gained rapid acceptance and accounted for 16.9 percent of the market by 1971.[5] Later, in 1958, Peritrate was combined with nitroglycerin. Together these drugs constitute the Peritrate product line and when the term Peritrate is used in this report it is used collectively. By 1956, the beginning of the time period here under study, the market for antianginal drugs was already dominated by Warner-Lambert and Peritrate accounted for 69.6 percent of the sales of sublinguals and long-term agents combined.

To explain Peritrate's success in the market over a long period of time, several avenues need to be explored. For example, protection from competition may be provided by patents, license arrangements, or control over the supply of raw materials, or a drug may attain a strong position by being the lowest-priced agent in the market. Furthermore, a drug may be an important new therapeutic development, or the sheer inertia of physicians to switch to other drugs after the entry and heavy promotion of a brand may be the major cause of that brand's dominance. Each of these areas will be examined in turn.

Patents, Licenses, and Sources of Supply:

As described in more detail in appendices C and D, patents, licenses, or control of the supply of the main generic ingredients offer no explanation for the high concentration or the dominance of Peritrate in this market. Peritrate itself was not patented, and the chemical was available in bulk form from 28 suppliers in the study period.

Given the absence of patent barriers and the easy accessibility of supplies of bulk generic ingredients, Warner-Lambert's success with Peritrate encouraged many firms to enter the market; and along with this entry, firms sought to differentiate their offerings. Known chemicals were introduced under new brand names. Barbiturates or tranquilizers were added to "nitrates" already on the market. New dosage forms, particularly the sustained-action form that was to become quite important, provided a basis for entry. And, much less frequently, a new chemical appeared. Both small, price-oriented firms and large, research and promotion-oriented

[5] Sustained-action dosage forms on "major" chemicals in this market have become quite important. Only PETN, isosorbide dinitrate, trolnitrate phosphate, and nitroglycerin have been offered in this form, and by 1971 sales amounted to 43.9 percent of all antianginal preparations. The sustained-action dosage form permits fewer pills to be prescribed in a given therapeutic regimen; i.e., one pill in a 12-hour period instead of four pills.

firms participated in this movement, but the vast majority of brands obtained only miniscule shares: 94.3 percent of the brands had shares less than one percent of the market in 1971.

Prices:

Price also must be eliminated as an explanation for high concentration in this market. The largest selling brands are also among the highest priced drugs. For example, Table IV.4 reveals that on each of three dosage strengths the average price of Peritrate exceeds the average price of all other PETN drugs over 1968–71. In two cases the price differences are very substantial indeed. On 10 mg. PETN, Peritrate's price is 578 percent higher than the average price of the other drugs; on 20 mg. PETN, Peritrate's price is 612 percent higher. Peritrate's marketing advantage is manifest not only by its high market share, but also by its high price.

TABLE IV.4.—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.			11
Mean price per thousand	$56.03	$53.67	
Sales	$41,828,098	$1,169,616	
Quantity (thousands)	746,544	23,653	

*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.

As did the oral diuretic price data, the antianginal price data illustrate that firms appear to be willing to compete on the basis of price. Physicians, however, seem to prefer prescribing drugs on some basis other than price. In this respect, physicians may act as deficient purchasing agents for consumers.

Therapeutic Gain:

During the early 1950's, pharmacological opinion about the value of long-term prophylactic therapy for angina was guarded.[6] In 1954, Kenneth Melville (1954, p. 31/13) wrote:

> For long-term prevention, the longer-acting nitrites, including sodium nitrite, erythrityl tetranitrate, and mannitol hexanitrate, are often used . . . On the whole, however, none of these agents have provided satisfactory and effectual long-term protection. Careful clinical observations have shown that none of these agents proved "to be much efficacious than a simple placebo mixture."

Warner-Lambert appears to have introduced Peritrate at a time when existing therapy for long-term prevention of angina was in need of improvement, and, in fact, the introduction of Peritrate occurred in conjunction with some favorable clinical reports. Nevertheless, a careful evaluation of the evidence suggests that Peritrate did not offer an important gain over already existing therapy. In reviewing the therapeutic merits of drugs introduced over the last 20 years, the Food and Drug Administration considered PETN to offer no better than little or no therapeutic gain.[7] Moreover, some clinical studies published some time after the introduction of Peritrate rated PETN no better than a placebo.[8] Writing two years after the introduction of Peritrate, the first appearance of pentaerythritol tetranitrate (PETN), Melville (1954, 31/3) concluded that

> "the therapeutic status of the newer nitrites triethanolomine trinitrate diphosphate [trolnitrate phosphate] and pentaerythritol tetranitrate has not been adequately established . . . preliminary results would appear to warrant further clinical studies with these agents."

Furthermore, Sollman (1957, p. 635) noted in 1957 that PETN acts slower and longer than other organic nitrites (e.g., erythrityl tetranitrate and mannitol hexanitrate). Even later, Friedberg (1966, p. 753) concluded that although Peritrate (PETN) is widely used and very favorable claims have been made for it, he has not found that

[6] A particular problem in determining the effectiveness of anginals is the presence of *subjective* elements in the evaluation. Pain may be relieved with the administration of an appropriate drug, but whether the chemical itself brought relief, or whether the pain was eased by the patient's strong desire to want relief and to believe that the consumption of the drug would bring that relief is difficult to determine. Modell (1970, pp. 11–12) notes:

> The patient's desire to get well and his response to the fact that he is receiving accredited attention and reassurance—the so-called placebo effects of treatment—tend to provide the illusion of effects from medication itself and to make it difficult to distinguish the difference between the specific effects of the medication and the inevitable nonspecific effects of the fact of receiving treatment.

[7] See *FDC Reports*, (1974).

[8] Charlier (1961, p. 72) noted that "therapeutically, pentaerythritol tetranitrate is considered excellent in angina by all clinicians who used purely subjective methods of assessment without employment of a double-blind system. . . . For the authors who favour objective methods, the results were hardly favourable." Reports supporting PETN appeared in 1949, 1950, 1952 (3), and 1955. Studies that did not endorse PETN were published in 1952, 1953, and 1955.

> Peritrate (or other long-acting nitrate compounds) is a valuable addition to the therapy of angina pectoris, or that it has given sufficiently consistent benefit to justify its recommendation.

To be sure, a review of pharmacological literature sheds little light on actual physician and patient experiences with the various antianginals, and it may be that physicians believed that they had greater success with PETN than with previously available drugs. Certainly the rate of physician acceptance was high in the early years, indicating that physicians' experiences with Peritrate must have been reasonably satisfactory. Just four years after its introduction, Peritrate accounted for nearly 70 percent of market sales. Therapeutically, Peritrate was a new chemical and may have been attractive in that light. Accompanied by the early favorable clinical studies, Peritrate was certainly no worse than the older available alternatives; furthermore, physicians had had many years of use with existing drugs, and patient tolerance to the nitrates on the market was a problem.[9]

Nevertheless, pharmacological literature suggests that therapeutic importance does not provide a satisfactory explanation for Peritrate's success, and Peritrate's declining market share over time offers some testimony to physicians' gradual realization that the drug was not therapeutically unique. Peritrate's strength in the market appears to have arisen from being the first antianginal drug to be heavily promoted.

Brand Promotion and Being First:

For physicians to prescribe individual brands, the existence and therapeutic properties of these brands must be made known to them. Such information is transmitted by drug salesmen (known as detailmen), advertising in medical journals, bulk mail distributions, the tendering of free drug samples, and presentations and displays at doctors conventions, to name the major techniques. The expense of promoting drugs can be considerable, as seen in the case of only a few of the numerous brands offered for the prevention of angina. The expense can also be quite minimal and, in fact, a fair proportion of small, price-oriented firms make no attempt to promote their antianginal brands. According to data

[9] Pharmacologist disenchantment with available "nitrate" therapy seems aptly expressed in the following statements. Goodman and Gilman (1965, p. 748) note that:

> This aspect [long-term prophylaxis] of the drug therapy is an unsatisfactory as the treatment of individual attacks is satisfactory. . . . Long-term use of an organic nitrate appears to be prescribed 'hopefully' rather than with real conviction. This lack of confidence is amply justified by the results of studies that appear to be adequately controlled and allow statistical evaluation of the results.

Modell (1970, p. 379) also argues that:

> The persistent failure of nitrites to provide prophylaxis presumably because of the development of tolerance, suggests that the search for still another nitrite is likely to be fruitless. A drug of another pharmacologic group should be sought—one against which tolerance does not develop.

submitted to the FTC, 47.7 percent of the brands with sales in 1971 were not promoted (i.e., zero expenditures were reported).

Warner-Lambert may have realized that physicians would respond favorably to promotional effort, and the promotion and use of the brand name Peritrate apparently have been key elements in this drug's initial success. Easy to remember and write, Peritrate was virtually the first product in this area to be offered under a brand name. A review of Drug Topic's *Red Book* for 1950–51 and 1951–52 revealed only one other brand name associated with drugs in this market—Nitranitol (a brand of mannitol hexanitrate).

Since Peritrate had already achieved dominance of the market by 1956, its initial promotional effort had obviously been successful. Promotional expenditures in the early years are not known since Warner-Lambert could provide data on Peritrate only for years subsequent to 1961. However, if pre-1962 promotion at least equaled post-1962 promotion, it would have been very intensive indeed. (As shown in Table IV.5, Peritrate promotion has ranged from $2.6 million to $3.9 million through the period 1962–1971.)

After achieving success, Peritrate appears to have benefited from the loyalty doctors attached to the brand. Doctors now tend to write prescriptions using the trade names of drugs; and with favorable use experience, they seem to remain loyal to these drugs. For drugs prescribed for the relief and prevention of angina pectoris, this condition may be even more prevalent. A marketing report for a competitor notes:

> Research shows that doctors will agree that our product is in many ways superior to Peritrate alone, but they are reluctant to try it on patients that are on Warner-Chilcott's preparations, the reason being that this type of patient is a constant risk and they do not want to make any changes which might disturb the patient.

The following year, a marketing report for the same drug notes the problem again:

> The coronary vasodilator market is peculiar in that one cannot hope to increase sales by getting a doctor to switch a cardiac patient from one successful product to another. This happens rarely, if ever. What one must do is snare the *new* cardiac patient.[10]

Another factor seems to be the frequency with which doctors see new patients. According to Roerig's analysts, the physician sees on the average only about seven new coronary patients a year. The reluctance of doctors to switch brands and the limited number of business from new patients are factors not conducive to easy entry and resultant large market shares.

[10] Other firms echo the same theme. Another marketing report for a late entrant notes that "while doctor reaction has been good, it is recognized that with a drug of this type, the doctor is reluctant to 'brand switch'. Promotion, accordingly, has been directed to use with new patients or for those patients with psychological problems where a change in therapy is indicated."

Hence, Peritrate's continued success is attributable in large part to prescriber inertia and the high volume of promotion designed to keep physicians loyal to the brand.

Table IV.5 presents the market shares and promotional indexes for the 16 most intensively promoted brands of antianginals. For the period 1956–71, these sixteen brands accounted for 94.1 percent of total promotion expenditures, and 91.2 percent of total market sales. The data reveal that Peritrate has clearly enjoyed the fruits of being first to devote a substantial dollar volume to promotion. Only in 1971 has Peritrate's promotional effort been exceeded and that by American Home Product's Ives Division on Isordil (isosorbide dinitrate). From 1962 to 1971, annual promotional effort on Peritrate has ranged from $2.6 million to $3.9 million in any given year. Promotion on Isordil reached $3.4 million in 1971, surpassing the $2.9 million spent on Peritrate.

It seems then that Warner-Lambert achieved a substantial product differentiation advantage by being first to use large-scale promotional effort to associate the use of the chemical with the prevention of anginal pain. Given that both patients and physicians desired a drug that would prevent pain, and given also that the drug was at least no worse than available alternatives, the heavy promotion of Peritrate apparently made many doctors aware of the potential and actual prophylactic properties of PETN and convinced them to adopt it for their patients. Repeat prescribing by physicians then sustained Peritrate's dominance for a long period.

The marketing advantage attained by Peritrate appears to have had two main implications for potential rivals seeking to overcome Peritrate's advantage. First, the data of Tables IV.5 and IV.6 suggest that late entrants had to promote their products at more intensive levels than Warner-Lambert incurred for Peritrate. Second, in order to erode the advantage of the early entrant, follower firms' brand introductions had to offer improvements in anginal drug therapy. These points may be illustrated by looking at the conduct and relative success of late arrivals on the market.

Overtaking Peritrate: The Experience of "Major" Rivals

As noted earlier, brands offered by a large number of small firms receive little or no promotion. Furthermore, most of these brands have offered no improvement in therapy, representing merely additional entry of known chemicals. The shares earned by these brands have been miniscule, a result in accord with the arguments raised above. Of greater interest though are a small number of brands on which at least a modest promotional effort was made.

TABLE IV.5.—Market Share, Promotion, and Promotion to Sales Ratios (P/S) of 16 Antianginals, 1956–71

Firm	Brand [Generic]		1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
W-L	Peritrate [Petn]																	
	Sales Share	%	69.6	69.8	66.5	63.6	64.5	62.4	62.6	61.3	58.6	55.0	51.9	47.3	43.6	38.3	33.8	30.4
	Promotion	$	?	?	?	?	?	?	2,760,900	2,634,700	3,094,600	3,700,600	3,187,700	3,547,700	3,926,500	3,445,200	3,268,400	2,872,900
	P/S	%							19.0	16.4	17.3	19.0	16.1	18.7	18.7	17.7	17.1	15.2
AHP (Ives)	Isordil [ISDN]																	
	Sales Share	%	NM	NM	NM	2.4	2.0	1.9	2.6	3.4	4.5	7.8	11.9	16.6	18.7	21.8	23.6	24.8
	Promotion	$				270,400	289,700	258,200	307,700	441,600	565,100	1,032,500	1,548,100	1,842,200	2,273,100	2,770,700	3,059,400	3,463,300
	P/S	%				77.6	89.1	68.4	51.5	49.6	41.5	37.4	33.9	27.7	25.3	24.9	22.9	22.5
AHP (Ayerst)	Inderal [Propranolol HCL]																	
	Sales Share	%	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	4.3	7.3	10.2	12.8
	Promotion	$													699,722	815,528	1,269,377	2,131,125
	P/S	%													33.7	21.9	22.0	26.8
AHP (Wyeth)	Equinitrate [Petn & Meprobamate]																	
	Sales Share	%	NM	NM	3.4	6.2	6.0	5.5	4.7	4.3	4.1	3.8	3.2	2.8	2.3	2.0	1.8	1.5
	Promotion	$			189,771	307,770	294,309	299,535	315,010	302,413	360,963	355,329	283,081	246,667	294,597	243,288	197,823	162,982
	P/S	%			46.5	34.7	29.9	27.5	28.5	26.8	29.1	26.5	22.8	21.7	26.7	23.7	19.4	17.2
B-W	Cardilate [Erythritol Tetranitrate]																	
	Sales Share	%	NM	NM	1.2	0.8	1.2	1.3	1.9	1.6	2.2	2.2	2.6	3.1	2.4	2.9	2.3	2.1
	Promotion	$			105,000	187,000	140,000	273,000	181,000	242,000	248,000	181,000	268,000	380,000	343,000	576,000	700,000	547,000
	P/S	%			72.9	173.1	68.3	108.8	40.9	56.5	37.6	22.8	27.3	31.0	29.6	39.0	54.2	41.4
C-W	Miltrate [Petn & Meprobamate]																	
	Sales Share	%	NM	NM	3.6	5.2	5.0	4.4	4.1	4.0	3.7	3.6	3.2	2.9	2.7	2.1	1.7	1.5
	Promotion	$			386,000	355,150	325,600	311,000	399,000	407,500	467,000	334,500	251,500	286,300	191,000	103,000	67,500	13,600
	P/S	%			90.6	47.7	39.7	35.7	42.1	38.8	40.8	26.2	20.6	24.3	14.5	9.8	7.1	1.5
R-M	Nitranitol [Mannitol Hexanitrate]																	
	Sales Share	%	7.6	5.6	4.5	3.1	2.2	1.6	1.2	0.9	0.7	0.5	0.4	0.3	0.3	0.2	0.2	0.2
	Promotion	$	268,362	165,913	119,289	65,697	49,065	34,850	31,256	27,546	24,522	22,389	19,880	17,767	18,024	18,174	16,028	14,326
	P/S	%	45.7	29.0	22.2	14.8	13.6	11.2	11.5	11.7	11.9	12.2	12.5	12.9	12.8	12.8	13.3	13.9

Armour	Pentritol [Petn]																
	Sales Share	%	NM	NM	NM	NM	1.0	1.4	1.5	1.7	2.2	2.2	2.3	2.3	1.7	1.5	1.3	1.3
	Promotion	$					61,367	99,542	157,925	164,048	232,621	272,340	313,478	277,497	314,361	230,405	267,589	239,390
	P/S	%					38.0	35.4	46.3	37.6	35.1	34.8	35.2	30.8	38.2	30.1	35.2	30.4
ICI	Sorbitrate [ISDN]																	
	Sales Share	%	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	1.5	2.2	3.5	4.4
	Promotion	$													1,467,000	1,511,000	1,469,000	1,702,000
	P/S	%													199.2	134.0	73.8	62.4
Geigy	Persantine [dipyridamole]																	
	Sales Share	%	NM	NM	NM	NM	NM	2.3	6.5	8.6	9.2	8.3	7.4	6.8	4.9	4.2	3.7	3.6
	Promotion	$						300,000	2,200,000	2,300,000	2,200,000	2,000,000	1,310,000	497,000	331,000	186,000	188,000	253,000
	P/S	%						65.9	145.1	102.0	78.1	67.8	46.6	18.4	13.9	8.6	9.0	11.2
Key	Nitroglyn [nitroglycerin]																	
	Sales Share	%	NM	2.7	4.6	4.3	2.9	2.5	1.9	2.0	1.9	1.8	1.6	1.6	1.3	1.2	1.2	0.7
	Promotion	$		?	?	?	?	?	243,000	413,000	221,000	197,000	180,000	185,000	193,000	265,000	223,000	174,000
	P/S	%							54.1	78.8	37.1	30.0	29.1	28.6	30.6	43.7	32.8	42.3
Marion	Nitrobid [nitroglycerin]																	
	Sales Share	%	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	1.0	2.5	3.3	3.9	4.7	5.7
	Promotion	$											495,000	855,000	924,000	1,492,000	1,366,000	519,000
	P/S	%											133.4	85.4	58.6	74.7	51.8	14.6
Marion	Duotrate [Petn]																	
	Sales Share	%	NM	NM	?	?	2.3	3.1	2.9	2.6	2.6	3.4	3.7	3.3	3.2	2.7	2.3	2.0
	Promotion	$			?	?	?	46,000	244,000	124,000	141,000	101,000	166,000	315,000	774,000	107,000	86,000	57,000
	P/S	%						7.5	36.2	18.3	17.8	8.3	11.8	23.8	50.4	7.9	6.6	4.6
Pfizer	Metamine [trolnitrate phosphate]																	
	Sales Share	%	?	?	?	?	?	?	?	?	0.7	2.1	1.8	1.4	1.1	0.9	0.7	0.5
	Promotion	$									54,400	272,500	67,500	19,100	752,600	27,000	29,400	7,800
	P/S	%									26.0	36.0	10.0	3.4	144.0	5.7	7.6	2.3

Table continued on following page. See footnotes at end of table.

TABLE IV.5.—Market Share, Promotion, and Promotion to Sales Ratios (P/S) of 16 Antianginals, 1956–71—Continued

Firm	Brand [Generic]		1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Pfizer	Cartrax [Petn & hydroxyquin hydrochloride]																	
	Sales Share	%	NM	3.6	1.6	2.5	2.1	1.6	1.4	1.3	1.3	1.2	1.1	1.1	0.9	0.8	0.6	0.6
	Promotion	$	?	?	?	?	?	?	?	162,500	130,600	198,000	103,400	194,900	55,500	10,700	8,700	1,200
	P/S	%								48.2	32.8	45.0	23.7	45.0	13.5	2.8	2.4	0.3
W-L	Perithiazide																	
	Sales Share	%	NM	NM	NM	NM	NM	2.0	0.3	0.5	0.4	0.3	0.3	0.2	0.1	0.1	0.04	NM
	Promotion	$						293,900	60,600	?	?	?	?	?	?	?	?	
	P/S	%						73.1	83.8									

NM = Not Marketed
? = Data not available

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

TABLE IV.6.—Promotion as a Proportion of Sales: Peritrate versus All Other Antianginals

Year	Peritrate (percent)	All Others (percent)
1956	—	17.9
1957	—	10.1
1958	—	23.7
1959	—	25.1
1960	—	21.9
1961	—	27.6
1962	19.0	49.1
1963	16.4	46.7
1964	17.3	38.2
1965	19.0	32.3
1966	16.1	28.5
1967	18.7	30.3
1968	18.7	35.6
1969	17.7	28.6
1970	17.1	26.9
1971	15.2	22.9

Note: Peritrate promotion data are not available prior to 1962

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

Table IV.5 reveals data for 16 brands, each of which received at least $100,000 in promotion in one or more years during the study period. These 16 drugs were the most heavily promoted of all the antianginal brands. By classifying them according to their relative therapeutic merit it becomes easier to see the influence of therapeutic merit in overcoming Peritrate's sales advantage.

Drugs Offering Little or No Therapeutic Gain:

Among the 16 drugs of Table IV-5, 14 added little to drug therapy in the treatment of angina pectoris. Duotrate and Pentritol were single-entity sustained-action PETN and differed from Peritrate-SA only in milligram strength. Both drugs were introduced in 1960 and supported with relatively large (for this market) promotional expenditures. Promotion to sales ratios were relatively high, though Duotrate's fluctuated to low levels at times. Nevertheless, these efforts were tiny: for years in which data were received, absolute promotion dollars never exceeded 10 percent of Peritrate's effort, and neither of these products captured more than 4 percent of market sales during the study period.

Three PETN combination products were introduced: Cartrax (PETN and hydroxyquin hydrochloride), Equinitrate (PETN and meprobamate), and Miltrate (the same as Equinitrate). The combination ingredient in each case was a tranquilizer. These drugs fared little better than Duotrate

and Pentritol, and while promotion was high relative to most brands, the effort was negligible compared with Peritrate. With respect to the above brands and some others to be discussed later, their performance seems in accord with Goodman and Gilman's (1965, p. 478) comment that "long-acting antianginal agents have quite uniformly followed a pattern of initial enthusiasm, followed by equivocal results in more or less controlled studies, and then progressive disuse."

Of the two sustained-action nitroglycerin products on the list, Nitrobid, introduced in 1966, appears to have had some success, its share of sales reaching 5.7 percent in 1971. By contrast, Nitroglyn, introduced in 1957, suffered a decline in share position, holding only 0.7 percent in 1971. Although long-acting nitroglycerin products have not been greeted with enthusiam by pharmacologists and are rated in the little or no therapeutic gain category by the FDA, the combined share of sales held by these chemicals increased in 1966 and later years, eventually accounting for 8.8 percent of the market in 1971. The stimulus for this increase in the face of not even a modest therapeutic gain seems due largely to Marion Laboratories' heavy promotion of Nitrobid. Nitrobid has of course been the prime beneficiary of this promotional effort that exceeded $1 million in 1969 and 1970, peaking at $1.5 million in 1969. Nitroglyn's promotional outlay from 1962 to 1971 has ranged between $174,000 and $413,000, and its low market share seems to reflect those relatively low levels.

Persantine (dipyridamole) offered what Modell (1970, p. 379) has suggested was needed, a new non-nitrite chemical. In this sense its differentiability may have been greater than any of the above discussed brands. Introduced in November 1961,[11] its promotional effort in its first calendar year, 1962, was $2,200,000, a level roughly maintained through 1965. This effort was the most intensive of any brand except Peritrate in the period 1962 to 1965. It appears that Geigy virtually attempted to match the Peritrate promotional effort in Persantine's initial years. Furthermore, the promotion-to-sales ratio for Persantine was above 65 percent in every year through 1965. If the analysis suggested by this report is correct, Persantine should have cut more deeply into Peritrate's share of the market than it did, since Persantine appeared to be therapeutically unique and received a massive promotional stimulus. Initially, the product succeeded, its share of the market rising quickly to 9.2 percent in 1964. However, from that point, market share declined and sales failed to rise, staying relatively constant at $2–3 million a year.

What went wrong? Marketing analysts point to several factors, one of which pertained to the claims that could be made for Persantine:

[11] Persantine had been previously marketed in Germany by Boehringer.

> Prior to 1966, the use of coronary vasodilators could be promoted for arteriosclerotic heart disease or any degenerative condition causing insufficient coronary artery blood flow. In 1966, these dilators were restricted so that the only approved indication was angina pectoris.

The analysts go on to say:

> Promotion now centers on reduction in the frequency and intensity of anginal attacks, and on dosage convenience. However, the former points have been restricted recently. This is especially true for Persantine after the "Dear Doctor" letter was mailed on February 15, 1968, to 300,000 doctors stating that past promotion was potentially misleading as some opinion does not support claimed effectiveness.

Persantine may have suffered more than other antianginal agents by the curb on the claims that could be made for it.

Furthermore, Persantine's therapeutic uniqueness did not represent a vast improvement in therapy. In 1967 one marketing report reveals:

> Persantine still has major difficulties in some medical circles as far as acceptance is concerned. Again this is primarily due to a lack of support by leading clinicians as well as proof of effectiveness in humans.
> In general, the problem with all coronary vasodilators is one of physician doubt about the actual effectiveness of these agents. Persantine's inefficiencies in this regard further impedes any potential progress.

Whether Persantine was hurt more than other antianginal products by the 1966 restriction permitting indication for use only in angina pectoris is difficult to judge, but it appears that Persantine had indeed claimed much more of the product than would be permitted later by the FDA.

Further light is shed on Persantine's problem in a marketing report analyzing the reasons for a competitor's (Isordil's) success:

> 1. The offer of a complete product line covering a multitude of market segments rather than a single product like Persantine.
> 2. The availability of a sustained-action dose to eliminate cumbersome doses involving multiple tablets.
> 3. Evidence that the drug dilates the coronary arteries in humans using the technique of cineangiography. No such evidence is currently available with Persantine.
> 4. Isordil retains complete support of leading influential American cardiologists. A favorable or unfavorable word from any of these specialists regarding a particular coronary vasodilator can have a profound effect upon the progress of the drug being discussed. Persantine has little, if any, support among the more influential cardiologists in the country.

5. Isordil is competitively priced with Peritrate and other leading Nitrites whereas Persantine is considerably more expensive.

Even though Persantine's market share declined, Geigy made no effort to bring the price down; price stayed relatively constant throughout the 1961–71 period, ranging between $52 and $55 per thousands pills. Since physicians seem not to regard price as an important element in the prescribing decision, Persantine's higher price may not have been a problem anyway.

Finally, the failure of sales to grow and the massive amounts spent on promotion caused Persantine to be unprofitable: only after four years on the market did total accumulated sales of $7,041,817 barely exceed the $7,000,000 expended on promotion.

In retrospect, Persantine's problem lay in the drug itself. The chemical was not the major development that the market was looking for. Initially succeeding, Persantine's market share had dwindled to 3.6 percent by 1971, its sales supported apparently by a small group of loyal prescribers to whom selective advertising was directed. As a Geigy analyst recommended in 1967:

> The 1967 promotional plan is to basically focus upon the small "hard core" group of Persantine prescribers in the country who are loyal to the product in an attempt to maintain or hold our current market position. A program of selective journal advertising and direct mail campaigns including sampling and mail questionnaires will be utilized in an attempt to further the interest of these physicians in Persantine and increase their overall prescribing for the product. (Geigy Marketing Memorandum).

But as Modell (1970, p. 376) noted:

> . . . although there are some optimistic reports from Europe, the well-controlled clinical and laboratory studies in the United States and Britain indicate that the drug has no usefulness in the anginal syndrome. . . . One author has put it this way: "The interesting drug dipyridamole, despite much study of its biochemical and pharmacological effects, is still looking for a disease to cure."

Drugs Offering Modest Therapeutic Gains:

Isosorbide dinitrate (ISDN) has been the only drug to make substantial inroads into Peritrate's share. The particular brand to accomplish this task was Isordil, introduced by American Home Product's Ives Division in 1959. Achieving sales of $15,378,300 compared with Peritrate's $18,107,886 in 1971, Isordil virtually overcame Peritrate's marketing advantage entirely. Isordil's success appears to lie in heavy absolute amounts of promotion, a promotion-to-sales ratio higher than evident for Peritrate,

and an element of therapeutic uniqueness that sets it off from the rest of the non-Peritrate products.

As noted previously, the anginal market is made up of rapid-acting agents for the relief of actual pain, and long-acting agents claimed to be useful for the prevention of future attacks of angina pectoris. All products on the list of Table IV.5 are long-acting prophylactics. Although not as rapid in action as sublingual nitroglycerin, which brings relief within one to three minutes of administration, sublingual Isordil provides relief in two to three minutes, a claim no other long-acting agent on the list can make.

Important as this therapeutic uniqueness was, even more significant in Isordil's success may have been the heavy promotion of the drug by American Home Products' Ives Division. Although relatively modest through 1964, promotional levels were raised sharply in 1965 and continued increasing steadily, reaching $3,463,000 in 1971. At this point Isordil's dollar promotion exceeded Peritrate's for the first time. This effort also resulted in a higher promotion-to-sales ratio for Isordil than for Peritrate: Isordil's promotion-to-sales ratio has always been above 22 percent, whereas Peritrate's ratio has always been below 20 percent for the years in which data were supplied—further evidence in support of the arguments advanced in this report.

The experience of another ISDN product, Sorbitrate, introduced by ICI's Stuart Division in March 1968 (at that time Stuart was a subsidiary of Atlas Chemical) also sheds light on the requirements for successful entry in this market. For its first four years, Sorbitrate's promotion averaged about $1.5 million. Since Persantine was the only other product to attempt entry on such a promotional scale, Sorbitrate's effort was relatively massive. Its promotion-to-sales ratio did not fall below 62 percent in those four years, as shown in Table IV.5, but its market share at the end of that period was only 4.4 percent. Sorbitrate was chemically similar to Isordil but appeared on the market nine years later. Hence, compared with Isordil, Sorbitrate was not therapeutically novel. And in 1969, after the introduction of Sorbitrate, one marketing report noted that "as a 'me too' product", Sorbitrate had no competitive handle that could be used to recommend Sorbitrate over Isordil in print or direct selling situations. In fact, this same report suggests that for Sorbitrate Stuart may not have been able to match the therapeutic claims made by Ives for Isordil.

Drugs Offering Important Therapeutic Gains:

A new chemical, propranolol hydrochloride, was introduced in the U.S. in 1968 by American Home Product's Ayerst Division under the brand name Inderal. Rated by the FDA as an important therapeutic development and heavily promoted, Inderal's rapid sales growth suggests that the drug fits in well with the analysis presented here.

Although market research information reveals that Inderal has been used primarily for the treatment of cardiac arrythmias, National Disease and Therapeutic Index (NDTI) data contained in marketing reports submitted to the FTC reveal that in 1969 26 percent of the actions desired of Inderal were for the treatment of angina pectoris, while cardiac arrythmia and control of the heart rate treatments received 33 percent and 21 percent of the desired action mentions, respectively.[12] Furthermore, while the treatment of angina pectoris was not an approved indication for propranolol hydrochloride during the period covered by this study, and the company claims never to have promoted this drug for the treatment of angina in this period, Inderal has clearly been used as an antianginal and as much as 26 percent of its sales may have been for that purpose. Hence, Inderal was included in the analysis without sales adjustment.[13]

[12] American Home Products, Ives Division, Marketing Report. In this same source, the author of the report noted that "although propranolol has not been approved by the FDA for this treatment, it is, however, accepted and routinely used by many physicians." FDA approval was finally granted (see *FDA Bulletin*, 1974), at which time the FDA noted that "propranolol appears to decrease anginal pain by decreasing cardiac work and oxygen consumption." However, it advised that propranolol is indicated in selected patients who have not responded to conventional measures such as weight control, reasonable restriction of activity, cessation of smoking, and use of sublingual nitroglycerin."

[13] The problem of accurately measuring drug markets defined narrowly on demand substitutability is compounded in many cases by the multiple uses of some prescription drugs.

CHAPTER V

SALES, PROMOTION, AND THE ADVANTAGE FROM BEING FIRST

The analyses of the markets for oral diuretic and antianginal drugs strongly suggest that the responses of brand sales to brand promotion differ substantially among brands in the same market and especially among brands that should be perfectly substitutable therapeutically. Such an observation in turn suggests that broad generalizations about the effect of promotion upon sales, even among brands in the same market would be misguided.

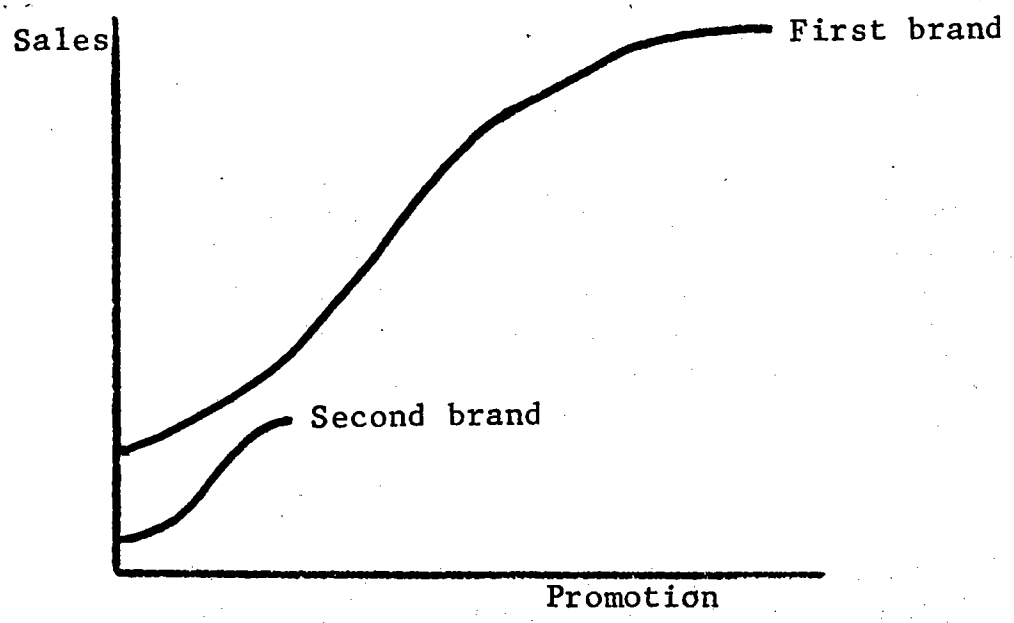
What the data have shown is that physicians are likely to respond much more favorably to the promotion of brands that are first to offer and promote some new therapeutic advantage than to the promotion of brands that merely duplicate existing therapy. In the case of oral diuretic drugs, the appearance of the first thiazide diuretic rendered previously used drugs practically obsolete. The advantage to Merck from introducing the first thiazide extended not only to its first brand, but also to a product line of related brands introduced somewhat later. In the case of antianginal drugs, the therapeutic advance achieved by the first PETN product was difficult to prove or disprove. A few pain-preventing drugs were available prior to the introduction of PETN, and, in retrospect, such drugs appear to have been at least as effective as PETN. Nonetheless, prior to the introduction of PETN, drugs used for antianginal therapy were not widely promoted, and Warner-Lambert appears to have received a long-term sales advantage from being the first firm to promote a drug to prevent anginal pain.

If, then, being first and being different are important determinants of physician response to promotion, the relationship of sales to promotion will vary among products according to the "firstness" or "differentness" of the brands. The relationships can be shown diagrammatically in much the same fashion as in Chapter II. For example, suppose there exists a market with two branded products identical to each other in every respect except the time of entry. The sales-response curves for promotion might appear diagrammatically as in Figure V.1.[1]

[1] The hypothetical sales-response functions presented in this section are drawn to imply that both the slopes and the intercepts are functionally related to being first and being different. Moreover, the functions are pictured as including an area in which there are increasing returns to promotion. Neither the assumption of different intercepts nor the assumption of increasing returns is critical to the analysis, however.

Note that every level of promotion yields a higher level of sales for the first than for the second brand and that no amount of promotion for the second

Figure V.1



brand can yield a sales volume equal to that attainable by the first brand.[2]

Figure V.2 presents a hypothetical set of sales-response curves including still a third product that enters offering some advantage to a subset, but not to all, of the potential buyers. Whereas the third "different" product may or may not outsell the first product, both the first and the different product will outsell the second product at any given level of promotion.

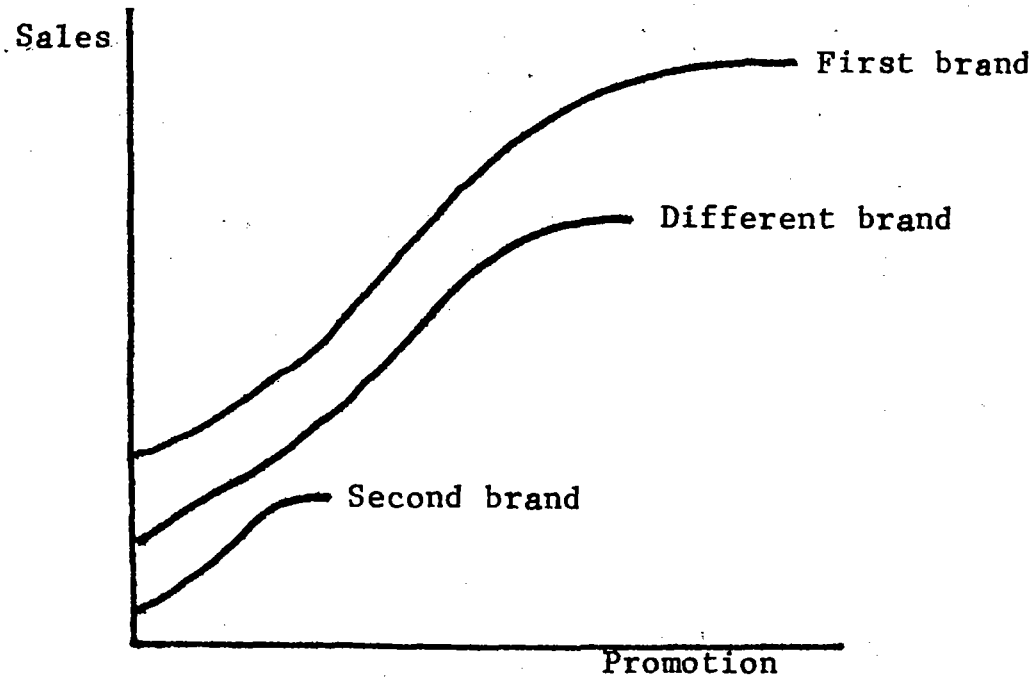
If firms attempt to maximize the profits from their brands, each firm will move to that point along its sales-response curve that yields the largest dollar volume of profits. If production costs are relatively constant, such a point would normally be along that portion of the curve where increasing amounts of promotion are yielding decreasing increases in sales (the upper

[2] The diagrammatic analysis presented here represents a convenient and simple way of incorporating an advantage to being first within an already existing framework (Simon 1970, and Comanor and Wilson 1974). The sales-promotion response curves must be viewed as relationships at a point in time with all other factors held constant. For example, the curve for each brand represents the relationship between sales and promotion with the price of that brand and other brands held constant, and with the promotion of other brands held constant at their profit-maximizing levels. Thus, the sales-promotion relationship for the second brand assumes that the first brand is being promoted at a level which maximizes the first brand's profits, with the prices of both brands being held constant.

The curves do not imply that the shapes and locations of the individual functions are independent. On the contrary, the curves are interdependent in the sense that the promotion of one brand at a level above or below that which maximizes its profits will shift the curves facing other brands. Moreover, since the advantages to being first and different probably decline over time, the various curves may be expected to shift toward one another as time passes. Hence, although the diagrammatic presentation provides a conveniently simple format for explaining how sales and promotion may be simultaneously determined by exogeneous variables, the curves are merely part of a more general and as yet unspecified model.

part of the *S*), the exact point depending upon the margin between costs and price.

Figure V.2



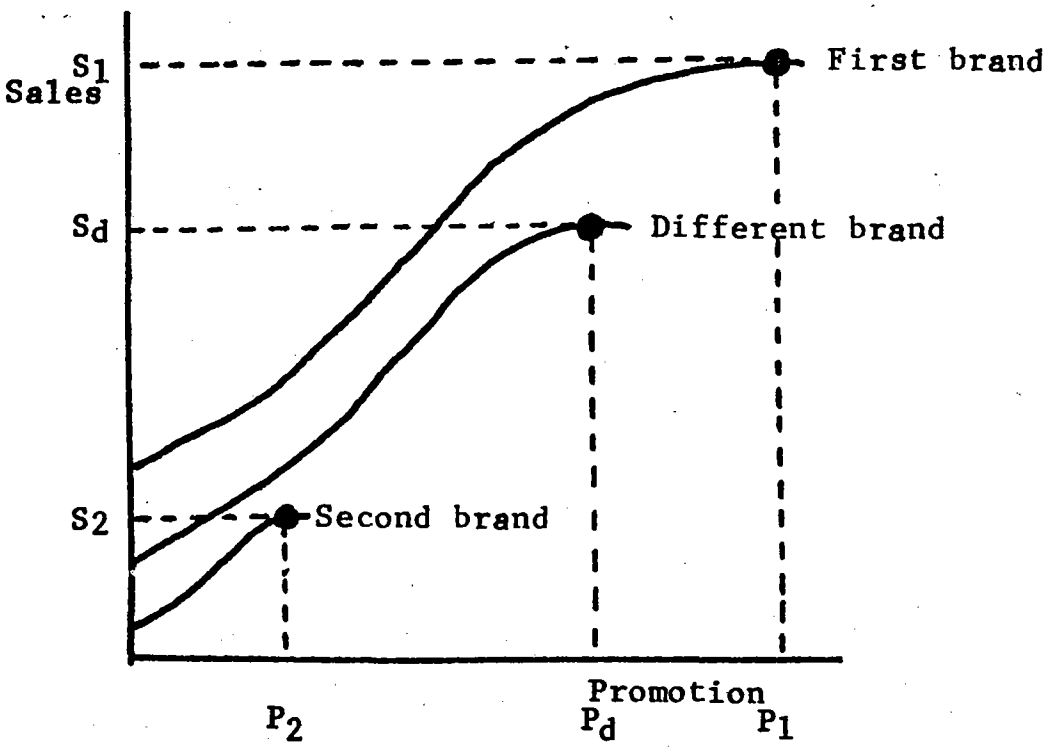
Now suppose that the first, second, and different brands are being promoted at the profit-maximizing points along their respective curves and that such points are approximated by those shown in Figure V.3.

At such points the first brand has sales of S_1 and promotion of P_1, while the second brand has sales of S_2 and so on. Any attempt to infer something about the response of sales to promotion by comparing the observable points would yield meaningless results. Yet, by connecting the three points as in Figure V.4, one might falsely conclude that any brand could achieve ever higher sales merely by spending more dollars on promotion—that promotion alone determined market share.

The probable existence of different sales-response curves for different brands presents problems for empirically estimating the relationship between sales and promotion. First, for every brand, both the profit-maximizing level of promotion and the sales attainable with that promotion are determined by product characteristics as well as by other variables. If there existed a unique curve for each and every brand, the true shape of any one curve might be estimated from time-series data only if production costs varied or if the firm varied promotion above and below the profit-maximizing amounts. If there existed several curves, each appropriate for a class of brands including several products, the true shape

of any one curve at a point in time might be estimated from cross-section data only if the firms had different production costs or if some firms

Figure V.3

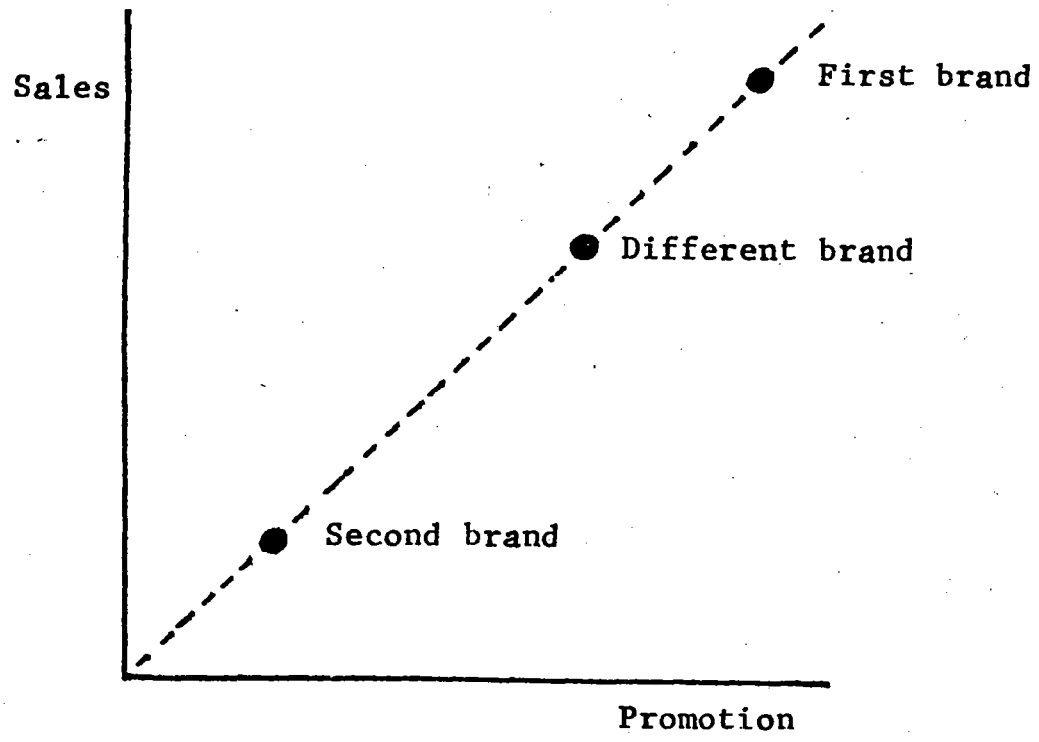


promoted more and others less than the profit-maximizing amount.

Second, the general shape of sales-response functions is unknown. It can be assumed with certainty, however, that sales-response functions are not linear. Ever increasing amounts of promotion cannot yield linearly increasing amounts of sales, since increasingly more resistant buyers must be encountered and market saturation must eventually be reached. But the knowledge that sales-response functions at least cannot be linear is small consolation. Curvilinear relationships might take any of several forms, and all such response functions must be shifting over time as market conditions change.

The techniques available for estimating statistically the shapes and locations of sales-response functions are relatively complex and not thoroughly developed (see Appendix A). Accordingly, this report relies only on descriptive statistics to identify approximately the different levels of observed sales and observed promotion associated with product differentiation characteristics in the two therapeutic markets here under study. The remainder of this chapter, then, seeks to demonstrate how both observed sales and observed promotion vary systematically according to the qualitative variables discussed in Chapters III and IV.

Figure V.4



Explaining Sales and Promotion

Although the sales and promotional data presented in Chapters III and IV provided substantial insight into the advantage from being first in a market, simple tabular data presentations cannot separate the independent influences of a number of variables. In this section the technique of multiple regression is used to provide a more systematic understanding of the relative impact upon sales and promotion of a number of different product characteristics. Although the theoretical statistical basis for multiple regression is complex, the technique does yield numerical estimates that can be readily understood even by those unfamiliar with statistics.

The variables to be explained are brand sales (SALES) and brand promotional expenditures (PROMO). The technique adopted for the present descriptive analysis is to suppress variation over time by summing the sales and promotion for each brand over all years for which data were available, the totals being divided by the number of years. For nearly all oral diuretic and most antianginal drugs, then, the average annual sales and promotion variables reflect sales and promotion over the entire market life of brands through 1971.

One advantage of the above procedure is that the high promotion usually associated with a product's introduction is averaged with promo-

tion for later years, in which promotion is more "normal." Of course, the averages for products introduced in the last few years of the period may still be unduly high relative to older brands. Nonetheless, averages based upon shorter time periods are probably subject to greater distortion. The annual sales and promotional data reveal a wide variety of behavior over time among brands. Some brands exhibit rapid sales growth from the date of introduction; others exhibit slower, but steadier sales growth. Most brands are promoted most heavily at introduction; yet, for some brands, promotion rises as sales grow. Longrun averages seem most likely to abstract from variation in firm strategies and miscalculations. As discussed in the technical appendix, use of the annual data to explain variation over time is the subject of future research.

A disadvantage of the use of long-term averages is that neither the sales nor the promotional outlay data have been adjusted for trends in the general price level. Since promotional costs have probably followed the upward movement of the general price level, promotional expenditures measured in nominal (unadjusted) dollars probably understate the real (adjusted) promotion of early entrants vis-a-vis late entrants. Hence, use of nominal dollars introduces a bias against finding higher promotional expenditures for early entrants. Similarly, although the prices of many, if not most, drug brands in the study have remained relatively constant, the costs of manufacturing and promoting the drugs have probably risen over time. Thus, although sales comparisons among brands using nominal dollars are probably little different from comparisons using real dollars, the use of nominal dollar sales probably understates the profitability advantage to early entry.[3]

To explain average annual sales and average annual promotion, a number of product characteristic variables were created. Many of those variables originally created proved to be of no value in explaining brand sales and promotion (see the statistical addendum at the end of this chapter). The variables to be explained and those that do provide insight into the problem are listed below:

Variables to be Explained

SALES—The average annual dollar sales of a brand over the entire time period the brand was marketed between 1956 and 1971.

PROMO—The average annual dollars of promotion spent on a brand over the entire time period the brand was marketed between 1956 and 1971.

[3] Evidence from the marketing reports suggests that firms learn to spend their promotional dollars more efficiently as time passes. Data are gathered to identify physicians most likely to respond to promotion, and fewer promotional dollars are wasted on broad-scale campaigns. Hence, although the prices of promotional inputs may be rising over time, increases in the productivity of promotional inputs will in part offset the effects of inflation. Simple price adjustments that ignore productivity changes would then bias upward the real promotion of early entrant vis-a-vis late entrant brands.

Explanatory Variables

TIME—The number of years the brand had been on the market in 1971.

SIZE—Total dollar sales of all prescription drugs by each firm in 1971.

FIRST—A dummy variable assigned to the "first" product in each market: Diuril in the oral diuretic market, and Peritrate in the antianginal market.

OTHMERCK—A dummy variable assigned to brands introduced by the firm marketing the FIRST brand that followed the FIRST brand: in this case Merck's brands other than Diuril.

SIZD—A dummy variable assigned to brands that were marketed by firms that were among the 30 largest pharmaceutical firms in terms of prescription drug sales in 1971.

SA—A dummy variable used in the antianginal drug analysis if a sustained-action dosage form was available under a given brand.

BRAND—A dummy variable used in the antianginal analysis if a drug was available under a brand or trade name; this variable was used only in the antianginal drug analyses.

IMPGAIN—A dummy variable assigned to the first brand on the market of a chemical given an important therapeutic gain rating by the FDA.

MODGAIN—A dummy variable assigned to the first brand on the market of a chemical given a modest therapeutic gain rating by the FDA.

The rationales for examining such product characteristics as being first on the market and therapeutic gain have been developed in previous sections of this report. Among other variables, several deserve further justification. Products with brand names have been distinguished from unbranded products since physicians may be prone to use brand names in writing prescriptions; time on the market was introduced to capture any promotional or sales advantages from early entry; and firm size is intended to distinguish the brands of larger, more prestigious firms from the brands of smaller, less well-known firms.

In developing the data sets for both orally effective diuretic and antianginal brands, the goal was to obtain brand observations such that the promotion of each was believed to affect the sales of only that brand. Nonetheless, where several brands in a product line have similar names, the proper level of aggregation for both sales and promotion is conceptual-

ly unclear. Efforts to determine the sensitivity of results to the specification of brands suggested that results were generally unaffected.[4]

The data sets are large and in effect represent the universe of the brand populations in both markets. A small number of firms was deleted from the antianginal data set either because relevant variable information was missing or because the accuracy of the information was questionable. Only one minor brand was deleted from the oral diuretic data set for the sales equation and only four minor brands were deleted for the promotion equations.

Explaining Brand Sales with Brand Promotion:

The discussion above suggests that where profit-maximizing promotion and the sales associated with that promotion are both determined by product differentiation characteristics, a naive analysis might lead one to believe that firms could achieve ever higher sales merely by increasing their promotion. The average annual sales and promotion data confirm that assertion. Simple two variable linear correlation of brand sales upon brand promotion yields the following equations for oral diuretic and antianginal brands, respectively:

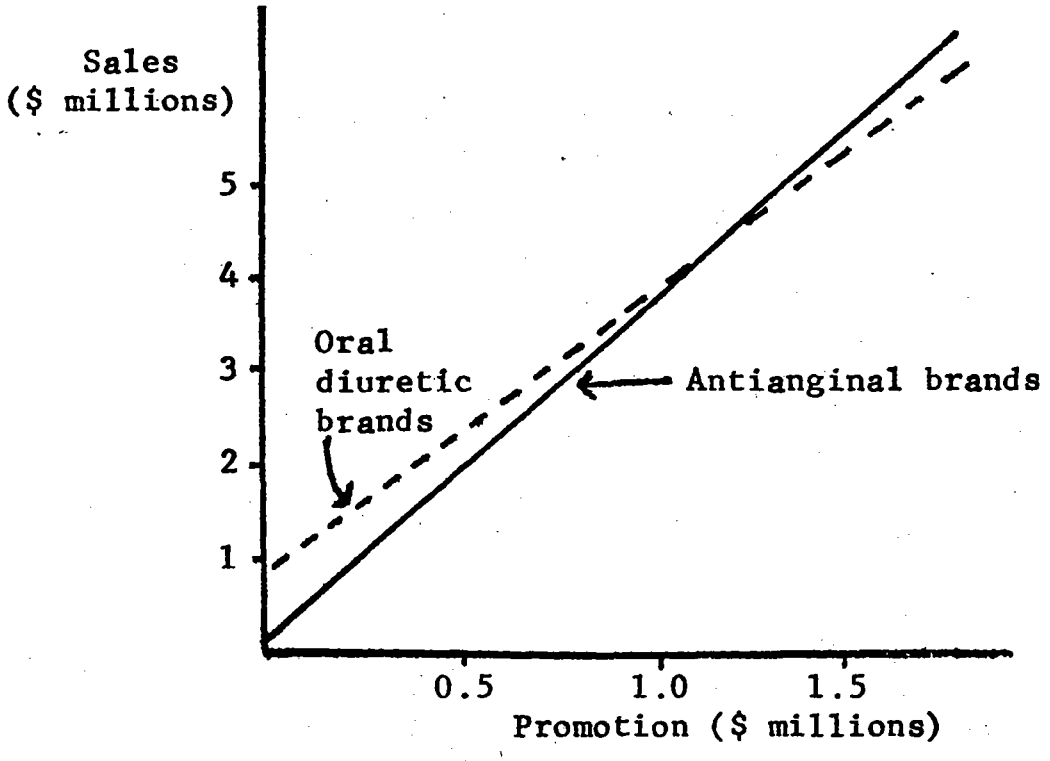
Oral Diuretic Brands: SALES = 0.814 + 2.914 PROMO r = .69 N = 64
Antianginal Brands: SALES = 0.024 + 3.631 PROMO r = .94 N = 182

Put simply, the above equations would lead one to believe that merely by spending $1.00 more on promotion the seller of an oral diuretic brand could increase his sales by $2.91, while the seller of an antianginal brand could increase his sales by $3.63. Diagrammatically, the estimated relationships look like those in Figure V.5.

But the analyses in Chapters III and IV revealed that each brand did not have an equal opportunity to gain sales via promotion. And the theoretical discussion in this chapter suggests that promotion, as well as sales, might be explained by product differentiation characteristics. Accordingly, the equations which follow are offered to demonstrate how variations in both observed sales and observed promotion can be explained by similar sets of qualitative variables.

[4] Since basic data were sometimes supplied at various levels of aggregation (some firms could provide more detailed data on promotion than others), some aggregation and disaggregation of the raw information was required. For example, in oral diuretics, Renese and Renese-R were treated in the present analysis as separate brands since the therapeutic indications for each are somewhat different. Nonetheless, Pfizer had submitted promotional data that covered both brands. To disaggregate this data, the ratio of promotion to sales was assumed to be the same for each brand. On the other hand, sales data for two different dosage forms of the antianginal PETN (for example, Peritrate and Peritrate-SA) were combined since each dosage form is indicated for the same ailment. Inevitably, however, the delineation of brand observations is an imprecise process.

Figure V.5



Explaining Brand Sales:

The following is the equation that "best" explains average annual brand sales of *oral diuretic* drugs:

$$\text{SALES} = -0.181 + 0.155\,\text{TIME} + 4.830\,\text{IMPGAIN} + 2.815\,\text{MODGAIN}$$
$$(2.045) \qquad (4.657) \qquad (2.282)$$

$$+ 11.661\,\text{FIRST} + 2.731\,\text{OTHMERCK} \ldots \bar{R}^2 = 0.574, \text{N} = 67$$
$$(4.481) \qquad (3.129)$$

Figures in parentheses are t values:

t values greater than 2.39 are significant at the 1% level
t values greater than 1.67 are significant at the 5% level
t values greater than 1.30 are significant at the 10% level

Put simply, the equation reveals the following:

1) Brands early to enter the market received higher average annual sales. For every year earlier a brand was on the market, the brand on average received an additional $155,000 in sales per year.

2) Brands offering *important* therapeutic gains had average annual sales $4.83 million per year higher than brands offering no therapeutic gain.

3) Brands offering *modest* therapeutic gains had average annual sales $2.82 million per year higher than brands offering no therapeutic gain.
4) Merck's Diuril, the first brand on the market, had average annual sales $11.66 million per year higher than other brands.
5) Merck's other or non-first brands had average annual sales $2.73 million per year higher than other brands.

Together these variables explained approximately 57.4 percent of the variation in the average annual sales of oral diuretics. The coefficients for the explanatory variables of therapeutic gain, first on the market, and the first firm's follow-on brands are all highly significant and proved to be quite stable regardless of the exact equation specification in which they were included. Interpretation of the time variable reported above and a size dummy variable not reported above requires further elaboration, however, and the interested reader is referred to the statistical addendum for further discussion. Other variables that were introduced but proved to be insignificant included a dummy variable distinction between single-entity and combination drugs (COMB) and a dummy variable distinction between potassium-supplemented and nonpotassium supplemented thiazide drugs (K) (see the statistical addendum at the end of this chapter).

Being first on the market and offering a brand incorporating a therapeutic gain proved to be highly significant on the antianginal market as well. Several formulations of a sales equation produced highly adequate explanations of sales. The following is the equation that "best" explains annual average sales of *antianginal* brands:

$$\begin{aligned} SALES = &-0.040 + \underset{(56.897)}{14.329}\,FIRST + \underset{(8.940)}{0.444}\,SIZD + \underset{(1.377)}{0.056}\,SA \\ &+ \underset{(1.564)}{0.061}\,BRAND + \underset{(17.604)}{4.407}\,IMPGAIN + \underset{(18.297)}{4.608}\,MODGAIN \ldots \quad \bar{R}^2 = 0.961,\ N = 182 \end{aligned}$$

Figures in parentheses are t values:
t values greater than 2.36 are significant at the 1% level
t values greater than 1.66 are significant at the 5% level
t values greater than 1.29 are significant at the 10% level.

Expressed simply, the equation reveals the following information:

1) Warner-Lambert's Peritrate product line, the first antianginal brand to be heavily promoted, has enjoyed average annual sales $14.3 million higher than other brands in the market.
2) Firms among the 30 largest prescription drug sellers enjoy average annual sales $444,000 higher than firms of smaller size.
3) The only brand offering an *important* therapeutic gain received average annual sales $4.407 million more than brands that offered little or no gain.

4) The only brand that offered a *modest* therapeutic gain enjoyed average annual sales $4.608 million higher than brands that offered little or no gain.

5) The use of a brand name or the offer of a sustained-action dosage form was worth an additional $50,000 to $60,000 per year to a brand.

Of the explanatory variables, which together explain approximately 96.1 percent of the variation in average annual sales, first on the market, therapeutic gain, and size of firm are extremely significant.[5] Sustained-action dosage forms and brand name rather than generic name usage are marginally significant determinants. In other formulations of the equation, the length of time a brand had spent on the market was not significant.

Explaining Brand Promotion:

For the *oral-diuretic* drugs, the following is the equation that "best" explains average annual brand promotion:

$$\text{PROMO} = 0.027 + 1.250\,\text{IMPGAIN} + 1.442\,\text{MODGAIN} + 0.396\,\text{SIZD}\ldots \overline{R}^2$$
$$(4.405) \qquad (3.964) \qquad (1.681)$$
$$= 0.370,\ N = 64$$

Figures in parentheses are t values:

t values greater than 2.39 are significant at the 1% level
t values greater than 1.67 are significant at the 5% level
t values greater than 1.30 are significant at the 10% level.

Put simply, the equation illustrates the following:

1) Brands offering *important* therapeutic gains were promoted on average $1.25 million more per year than brands offering no therapeutic gain.

2) Brands offering *modest* therapeutic gains were promoted on average $1.44 million per year more than brands offering no therapeutic gain.

3) Firms among the 30 largest pharmaceutical firms in 1971 spent $396,000 more per year promoting their brands than did smaller firms.

Together the explanatory variables account for approximately 37.0 percent of the variation in annual average promotion. The insignificance of the FIRST variable (See Table V.1, Equation 11) may be attributable to any of several factors. First, several late-arrival brands were heavily promoted. Second, since the first brand was also an important therapeutic gain, the absolutely large promotional expenditures on that brand are explained in part by the therapeutic gain variable. Finally, the use of promotional

[5] The modest gain product, Isordil, earned slightly higher average sales than the important gain product, Inderal. This result is due to Isordil's lengthier time on the market—13 years compared with 4 years—and to Inderal's failure to obtain FDA approval for the antianginal indication until after the study period (see the discussion of this drug at the end of chapter IV).

expenditures unadjusted for price changes tends to understate the promotion of early-entrant brands relative to late-entrant brands. In experimenting with other forms of the equation, the inclusion of alternative variables resulted in lower values for $\overline{R}^2$.

For the *antianginal* drugs, several equations offer highly adequate explanations of average annual promotion expenditures, the "best" of which is the following:

$$\begin{aligned}\text{PROMO} = 0.009 &+ \underset{(19.719)}{3.052}\,\text{FIRST} - \underset{(-1.595)}{0.444}\,\text{TIME} + \underset{(6.306)}{0.192}\,\text{SIZD} \\ &+ \underset{(1.679)}{0.047}\,\text{BRAND} + \underset{(6.407)}{0.995}\,\text{IMPGAIN} + \underset{(7.715)}{1.192}\,\text{MODGAIN}\ldots\ \overline{R}^2 = 0.774,\ N = 182\end{aligned}$$

Figures in parentheses are t values:

t values greater than 2.36 are significant at the 1% level
t values greater than 1.66 are significant at the 5% level
t values greater than 1.29 are significant at the 10% level.

This equation indicates the following:

1) The average annual promotion on the Warner-Lambert Peritrate product line is $3.052 million more than on any other brand.

2) For every additional year a brand continues in the market, average annual promotion is reduced by $4,000. The TIME variable was only marginally significant.

3) Firms that are among the 30 largest sellers of prescription drugs spend $192,000 more each year on promotion on the average than do smaller sized firms.

4) Average annual promotion on drugs that are offered under brand names is $47,000 higher than for drugs not offered under brand names.

5) Drugs offering *important* therapeutic gains are promoted on average $995,000 more per year than drugs that offer little or no therapeutic gain.

6) Drugs that offer *modest* therapeutic gains are promoted on average $1.192 million more than drugs that offer little or no therapeutic gain.

Together the explanatory variables account for approximately 77.4 percent of the variation in average annual brand promotion. For explaining average annual promotion of antianginal brands, then, the most significant variables are being first on the market, therapeutic gain, the size of the firm, and using a brand rather than a generic name.

Summary

The diagrammatic presentation and the regression estimates presented in this chapter illustrate how both observed sales and observed promotion vary according to product differentiation characteristics. Although the

regression estimates cannot be used to derive the exact shapes and locations of individual sales response curves, they do reveal that being first and being therapeutically novel are important determinants of actual sales and promotion. The first and therapeutic gain brands tend to have higher promotion and higher sales than late-entering substitute brands.[6]

Although many of the same explanatory variables were significant in both the oral diuretic and the antianginal equations, certain differences do appear. Some of those differences may be readily explained. For example, the BRAND variable, introduced in the antianginal equations, does not appear in the oral diuretic equations since all oral diuretics were marketed under brand names. Furthermore, the SIZD variable, significant in the antianginal sales equation, may have been insignificant in the oral diuretic sales equation sales equation, because of collinearity between the SIZD and TIME variables (see the following statistical addendum).

Other differences are more difficult to reconcile. The advantage to Merck from being first to offer and promote an orally effective diuretic appears to have spilled over to other Merck brands.[7] The advantage to Warner-Lambert from being first to promote a pain-preventing antianginal did not spill over to the only other branded antianginal offered by Warner-Lambert (Perithiazide, a unique and unsuccessful combination drug containing PETN and hydrochlorothiazide).[8] Finally, the significance of time on the market (TIME) varied between markets in both the sales and the promotion equations.

Statistical Addendum:

Although the equations reported above appear to provide the most useful insights into the determinants of sales and promotion, certain unreported equations do shed light upon more technical issues. Tables V.1 and V.2 report additional sales and promotion equations for oral-diuretic and antianginal brands, respectively. Aside from revealing the insignificance of variables not included in the equations reported above (see

[6] The discussion at the beginning of this chapter suggested a framework in which profit-maximization by firms could lead to a positive association between sales and promotion across brands. Some a priori basis for expecting non-profit-maximizing behavior at the brand level may exist. Where a single firm markets more than one brand, profit-maximization at the firm level could imply something other than profit-maximization for each of the firm's individual brands. In particular a two-brand firm might hope to maximize its profits by under-promoting its second brand so as to protect its first brand from sales erosion. The promotion equations for oral diuretic drugs, however, suggest that the effects of any such behavior may be minimal. Equation 11 in Table V.1 reveals that Merck, the leading firm in oral diuretics, did not promote its follow-on brands significantly less than its first brand when therapeutic gain is held constant.

[7] After Diuril was introduced in late 1957, Merck's follow-on brands in order of introduction were: Diupres (1959); Hydrodiuril (1959); Hydropres (1959); Cyclex (1960); Hydrodiuril-KA (1960); Hydropres-KA (1960); Aldoril (1963); Edecrin (1967); and Aldoclor (1968).

[8] For the equations reported here, all combinations and dosage forms of Peritrate were treated as a single brand. In another equation, the original dosage form of Peritrate was treated as a brand distinct from other dosage forms and combinations. The original Peritrate was treated as the FIRST brand while other Peritrate forms were assigned an OTHER WARNER designation analogous to the OTHER MERCK variable. In the unreported equation, the advantage from being first extended even to those forms of Peritrate that were introduced after the original form.

Equations 7 and 11 for oral diuretics and Equations 4 and 8 for antianginals), the equations provide further information on the relationships between firm size and brand sales and promotion. Equations 3, 4, 8, and 9 for oral diuretics, and Equations 1, 2, 5, and 6 for antianginals reveal that the dummy variable representing the brands of the 30 largest firms better explains sales and promotion than does the continuous size variable. Equations 6 and 10 in oral diuretics and Equations 3 and 7 in antianginals reveal that the relationships between firm size and sales and promotion are discontinuous: among brands of the 30 largest firms, firm size has no significant impact upon sales or promotion.

Equations 1, 2, 3, and 5 in Table V.1 collectively suggest that SIZD may have a positive effect upon brand sales for oral diuretics as well as for antianginals. The equations also imply that the significance of the TIME variable may be less clear-cut than Equation 1 (reported in the text) would suggest. Note that in Equation 3, where SIZD is introduced without TIME, the effect of SIZD is both positive and significant. Similarly, in Equation 1, where TIME is introduced without SIZD, the effect of TIME is both positive and significant. But in Equation 2, where both TIME and SIZD are included, the significance of each variable is substantially reduced, and the coefficient for SIZD has a value radically different from that in Equation 3.

The unstable results appear to arise because most of the brands (53 of the 67) are in fact marketed by the 30 largest firms. Equation 5 suggests that among such brands, the coefficient for TIME is positive but statistically insignificant at the 10 percent level. Brands not marketed by the 30 largest firms were typically (in 9 of the 14 cases) marketed for 3 or fewer years. Hence, most of the observations having SIZD = 0, also had low values for TIME. Although the collinearity between SIZD and TIME prevents an entirely accurate assessment of the relative contribution of each, Equations 1, 2, 3, and 5 together suggest that both SIZD and TIME may have some positive influence upon oral-diuretic brand sales.

TABLE V.1.—Sales and Promotion Equations: Oral Diuretic Drugs

Dependent Variable	Sample	Constant	Independent Variables									$\bar{R}^2$	N
			FIRST	OTHMRK	IMPGAIN	MODGAIN	TIME	SIZD	SIZE	COMB	K		
1. SALES	All Brands (In text)	–0.181	11.661[a] (4.481)	2.731[a] (3.129)	4.830[a] (4.657)	2.815[b] (2.282)	0.155[b] (2.045)					.574	67
2. SALES	All Brands	–0.282	11.769[a] (4.486)	2.639[a] (2.958)	4.749[a] (4.512)	2.667[b] (2.106)	0.122 (1.27)	0.540 (0.572)				.570	67
3. SALES	All Brands	0.250	12.264[a] (4.703)	2.596[a] (2.898)	4.704[a] (4.45)	2.476[b] (1.959)		1.268[c] (1.679)				.565	67
4. SALES	All Brands	0.875	11.871[a] (4.314)	2.406[a] (2.103)	4.965[a] (4.656)	2.704[b] (2.107)			0.000 (0.684)			.548	67
5. SALES	Brands of 30 largest firms	–0.176	11.599[a] (3.896)	2.654[a] (2.640)	4.765[a] (4.017)	2.733[b] (1.907)	0.164 (1.175)					.523	53
6. SALES	Brands of 30 largest firms	–2.135	12.987[a] (4.129)	3.220[b] (2.333)	4.576[a] (3.775)	2.506[c] (1.751)			–0.004 (0.666)			.514	53
7. SALES	All Brands	–0.143	11.501[a] (4.314)	2.798[a] (3.134)	4.748[a] (4.455)	2.710[b] (2.146)	0.17[b] (2.096)			–0.244 (–0.392)	–0.433 (–0.459)	.562	67

Table continued on next page. See footnotes at end of table.

TABLE V.1.—Sales and Promotion Equations: Oral Diuretic Drugs—Continued

Dependent Variable	Sample	Constant	Independent Variables									$\overline{R}^2$	N
			FIRST	OTHMRK	IMPGAIN	MODGAIN	TIME	SIZD	SIZE	COMB	K		
8. PROMO	All Brands (In text)	0.027			1.250[a] (4.405)	1.442[a] (3.964)		0.396[b] (1.681)				.370	64
9. PROMO	All Brands	0.295			1.317[a] (4.557)	1.519[a] (4.117)			0.000 (0.365)			.342	64
10. PROMO	Brands of 30 largest firms	0.606			1.263[a] (4.045)	1.424[a] (3.557)			–0.001 (–0.829)			.315	53
11. PROMO	All Brands	0.126	–0.376 (–0.477)	–0.114 (–0.428)	1.254[a] (3.938)	1.298[a] (3.378)	–0.024 (–0.785)	0.682[b] (2.059)		–0.120 (–0.620)	–0.279 (–0.992)	.344	64

t values in parentheses
a = significant at the 1% level.
b = significant at the 5% level.
c = significant at the 10% level.

TABLE V.2.—Sales and Promotion Equations: Antianginal Drugs

Dependent Variable	Sample	Constant	Independent Variables								$\bar{R}^2$	N
			FIRST	IMPGAIN	MODGAIN	TIME	SIZD	SIZE	BRAND	SA		
1. SALES	All Brands (in Text)	–0.040	14.329[a] (56.897)	4.407[a] (17.604)	4.608[a] (18.297)		0.444[a] (8.940)		0.061[c] (1.564)	0.056[c] (1.377)	0.961	182
2. SALES	All Brands less 13 for which size data were not available	–0.034	14.353[a] (48.573)	4.241[a] (14.030)	4.450[a] (14.580)			0.002[a] (5.184)	0.121[a] (2.606)	0.047 (0.975)	0.951	169
3. SALES	Brands of the 30 largest firms	0.010	14.084[a] (21.667)	4.179[a] (6.214)	4.267[a] (6.303)	–0.010 (–0.510)		0.001 (0.574)	0.443[c] (1.547)		0.953	34
4. SALES	All Variables All Brands	–0.037	14.331[a] (56.517)	4.404[a] (17.425)	4.609[a] (18.231)	–0.0004 (–0.120)	0.444[a] (8.905)		0.062[c] (1.535)	0.055[c] (1.327)	0.960	182
5. PROMO	All Brands (in Text)	0.009	3.052[a] (19.719)	0.995[a] (6.407)	1.192[a] (7.715)	–0.004[c] (–1.595)	0.192[a] (6.306)		0.047[b] (1.679)		0.774	182
6. PROMO	All Brands less 13 for which size data were not available	0.017	3.107[a] (17.629)	0.996[a] (5.437)	1.194[a] (6.576)	–0.004[c] (–1.391)		0.0005[a] (2.500)	0.073[a] (2.584)		0.733	169
7. PROMO	Brands of the 30 largest firms	0.206	3.094[a] (8.331)	0.864[a] (2.140)	1.201[a] (3.112)	–0.019[c] (–1.545)		–0.0001 (–0.218)	0.279[b] (1.663)		0.723	34
8. PROMO	All Variables All Brands	0.002	3.037[a] (19.424)	1.003[a] (6.435)	1.177[a] (7.551)	–0.003[c] (–1.422)	0.195[a] (6.345)		0.042[b] (1.679)	0.020 (0.769)	0.774	182

t values in parentheses; a = significant at the 1% level; b = significant at the 5% level; c = significant at the 10% level.

CHAPTER VI

CONCLUSIONS

The institutions that govern the distribution of prescription drugs from manufacturer to user differ from those in most markets. The ultimate consumer of drugs has only indirect control over the drug purchase decision. As one economist has noted, when the consumer chooses among physicians, he selects a "very complicated joint product which includes the drugs prescribed. . . ." (Telser 1975, pp. 212–213.)

Since physicians select but do not pay for the drugs they prescribe, market forces would require physicians to consider price in their prescribing decisions only if consumers were willing and able to make informed decisions about physicians' prescribing habits when they shopped for medical care. Numerous institutional constraints limit the ability of consumers to shop and reduce the effectiveness of such shopping as takes place: First, consumers have limited knowledge about the quality of and alternatives to their present medical care, including drug therapy; second, the supply of physicians is limited via institutional mechanisms, a limitation which probably reduces the incentive for individual physicians to expand their practices by offering lower prices and prescribing lower-priced drugs (Kessel 1958; Feldstein 1970; Fein 1967); third, laws and professional codes prohibit physicians from disseminating price and other information through advertising;[1] and finally, state laws prohibit pharmacists from advertising the retail prices of prescription drugs[2] and from honoring a consumer's request to fill a brand-name prescription with the lowest-priced brand (Green 1972, p. 108).

The Prescription Drug Study Report cannot identify the relative impact of the many individual constraints that pervade the drug distribution system. The study does reveal, however, that the constraints lead to an interaction between physician behavior and firm conduct that has a profound effect upon the prices, promotion, and sales of prescription drugs.

The structure and conduct observed in the prescription drug industry can be understood only within the context of physicians' revealed

[1] See Report of the National Advisory Commission on Health Manpower (1967, pp. 312–313).

[2] The United States Supreme Court in *Virginia State Board of Pharmacy* v. *Virginia Citizens Consumer Council*, 425 U.S. 748 (1976), struck down state laws which prohibit or unnecessarily restrict the advertising of prescription drug price information. Because this decision may accomplish by First Amendment means the same result as the Federal Trade Commission's proposed Trade Regulation Rule (40 FR 24031), further consideration of that rule has been deferred pending an evaluation of the impact of the Court's decision.

preferences for prescribing by brand rather than generic name. A private market research source estimates that about 90 percent of all new prescriptions are written by the brand name of the drug.[3] The survey data presented in this report confirm such behavior and reveal further that physicians as a group tend to prefer only a few of the many brand names available in individual markets.

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, and the proliferation of brand names means that physicians can learn and work with only a few (U.S. Senate 1972, p. 43).

Although physicians' preferences for brand-name drugs have been widely documented prior to this report, the Prescription Drug Study provides interesting and unexpected insight into the characteristics of the brands that are most preferred. First, strong preferences are revealed for brands that are the first of their kind to appear on the market. These preferences wane only slowly over time and also spill over to follow-on brands marketed by the first firm in the market. Second, the data also reveal that physicians can be persuaded to prescribe late-entering brands if those brands offer some therapeutic gain useful to a subset of patients. Overall, the effect of these prescribing habits is to raise promotional expenditures as a proportion of sales to late-entering firms and to minimize the incentives for price-cutting on large-selling brands.

While physicians' preferences for drugs that seem to offer therapeutic improvements may be associated with the substantial early promotion of such drugs, the long-term dominance of these drugs cannot be attributed to promotion alone. Data for the oral-diuretic market reveal that some late-entrant brands received heavier promotion than the first brand without dislodging the first brand from its dominant sales position. Data for both markets showed that firms offering follow-on substitute brands generally refrained from spending large sums of money on promotion. Case examples revealed that where firms did attempt to promote heavily such follow-on brands, the futility and unprofitability of such efforts were recognized and promotional efforts were cut back. Hence, physicians appear to be searching for improvements in drug therapy and are responsive to the promotion of brands that seem to offer such improvements.

[3] See "Generics Pose No Threat to Big Drug Firms" (1974, p. 8).

The advantage to firms from being first to offer a new type of drug is considerable, and physician's long-term preferences for the first brands appear to insulate firms from competition even more effectively than do patents. In the oral diuretic market the dramatic sales achieved by the first brand stimulated other firms to invent around the controlling patent and to enter with closely substitutable drugs. In the antianginal market the first and dominant brand was protected by no patents. The trademark protection of brand names then appears to bar the success of low-priced, substitute brands and, within the framework of the present drug distribution system, that barrier appears to be far more powerful than patent protection.

Generality of Results

Although the Prescription Drug Study focuses upon only two prescription drug markets, there is little reason to believe that the results presented here might not apply to other segments of the prescription-drug industry. Indeed, the preference of prescribers for first and novel brands might well explain the structure and conduct observed in many non-drug markets. Research in non-drug areas would appear to be warranted.

Both classes of drugs investigated here are primarily maintenance drugs. Patients receiving drug therapy for both high blood pressure and angina tend to be placed on a regimen of *long-term* drug therapy. Once the physician finds that a patient has responded satisfactorily to a particular brand drug, the physician may refrain from switching the patient to a potentially substitutable brand. Thus, it could be argued that the pattern of market structure and conduct would be different in non-maintenance drug markets where therapy is typically of a short-term nature.

Yet, physicians may be reluctant to switch to substitute drugs in any therapeutic area, and patients may be more sensitive to the prices of maintenance than to the prices of non-maintenance drugs. Once satisfied with one or a few brands, the physician may continue to prescribe those brands until a new and better drug provides him with a reason to switch. Furthermore, patients receiving long-term drug therapy have greater financial incentives to ask physicians to switch to low-cost drugs than do patients who receive a single prescription as part of short-term therapy.

A priori arguments notwithstanding, examination of market research data for a non-maintenance antibiotic drug, ampicillin, suggests that the sales advantage from being first may apply to non-maintenance as well as maintenance drugs. Introduced in December, 1963, Polycillin, the first brand of ampicillin, had 1968 sales of $52.2 million. The nearest sales rival

to Polycillin was Penbritin which was introduced nearly one year later. The 1968 sales of Penbritin totaled only $14.0 million.[4]

Policy Implications

The patterns observed in the oral diuretic and antianginal markets have social implications that extend beyond merely explaining the relative success and failure of individual brand drugs. Physician's preferences for the first brand to offer new and different therapy bestow substantial financial rewards upon innovating firms. Such rewards from product differentiation influence both the distribution of income and the allocation of resources.

As a matter of policy, society actively chooses to stimulate inventive activity by rewarding it through the patent grant. Under the patent system the right of innovators to collect excess profits is protected legally by foreclosing the entry of competition. But patent protection is intentionally limited in both duration and scope. Patents expire after 17 years. Patents do not cover products that occur in nature. Patents do not preclude others from achieving the same end by different means. And patents do not cover new uses of products or ideas that are already in the public domain. The evidence presented in this report suggests that through product differentiation innovating firms receive substantially greater financial rewards than they would from a patent system alone. The rewards are particularly evident in cases where the trademarked name of a drug is continually and heavily prescribed even when no patent exists.

The product differentiation rewards to innovation undoubtedly stimulate firms to invest more in the discovery and development of new drugs than they would with patent protection alone. Accordingly, product differentiation could benefit society by increasing the speed with which firms develop and market new drugs.

But the financial rewards bestowed upon innovating firms by the present institutional framework appear to continue for a very long time, and such long-term rewards do impose a cost upon society. The most obvious effect of physicians' general failure to substitute lower-priced, follow-on brands for higher-priced, first brands is a distributional one. Income is taken from those who use drugs and given to those who produce them. To the extent that patients fail to seek medical care or fail to fill prescriptions because of high drug prices, product differentiation may also adversely affect the health of individual patients.

The total benefits and costs to society from prescription-drug product differentiation cannot be estimated. It is not possible to know what innovative activity would have been in the absence of product differentia-

[4] Sales data obtained from *U.S.* v. *Bristol-Myers Company, et al.* (1970, p. 5).

tion; neither is it possible to estimate accurately the effects of high drug prices upon individuals' health. Nonetheless, 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.[5]

Potential Remedies

The complex institutional constraints surrounding distribution of prescription drugs increase substantially the prices consumers must pay for drug therapy. The sales and promotional data examined in this study suggest that it is physicians' preferences that tend to determine both the promotion and the sales of drug brands. Accordingly, public policy should focus more closely upon the prescribing process. Alteration in the institutional process by which physicians' prescriptions determine the sales of individual brand drugs will affect drug promotion as well as drug sales. In that process it is the trademarked brand name that plays the most critical role.

Trademarks serve a socially useful purpose. Trademarks allow consumers to select products they prefer and to reject products they dislike. Without trademark identification, shopping on the basis of both quality and price might be very difficult. But many consumer goods and most prescription drugs are protected by two trademarks: the trademark which identifies the name of the manufacturer and the trademark which identifies the brand name of the generic product. In the distribution of prescription drugs, it is the widespread use of the brand-name trademark that hinders rather than facilitates shopping.

The physician has little, if any, financial incentive to shop among drug brands on the basis of price. And if the physician prescribes drug therapy by using trademarked brand names, he effectively prohibits shopping by the only principals in the distribution process who do have financial incentives to make price comparisons: the pharmacist and the patient. The pharmacist may not substitute a lower-priced brand for the brand that the physician prescribes even if requested to do so by the patient.

In markets for most consumer goods, both retailers and consumers have incentives to shop among manufacturers' brands on the basis of both quality and price. To attract customers, the retailer has an incentive to

[5] 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% of total antianginal sales in 1971.

offer quality merchandise. To compete with other retailers, each retailer also has the incentive to limit his inventory to quality merchandise purchased at the lowest possible prices. Similarly, the consumer who wishes to spend his income wisely has the incentive to select among brands of equal quality on the basis of price and to evaluate any quality differences among brands on the basis of price differences. Such market forces serve to limit any discretion which manufacturers of consumer goods may have over price.

Through their pharmacists, consumers should have the ability to substitute lower-priced for higher-priced brands. Two approaches to facilitate such substitution should be explored. The first is the repeal of State antisubstitution laws that prohibit pharmacists from substituting lower-priced brands for brands physicians prescribe. The second is the limitation of brand-name trademark protection for prescription drugs.

State antisubstitution laws limit the ability of follow-on substitute brands to compete on the basis of price. Since antisubstitution laws prohibit the pharmacist from filling prescriptions with brands other than those prescribed, sellers of follow-on brands must promote their brands directly to physicians. As the data have shown, physicians are generally unlikely to switch to a drug that offers equal, but no better, therapy. If pharmacists were allowed to substitute, sellers of follow-on brands would have incentive to persuade pharmacists to stock and sell their brands by offering equivalent drug therapy at a lower price. Enhanced competition from follow-on brands could in turn force first brands to protect their sales by offering a lower price.

Repeal of the state antisubstitution laws represents one approach toward the enhancement of price competition. Limitation of trademark life offers another. Trademarks are registered by the U.S. Patent Office for a period of 20 years and may be renewed indefinitely so long as they are in use. To the extent that trademark protection induces firms to promote important new drugs and to provide information about new therapeutic techniques, brand-name trademarks provide valuable incentives. Moreover, the promise of trademark protection for an unpatented chemical may induce firms to discover and promote new therapeutic uses for old chemicals.

Nonetheless, unlimited trademark life does exact social costs. Once the use of a drug has become widely known and described, the use by follow-on sellers of various trademarked brand names serves only to discourage and obscure substitutability. And the data in this report suggest that the failure to substitute is very costly. Therefore, the trademark, like the patent, might be given a limited life.

As in the case of patents, there exists no simple and general rule that might be used to determine the optimal life for the trademark protection of brand-name prescription drugs. One simple expedient would be to deny the renewal of brand-name drug trademarks, effectively limiting the life of

such trademarks to 20 years. Since the trademark protecting the name of the manufacturer or distributor would not expire, the limitation of brand-name trademarks should not reduce the incentives for firms to maintain quality and quality control. Furthermore, a 20 year life should ensure that the impact of such a limitation upon future innovation would be minimal.[6]

The detailed design of effective and efficient policy is beyond the scope of this report. The repeal of antisubstitution laws and the limitation of trademark life are but two of several approaches towards solving the problems manifest in the distribution of prescription drugs. The Prescription Drug Study does, however, cast new light upon the underlying causes of the problems and emphasizes once again that the benefits to consumers from the adoption of appropriate public policy could be substantial.

[6] The profitability of any investment is determined by calculating the present value of the expected future earnings resulting from the investment. Present values are obtained from expected future earnings by a process known as *discounting*. Earnings that are to be received in the future must be *discounted* since money received in the future is not worth as much as money received today. For example, if one could ordinarily earn 6 percent by putting money in the bank, the promise of $100 one year from now would not be the same as the promise of $100 today. If $100 were received today and were put in the bank for one year, the bank account would be worth $106 at the end of the year. Hence, the promise of $100 one year from now must be discounted by 6 percent, and its present value is equal to $100 ÷ 1.06 = $94.34.

In the case of a 20-year limit upon trademark life, any income lost as a result of the limitation would occur very far in the future. The further in the future that income is earned, the less is its present value. At a 10 percent rate of discount, a rate more realistic for firm investment decisions, the promise of $100 in 20 years would have a present value of only $14.86 today. Thus, if a firm were computing the present value of investing in a new drug, a reduction in income that occurred 20 years in the future would have a minimal effect upon the present value of total expected earnings.

Since any new product is more and more likely to be rendered obsolete after some period of time, the expected future earnings from investing in a trademarked drug would be declining after some point, even before those earnings were discounted. When combined with the discounting process, the decline in expected future income means that the percentage reduction attributable to a 20-year limitation upon that income would be very small indeed. If, for example, the expected future income from a trademark declined in a straight-line manner (i.e., by a constant number of dollars each year) to a value of zero after 50 years, removal of all expected income after the 20th year would reduce the present value of future income by less than 8 percent at a discount rate of 10 percent.

APPENDIX A

TECHNICAL DISCUSSION

This report reveals the existence of a marketing advantage from being first to enter a market with an entirely new or a somewhat better product. Inductive techniques were used to demonstrate within a theoretical framework how both profit-maximizing sales and promotion might be related to being first and being different. Descriptive statistics were employed to show that, in fact, variation in both observed sales and observed promotion was significantly associated with the qualitative variables.

The results of the study suggest new insight into an aspect of physician (and perhaps other consumer) behavior that has received little attention. Yet, this report merely documents that an advantage to early entry does in fact exist. Economists will recognize that the descriptive statistical work herein is essentially with equations of a reduced-form nature. Equilibrium values of endogenous variables (price times quantity, and promotion) were related to strictly exogenous variables. No attempt has been made to estimate the structural equations of the simultaneous system within which equilibrium is attained. Accordingly, numerous interesting questions remain unanswered.

Success in estimating the parameters of a general model of the demand for prescription drug brands could provide valuable information about the precise way in which price and promotion interact with the advantages from being first and being different. Yet, although the payoff to such an analysis could be substantial, the obstacles to specifying and testing such a model in a theoretically sound manner are considerable. Accordingly, whether or not such an analysis can yield meaningful results is at present rather uncertain. The purpose of this appendix is to discuss briefly the problems encountered in specifying and testing a general model and to sketch the planned course for future research.

Previous Work

The complexities of analyzing the prescription drug survey data in a generalized framework can be understood by recourse to the experience of previous studies. However, only a limited number of econometric investigations have attempted to explain brand or firm sales/shares, and,

as the following brief review of a representative sample of this literature indicates, most of the work is subject to one or both of two debilitating criticisms. First, where market share has been incorporated as a dependent variable, models have been almost always misspecified: analysts have failed to constrain predicted market shares to sum to one. Second, where ordinary least squares have been used as an estimation technique, the simultaneity between sales and promotion will have biased the estimates.

Cowling et al.

In a series of papers, Cowling and others (Cowling and Rayner, 1970; Cowling and Cubbin, 1971; and Cowling, 1972) reported the results of their attempts to relate advertising to sales shares within a number of markets in the United Kingdom: tractors, automobiles, toothpaste, margarine, and instant coffee. Models were modified to fit the characteristics of each market, but the general approach involved regressing market shares against relative prices, advertising shares, and lagged market shares. The chief problem with these studies is a failure to constrain the predicted market shares to sum to unity.

In the analysis of tractor manufacturers' shares, Cowling and Rayner used a single equation format. Arguing that simultaneity between advertising and sales was not present, because tractor demand was highly seasonal, leaving little time for retaliatory advertising to occur in the same period as sales were made, the authors thus defused a potential problem area. Cross-section and time-series data were pooled, and the authors attempted to render the observations homogeneous by adjusting prices for product quality differences. For the record, the advertising share variable proved to be a positive and significant explanator of firm market shares.

The simultaneity problem was present, however, in the analyses of the other markets. For the automobile industry, Cowling and Cubbin employed both ordinary least squares (OLS) and two-stage least squares (TSLS) techniques to estimate firm market share equations. Again, cross-section and time-series data were pooled. Although advertisting share was a positive and significant explanator of market share, the authors concluded that the OLS coefficients were biased downward and that the TSLS estimates were plagued by collinearity between the first stage predicted market shares and the lagged market shares.

Dropping from firm to brand levels in examining the shares of toothpastes, Cowling reported only the OLS results. Although the advertising share coefficient had the expected sign and was significant, the results were of dubious value because of the obvious simultaneity problem. Cowling, aware of this problem, simply noted that TSLS "... gave unsatisfactory results with exploding standard errors—the problem caused by multi-collinearity has been intensified as we might expect" (1972, p. 99).

The author made no attempt to control for different brand characteristics, suggesting that they were probably unimportant. A new brand introduction variable was utilized, however, which proved to have no important effect.

Cowling also used similar techniques to analyze quarterly observations on margarine brands. Again pooling data, OLS and TSLS methods were applied, with only the OLS results being reported. Of interest was the use of intercept and slope dummy variables to control for potential quality differences and for a possible interaction between quality and time variables (on the assumption that quality may improve over time). Cowling reported large standard errors for the advertising equation in the TSLS format. However, advertising share had the expected sign and was significant, with better quality brands earning on average each year a higher market share than lower quality brands. The significance also of the interaction variable incorporating quality and time suggested that better quality brands improved their share positions over time.

With respect to the instant coffee market, Cowling obtained unsatisfactory results, indicating only that the TSLS estimates of the market share equation seemed better than the OLS estimates.

Peles

Peles (1971) attempted to measure the lagged effects of advertising on firm sales and market shares in three U.S. industries: beer, cigarettes, and new passenger cars. Using single equation models, Peles sought to explain current sales as a function of current advertising, past advertising, and other variables. Although dummy variables were used to test for possible differences between products and firms, only a national-local regional distribution variable for the beer industry appeared to be significant. Although current advertising was a significant explanator of sales, simultaneity bias was potentially present, and the author made no explicit recognition of this problem.

Telser

Telser (1962) analyzed time-series data for cigarette brands using single-equation models in linear, semi-log, and double-log form. Quantity sold was regressed against advertising, prices, real income, and a time trend variable. No attempt was made to account for simultaneity between advertising and sales. In another model, market sales shares were regressed against advertising shares and lagged market shares. Again, the simultaneity problem was not discussed, and the predicted market shares were not constrained to add to unity.

Telser also attempted to explain market shares of individual firms in terms of lagged market share, advertising share, and a product innovation variable. Since the product innovation variable measured a firm's ability to maintain position in the sub-classes in which it offered brands, the variable was probably one that should have been a dependent rather than an independent variable.

Bass and Parsons/Schmalensee

Recent works by Bass and Parsons (1969) and Schmalensee (1972) are subject to neither of the criticisms discussed above. Yet, although the models employed appear to have been well specified and properly estimated, the results from the tests were rather disappointing.

Bass and Parsons—Noting that single-equation regression models were seriously deficient in identifying the advertising-sales relationship, Bass and Parsons formulated a model to take into account the simultaneous relationship. Constraints were placed on the magnitude of the structural parameters, and reduced-form equations were derived from a system of simultaneous structural equations. The model was then applied to bimonthly time-series data for the leading brand and to all other brands combined. Dummy variables were used only to test for seasonality. The predictive qualities of the model appeared to be good. However, own advertising was not a significant explanator of the variation in sales.

Schmalensee—Probably the most significant contribution to the estimation of advertising-sales relationships is that of Richard Schmalensee. Highly critical of previous work on the subject, Schmalensee demonstrated that properly specified market share models must be constrained so that predicted market shares sum to one.

In his own empirical work Schmalensee attempted to address the problems of sum constraints and simultaneity. Pooling cross-section and time-series data for six cigarette firms, Schmalensee attempted to explain the change in firm market share using current advertising share, lagged market share, and lagged advertising share as independent variables. Additionally, a dummy variable for each firm was included. The equations were sum constrained and the simultaneity problem was addressed through the use of the instrumental variable technique.

Although the equations did explain the pooled data well, Schmalensee noted that the preponderance of the explanatory power was attributable to the firm dummy variables. When he applied his best-fitting equation to the firms individually, the equation worked well for only one firm. Moreover, upon testing for the appropriateness of the sum constraints imposed,

Schmalensee was forced to conclude that the linear market share models were misspecified.

Schmalensee also attempted to estimate equations using firm sales as the dependent variable. Although 288 equations were estimated, again using the instrumental variable technique, the results from these firm sales equations were no more impressive than those from the market share equations. Neither the firm's own nor its competitor's advertising proved to be significant.

A Course for Further Research

Measuring the impact of promotion upon market shares has remained an elusive goal in economics literature. As the discussion above has demonstrated, meaningful analyses of the determinants of market shares must be sum constrained and must take account of simultaneity.

Schmalensee (1972) has shown that sum constraints severely limit the form a market share model may take. He shows that: (1) the sum of the intercepts must be equal to one minus the sum of the slope coeficients across brands; (2) each independent variable must sum across observations to the same constant; and (3) the slope coefficient for a given independent variable must be the same for all brands. The constraints are defined only for a static linear model. Whether or not appropriate constraints can be developed for non-linear models is unknown. Moreover, the introduction of a dynamic system in which the first firm controls 100 percent of the market in the first time period requires still additional sum constraints: that the constant term for the first firm must be equal to one minus the sum of the slope coefficients and that the constant terms of non-first brands sum to zero.

Because of the simultaneous relationship between sales and promotion, ordinary least squares estimates of the impact of promotion upon sales will be biased upward. While simultaneity is hardly a problem new to econometric analysis, variation in annual data may be insufficient to yield estimates of true relationships. Evidence from the marketing reports of the firms suggests that even when promotion is systematically varied across matched marketing territories, the impact of promotion upon sales may be difficult to evaluate.[1] The Prescription Drug Study data base is far less detailed, and it is on an annual basis. Since firms can and do get feedback concerning the impact of promotion upon sales within relatively short

[1] During a four-month period, one firm conducted tests to determine the effect of adjustments in journal advertising on the sales of two brands. From a total of 700 territories, 39 triplets (sets of three territories) were chosen for the experiment, and in each triplet, territories were matched on the basis of demographic similarities (17 demographic criteria were used). Then within each triplet, territories were randomly selected and designated to receive either an increase, a decrease, or no change in advertising expenditures. None of the variations in sales recorded in the test period was statistically significant at the 99 percent level, and the study concluded that variations in journal advertising had no discernible effects on the sales of brand A or brand B.

periods of time, annual data are inevitably contaminated by simultaneity. The work of Richard Schmalensee (1972) demonstrates that such contamination can cause even unusually well-specified models to yield nonsense results. Schmalensee concludes:

> A likely explanation is that the relationship between advertising and sales is quite complex. . . . The effectiveness of any firm's advertising may vary considerably from year to year. Also, when a brand or product is heavily advertised, the marginal effects of additional spending are apt to be small on average. Since our sample does not contain great fluctuations in any firm's advertising outlays, the effects we are trying to capture are thus likely to be small and variable. When the problem of disentangling advertising's effects on sales from the impact of sales on advertising budgets is also considered, it is perhaps not surprising that we failed to find any persistent advertising effects. . . . Time-series analysis may never be able to shed adequate light on the effects of advertising on demand unless substantial data covering periods shorter than a quarter become available (pp. 211–215).

A "Dominant Firm" Model

The works discussed above treat all brands or firms in a symmetric manner. Generally, the same equation, with perhaps firm or brand specific coefficients, is *assumed* to explain market shares or sales for all brands or firms. The findings reported here suggest that the first firm is in a qualitatively different and advantageous position vis-a-vis later entrants. This in turn suggests that the primary focus of the analysis should be on the decisions of the first entering firm. The "dominant firm" model recently advanced by Gaskins (1970, 1971) appears to be a promising framework for this kind of analysis. A simple version of the Gaskins model is offered here to help provide a theoretical framework for interpreting the findings reported in Chapter V.

When the firm pioneers a new market, it is, by definition, a monopolist. In the absence of complete patent protection, however, the firm must expect that higher than competitive profits will attract new entry. If the first firm has a cost advantage relative to latecomers, then it could set a "limit price" that would yield higher than normal quasirents and yet preclude new entry. The limit price is defined as that price at which the rate of new entry is zero. On the other hand, the first firm could choose to "make hay while the sun shines" and right away exploit its monopoly power to the hilt. The cost of this policy would be the rapid erosion of market share and the eventual loss of all market power. Gaskins has demonstrated that neither extreme policy is likely to maximize long-term profits and that, under fairly general conditions, the optimal price will always be less than the myopic profit-maximizing price.

The Gaskins model can be adapted to the purpose here by making the simplifying assumption that the dominant firm chooses a single price over

its planning horizon, rather than a price path. Gaskins (1970, pp. 22–24) has shown that in many cases a constant price is almost optimal. If there is a significant cost to making price changes, a constant price will be optimal. For the drug markets studied in this report, it has been found that constant prices over a 12– to 14–year period are the rule, though there are important exceptions. One reason for such behavior is cited in the marketing reports: a substantial price reduction may create an unfavorable image in the minds of physicians, since they may conclude that the firm has previously been exploiting its market power.

Assuming a constant price over the planning horizon, Gaskins model reduces to

$$(1) \qquad \text{maximize } p \int_0^T (p-c)\, q(t) e^{-rt} dt$$

where

$$q(t) = a - bp - x(t)$$

and

p is the dominant firm's price; and
c is the dominant firm's average cost, including a normal return on its investment.
q(t) is the quantity sold by the dominant firm at time t.
x(t) is the quantity sold by all other firms at time t.

The key element of the model is that the rate of increase in other firms' output ($\dot{x}$ (t)), either through new entry or through expansion by existing producers, is a positive function of the expected profits to be earned. This notion can be captured by making the rate of entry a function of the difference between the dominant firm's price (p) and the limit price ($\bar{p}$).

$$(2) \qquad \dot{x}(t) = k(p - \bar{p}) = 0,\ k>0.$$

It should be noted that the difference between the limit price ($\bar{p}$) and the dominant firm's unit costs (c) is the measure of the dominant firm's cost advantage. In the case of the drug products examined here, the cost advantages appears to be mainly in the "effectiveness" of promotional expenditure. For example, Merck spent between 6 and 14 cents to generate a dollar of sales in the diuretic market between 1958 and 1971, while the latecomers on average spent between 21 and 59 cents per dollar of sales. Merck's cost advantage did decline steadily throughout the period. Similarly, between 1962 and 1971, Warner-Lambert spent between 15 and 19 cents per dollar of sales in the antianginal market, while rivals on average spent between 23 and 49 cents per dollar of sales. Again, the cost advantage held by the dominant firm declined throughout the period. Equation (2) does not incorporate the observed decline in the cost advantage held by the early entrant, but this extension will be made after the simpler case is studied.

Since p and $\bar{p}$ are assumed to be constant over the planning horizon from time o to time, T, it is easy to solve for the output of the "fringe" explicitly. The solution is given by equation (3).

$$(3) \quad x(t) = k(p-\bar{p})t$$

Equation (3) can then be substituted into equation (1) to get

$$\Pi = \int_0^T [(p-c)(a-bp - k(p-\bar{p})t)]e^{-rt}dt$$

Performing the indicated integration, we get

$$(4) \quad \Pi = (p-c)(a-bp)\left[\frac{1-e^{-rT}}{r}\right] - k(p-\bar{p})(p-c)\left[\frac{1-(1+rT)e^{-rT}}{r^2}\right]$$

For convenience, call the first bracketed term in equation (4) "A" (i.e., $A = 1-e^{-rT}/r$) and the second bracketed term, "B". By taking the derivative of (4) with respect to the dominant firm's price (p), we can solve for the optimal constant price (p*).

$$(5) \quad p^* = \frac{\left[\frac{a+bc}{2b}\right]bA + \left[\frac{\bar{p}+c}{2}\right]kB}{bA+kB}$$

Equation (5) has a simple interpretation. The first term in brackets on the right-hand side is simply the price that a monopolist would charge if entry were completely blockaded. The second bracketed term is a simple average of the limit price ($\bar{p}$) and the price that would yield a normal rate of return to the dominant firm (c). If the dominant firm has no cost advantage relative to entrants (i.e., $\bar{p} = c$), then the second term is simply the equilibrium competitive price. Thus, in this simple case, *the optimal price is a weighted average of the myopic monopoly price and a simple average of the limit price and competitive price.* In general, the optimal price will exceed the limit price and the dominant firm will continually lose market share.

Given the dominant firm's optimal price, it is easy to solve for the total sales of both the dominant firm and the fringe firms over the time period 0 to T. These sales equations are "reduced forms" which depend basically on which firm was first to enter, the extent of the cost advantage enjoyed by the first entrant, certain demand equation parameters, and the speed of competitive response (k). The sales equations would be conceptually similar to the sales equations estimated in chapter V, except that: 1) it is clear that the cost disadvantage suffered by the latecomers declines over time; 2) the simple model here assumes that all fringe firms are on an equal footing, whereas, in fact, those that enter early with an improved product ("gain") are better off than the others; and 3) the model here assumes no growth, whereas, in fact, both drug markets studied here grew at rapid

rates. The latter point is important only if growth affects the dominant and fringe firms differentially, as Gaskins (1970, pp. 65–82) assumes.

The model above can easily be extended to the case where the dominant firm's cost advantage declines over time. As Gaskins notes:

> Conceivably, the cost advantage, (as measured by the difference between dominant firm cost and the limit price) narrows as rival products slowly build up brand loyalty. (Gaskins 1970, p. 54.)

Gaskins represents this case by assuming that the limit price exponentially declines toward the dominant firm's unit cost.

$$(6) \qquad \bar{p}(t) = (\bar{p}_0 - c)e^{-\sigma t} + c$$

where p_0 is the initial level of the limit price. The rate of entry now becomes,

$$(7) \qquad \dot{x}(t) = k(p-c) - (\bar{p}_0 - c)e^{-\sigma t}, \; x(0) = 0$$

The solution to this differential equation is

$$(8) \qquad x(t) = k\left[(p-c)t - (\bar{p}_0 - c)\left(\frac{1-e^{-\sigma t}}{\sigma}\right)\right]$$

Substituting (8) into (1), we derive a new expression for the present value of the dominant firm's profits, given by (9).

$$(9) \qquad \Pi_d = (p-c)(a-bp)A - k(p-c)^2 B + k(\bar{p}_0 - c)(p-c)C$$

where,

$$C = \frac{\sigma - (r+\sigma)e^{-rT} + re^{-(r+\sigma)T}}{\sigma r(r+\sigma)}$$

Taking the derivative of (9) with respect to p and equating to zero, we find the optimal price with a declining cost advantage to be

$$P_d^* = \frac{\left[\frac{a+bc}{2b}\right]bA + \left[c + (\bar{p}_0 - c)\frac{C}{2b}\right]kB}{bA + kB}$$

Again, the optimal constant price turns out to be a weighted average of the monopoly price and a price that is lower than the average of the limit price and the unit cost. Note that the weights are identical to those in the simpler model. It is not too surprising that if the dominant firm's advantage is declining, the optimal price is generally lower than it would otherwise be. A more important distinction between this model and the earlier one is that the dominant firm's market share will fall exponentially rather than linearly over time. An exponentially declining market share more closely approximates the data presented in Chapters III and IV than does a linear trend.

Conclusions

This appendix has focused upon the theoretical and empirical obstacles to exploring further the relationship between sales and promotion within the context of an advantage to early entry. The discussion reveals that virtually all empirical work on the subject either has been subject to important criticisms or has failed to generate a significant relationship between sales and promotion. The appendix also suggests that the findings of this report might be integrated into a dominant firm model and offers a preliminary framework within which one might analyze the behavior over time of a first firm. Perhaps the most obvious void in the present analysis is the absence of a testable theory of consumer behavior that explains an advantage to being first. Comanor and Wilson (1974) have made progress with a model applicable for static analysis, and although no dynamic model appears to exist, analyses of consumer panel data have revealed predictable regularities in consumer repeat purchase activity (Ehrenberg 1972). Until more is known about consumer behavior, models purporting to relate the market shares of differentiated products to their promotional activity must be viewed with a healthy degree of skepticism.

APPENDIX B

SURVEY SCOPE AND PROCESS OF DATA COLLECTION

On November 8, 1973, in accord with its powers provided by Section 6 of the Federal Trade Commission Act, the Federal Trade Commission adopted a resolution authorizing the investigation and collection of data pertaining to certain prescription drugs: oral diuretics and combination diuretic-antihypertensive agents, antianginals, and metronidazole. For each drug category, firms were requested to supply information on: 1) quantities sold and dollar sales by dosage strength; 2) promotional expenditures by brand; 3) patents and/or licenses held; 4) sources of supply of the principal generic ingredients; and 5) copies of marketing documents.

The data were collected by means of mail questionnaires. Two report forms were used. Special Report I was concerned with oral diuretics, combination diuretic-antihypertensive agents, and antianginal agents, and was sent to 250 firms. Special Report II, which was identical to Special Report I, gathered information from the lone producer of metronidazole (data for metronidazole were not utilized in this report). Copies of both questionnaires, and the Commission's resolution and order are attached at the end of this Appendix.

With the aid of pharmacologists and representatives of the Food and Drug Administration, the staff determined the products that lay within the three therapeutic areas of interest. The staff then attempted to compile a list of all firms engaged in marketing these drugs at any time during the 16-year span of the Survey, 1956–1971. The list of firms was compiled from the following sources:

American Druggist Blue Book, New York, 1955–1972.
Burack, Richard, *The New Handbook of Prescription Drugs*, New York, 1970.
Drug Topics Red Book, New York, 1955–1972.
Dun & Bradstreet Middle Market Directory, New York, 1955–1972.
Dun & Bradstreet Million Dollar Directory, New York, 1955–1972.
Dun & Bradstreet Reference Book, New York, September 1972.
Kern, Kenneth R., ed., *Executive Directory of the Pharmaceutical Industry*, Princeton, 1972.
Moody's Industrial Manual, New York, 1955–1972.
Moody's OTC Industrial Manual, New York, 1972.
Physicians' Desk Reference to Pharmaceutical Specialties and Biologicals, Oradell, 1973.

Thomas Register of American Manufacturers and Thomas Register Catalog File, New York, 1972.
Wilson, Charles O., and Tony E. Jones, *American Drug Index*, Philadelphia, 1971.
U.S. Department of Health, Education and Welfare, *National Drug Code Directory*, Washington, D.C., June 1972.

According to these sources, 238 firms marketed drugs classified as antianginals, and 18 marketed drugs classified as diuretics and combination diuretic-antihypertensive agents. A few firms which were merged or acquired in 1970 or 1971 supplied separate data and were treated as separate firms in the Survey. These firms were Ciba and Geigy, Wolins and Western Research (now Generics Corp.), and Leo Linden and Chromalloy.

Usable data were obtained from 132 respondents. Of the remaining firms dropped or excluded from the Survey, 42 firms (16.5%) had drugs which upon further analysis proved to be irrelevant for the purposes of this report. In addition, 15 firms (5.9%) were no longer in business, 15 firms (5.9%) were unable to locate company records, and 48 firms (18.9%) could not be located after repeated mailings and several telephone calls. Any effect of the ommissions is to understate the sales in the early years of the survey by the amount of sales of the firms which were not contacted or which were excluded because they could not be located or they were no longer in business. The potential error created by the ommission of firms is unknown, but it is probably small.

Survey Firms Providing Data Analyzed in This Report

Abbott Laboratories
Ambort Medical, Inc.
American Cyanamid Co.
American Hoechst Corporation[1]
American Home Products Corp.
American Hospital Supply Corp.
Approved Pharmaceutical Corp.
Arcum Pharmaceutical Corp.
Armour-Dial, Inc.
Barre Drug Co., Inc.
Barry-Martin Pharmaceuticals, Inc.
Barth-Spencer Corp.
Beatrice Scientific Co.
Bell Pharmacal Corp.
Blaine Co., Inc.
Blueco, Inc.
Blue Line Chemical Co., The
Bock Pharmacal Co.
Bowman, Inc.
Bristol-Myers Co.
Bundy, C.M., Co., The
Burroughs Wellcome Co.
Geigy Pharmaceuticals[2]
Halsey Drug Co., Inc.
Hance Bros. & White Co.
Hartford Laboratories
Hoffmann-La Roche, Inc.
Hyrex-Key Pharmaceuticals Co., Inc.
Canfield, C.R., & Co.
Canright Corp.
Carnrick, G.W., Co.
Carter-Wallace, Inc.
Central Pharmacal Co., The
Century Pharmaceuticals, Inc.
Chromalloy American Corp. (Leo Linden)
Ciba Pharmaceutical Co.[2]
Colgate-Palmolive Co.[3]
Columbia Medical Co.
Consolidated-Midland Corp.
Corvit Pharmaceuticals
Darby Drug Co.
Dart Industries Inc.
Daylin, Inc.
Doric Corporation
Elder, Paul B., Co.
Evron Pharmaceutical Co., Inc.
Ferndale Laboratories, Inc.
First Texas Pharmaceuticals, Inc.
Fleming & Co.
Foy Laboratories, Inc.
Pennwalt Corp.
Pfizer, Inc.
Physicians & Hospitals Supply Co.
Purepac Laboratories Corp.
Recsei Laboratories, The
Reid Provident Laboratories, Inc.
Revlon, Inc.

ICI America Inc.
ICN Pharmaceuticals, Inc.
Interstate Drug Exchange, Inc.
Invenex Pharmaceuticals
Jenkins Laboratories, Inc.
Johnson & Johnson
Kay Pharmacal Co., Inc.
Kenwood Laboratories, Inc.
Ketchum & Co., Inc.
Key Pharmaceuticals, Inc.
Kingsbay Pharmaceuticals, Inc.
Kirkman Laboratories, Inc.
Kremers-Urban Co.
Lannett Co., Inc., The
Lemmon Pharmacal Co.
Len-Tag Co.
Lilly, Eli, and Co.
Mallard, Inc.
Mallinckrodt Chemical Works
Marion Laboratories, Inc.
Mayrand, Inc.
Medical Arts Supply Co.
Medics Pharmaceutical Corp.
Merck & Co., Inc.
Meyer Laboratories, Inc.
Minnesota Mining and Manufacturing Co.
Missouri Pharmaceutical Mfg. Co.
Morton Pharmaceuticals, Inc.
Natcon Chemical Co., Inc.
North American Pharmacal
North American Philips Corp.
Ormont Drug & Chemical Co., Inc.
Pan American Laboratories, Inc.
Para-Medical Enterprises, Inc.
Parkway Distributors, Inc. (H.L. Moore Drug Exchange)
Pasadena Research Laboratories, Inc.
Richardson-Merrell Inc.
Richlyn Laboratories, Inc.
Robins, A.H., Co.
Robinson Laboratory, Inc.
Rohm & Haas Co.
Rorer-Amchem, Inc.
Rowell Laboratories, Inc.
Rucker Pharmacal Co., Inc.
Sandoz-Wander, Inc.
Schein, Henry, Inc.
Schering-Plough Corp.
Searle, G.D., & Co.
Smith Kline & French Laboratories
Sperti Drug Products, Inc.
Squibb, E.R., & Sons, Inc.
Stayner Corp.
Sterling Drug, Inc.
Sutliff & Case Co., Inc.
Tennessee Pharmaceutical Co., Inc.
Towne, Paulsen & Co., Inc.
Truxton, C.O., Inc.
Tutag, S.J., & Co.
U.S. Ethicals Inc.
United Pharmaceuticals, Inc.
United Research Laboratories, Inc.
Vale Chemical Co., Inc., The
Vita-Fore Products Co., Inc.
Vitamin Research Corp.
Walgreen Laboratories, Inc.
Warner-Lambert Co.
Wayne Laboratories
West Chemical Products, Inc.
Western Research Corp.
West-Ward, Inc.
Winsale Drug Co.
Winston Pharmacal Corp.
Wolins Pharmacal Corp.
Zemmer Company, The
Zenith Laboratories, Inc.

[1] Now Hoechst-Roussel Pharmaceuticals Incorporated.

[2] Now Ciba-Geigy Corporation.

[3] The Lakeside Laboratories division of Colgate-Palmolive has since been merged into the Merrell-National Laboratories division of Richardson-Merrell Inc.

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION

COMMISSIONERS: Lewis A. Engman, *Chairman*
Paul Rand Dixon
David S. Dennison, Jr.
Mayo J. Thompson

RESOLUTION AUTHORIZING AND DIRECTING THE COLLECTION OF ECONOMIC REPORTS

WHEREAS, the Federal Trade Commission is authorized by Section 6 of the Federal Trade Commission Act to gather and compile information concerning, and to investigate from time to time the organization, business,

conduct, practices and management of corporations (as specified in the Federal Trade Commission Act) engaged in commerce, and their relation to other corporations and to individuals, associations, and partnership; and

WHEREAS, the Federal Trade Commission may require that such corporations file annual or special reports, or both, furnishing to the Commission such information as may be needed as to their organization, business, conduct, practices, management, and their relation to other corporations, partnerships and individuals; and

WHEREAS, it is deemed necessary in the public interest for the Federal Trade Commission to gather information about corporations engaged in the manufacture, sale or distribution of prescription drugs, including, among other things, information as to the nature of business and relation of such corporations to other corporations, individuals, associations, or partnerships, as to the quantities, the value of sales and promotional expenditures for certain products of such corporations, as to the patents and patent licenses governing the production or sale of certain products of such corporations, and as to the indentities of other corporations, individuals, associations, or partnerships that supply certain material to such corporations for the purpose of making the reports authorized under Section 6 (f) of the Federal Trade Commission Act and aiding in the enforcement and administration of statutes committed to the Commission.

NOW, THEREFORE, IT IS HEREBY RESOLVED that the Federal Trade Commission, in the exercise of the powers vested in it by Section 6 of the Federal Trade Commission Act, and with the aid of any and all powers conferred upon it by law and any and all compulsory processes available to it, do forthwith proceed to investigate and collect information, including information in the form of reports of the nature and for the purposes herein above stated, from such corporations engaged in commerce as may be designated by the Commission pursuant to general or special orders.

By direction of the Commission.

/S/ CHAS. A. TOBIN
Secretary

Date: November 8, 1973

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION

In reply refer to
Division of Industry
Analysis, Bureau of
Economics

COMMISSIONERS:

Lewis A. Engman, *Chairman*
Paul Rand Dixon
David S. Dennison, Jr.
Mayo J. Thompson

ORDER TO FILE SPECIAL REPORT

To:

The Federal Trade Commission, in the exercise of the powers vested in it by Section 6 of the Federal Trade Commission Act, has adopted and entered of record a resolution (copy attached) authorizing and directing the collection of reports from corporations (as defined in Section 4 of the Federal Trade Commission Act) engaged in commerce as to their business and relation to other corporations, partnerships, proprietorships, and associations.

Pursuant to the powers conferred upon it by law, the Commission hereby requires you to file with it, within sixty (60) days following receipt of this Order, a completed copy of the attached FTC Form, "Prescription Drug Survey".

You are advised that penalties may be imposed under applicable provisions of Federal law for failure to file special reports or for the filing of false reports.

Dated at Washington, D.C., November 8, 1973

By direction of the Commission.

/S/ CHAS. A. TOBIN
Secretary

THIS REPORT IS DUE WITHIN 60 DAYS OF RECEIPT

OMB No. *56–573020*
Expires *December 31, 1974*

FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

Prescription Drug Survey

SPECIAL REPORT I

PATENT AND LICENSE STATUS SALES AND PROMOTIONAL EXPENDITURES OF PRODUCTS IN SELECTED PRESCRIPTION DRUG MARKETS

THIS REPORT IS REQUIRED BY LAW. It is mandatory under the authority of the Federal Trade Commission (15 U.S.C. 46).

REPORTING DATE. Within 60 days following receipt of this Report, complete and return one notarized copy of the reporting company's response with a certification attached thereto.

This Report is intended for parent companies. Efforts have been made to establish the identities of parent companies. If, however, recipient is controlled by a parent organization, this Report should be forwarded to such parent for completion and submission. If the parent is not a domestic company, this Report should be completed and submitted by its controlling domestic subsidiary.

Each parent company should include the requested information for its own operations as well as for the operations of subsidiaries which it controls. (Control for the purpose of this Report is ordinarily based upon the ownership of a majority of stock interest; that is, more than 50 percent. Control means the determination of basic business policies such as investment in plant and equipment, price policies, and product development and can also be based upon ownership of a less than majority stock interest).

Return all Special Reports and direct any written inquiries to:

Chief, Division of Industry Analysis
Bureau of Economics
Federal Trade Commission
Washington, D.C. 20580

Telephone inquiries may be directed to Dr. David F. Lean or Dr. Ronald S. Bond, telephone 202–254–7690.

State name and address of parent company responding to this Report:

Name _____

Address _____

_____

_____

_____

State name, address, and basis of control of each subsidiary engaged at any time from 1956 to 1971, inclusive, in the sale of drugs defined in this Report. If control over any subsidiary was assumed or relinquished at any time during the above period, state in a separate enclosure: (a) the name(s) of any predecessor(s) or successor(s) in interest and (b) the dates on which control was assumed or relinquished.

Name _____

Address _____

_____

Basis of Control _____

Name _____

Address _____

_____

Basis of Control _____

Name _____

Address _____

_____

Basis of Control _____

State number of *Patent and Pending Patent Questionnaires* filed in this report. ____
State number of *License Questionnaires* filed in this Report. ____
State number of brands for which sales and quantities, promotion, and ingredient supply data were submitted.
Sales and Quantities ____
Promotion ____
Ingredient Supply ____

CERTIFICATION

This Special Report has been prepared by me or under my personal supervision from records of:

(Name of parent company)
and is correct to the best of my knowledge and belief.

_____ _____
(Signature of official) (Title)

_____ _____
(Typed signature of above official) (Office telephone number)

Date _____
Subscribed and sworn to before me this ___ day of _____, 197___

_____
Notary Public

My commission expires _____

INSTRUCTIONS

1. This Report requests information related to certain drugs marketed during the time period 1956 to 1971. If the parent company and/or any of its subsidiaries currently markets drugs which were obtained by acquisition or merger from a predecessor in interest during this time period, then the reporting company should submit data for the entire period, noting for each year and each brand the name of the appropriate parent company.

2. Answers to specific questions should be derived from company books and records. If records are not available, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the brand name of the product to which such enclosure refers.

3. When an item is not applicable, so indicate with the letters "NA".

4. All references to year refer to calendar year. However, if calendar year information is unavailable, then estimate calendar year and furnish fiscal-year data as well, indicating the 12-month period covered.

5. Additional copies of this Special Report may be reproduced from this copy or may be obtained by writing to: Chief, Division of Industry Analysis, Bureau of Economics, Federal Trade Commission, Washington, D.C. 20580.

DEFINITIONS

1. The term *antianginal* refers to drugs which manufacturers claim to be indicated for the treatment of angina pectoris, and *also* refers to other drugs which physicians use in the treatment of angina pectoris. These agents include, *but are not necessarily limited to*:

the so-called rapid-acting nitrites,
the long-acting nitrites,
papaverine and derivatives,
dipyridamole, and
propranolol hydrochloride

2. The term diuretic refers to drugs which manufacturers claim to be indicated for the treatment of edema, and *also* refers to other drugs which physicians use in the treatment of edema. These agents include, *but are not necessarily limited to*:

thiazides and related sulfonamides,
spironolactone,
triamterene,
furosemide
ethacrynic acid, and
mercurial compounds

3. The term *combination diuretic-antihypertensive* refers to those thiazide and related sulfonamide compounds which are combined with other drugs (i.e., reserpine, etc.) for the treatment of hypertension.

Section I

Patents and Pending Patents

A. Section I is concerned with patents and pending patents that you have owned or controlled and which relate in any way to any antianginal, diuretic, or combination diuretic-antihypertensive drugs that you marketed at any time during the period 1956 to 1971. For each such patent and pending patent, please complete a copy of the following three-page patent questionnaire.

B. Submit copies of all patents and applications for pending patents listed in response to part A.

C. Submit copies of any agreements entered into in connection with the settlement of interference proceedings instituted by the U.S. Patent Office, in consequence of which you were a successful applicant for the patent.

D. Submit copies of all license agreements for patents listed under Part A of this section, without regard to their dates and regardless whether the licensor was your company or a predecessor in interest.

Patent and Pending Patent Questionnaire
Page 1

1. United States Patent (Pending Patent) Number _____
☐ Check if pending patent
Instruction: Write the above patent (pending patent) number in the appropriate spaces in the upper right-hand corners of pages 2 and 3 of this questionnaire.
2. Type of patent (check one)
a. Pertains to product ☐
b. Pertains to process ☐
c. Pertains to both a and b ☐
3. In the Table below, provide the following information:
a. In column (a), list the generic ingredient(s) covered by the above patent.
b. For *each* generic ingredient listed, write, in column (b), your brands in which the ingredient is incorporated.

(a) Generic Ingredient(s)	(b) Brands

Patent (Pending Patent)
Number _____

Patent and Pending Patent Questionnaire
Page 2

4. Date of patent issuance (application date for pending patent) _____
5. Expiration date of patent _____
6. Calendar years in which patent (pending patent) was worked (used) by you _____
☐ Check if never worked (used)
7. If patent was acquired from another firm, then state:
a. Name of firm from which patent was acquired _____
_____
b. Date of patent acquisition _____
8. In Table I. submit the following information

Column

a. List the name of each licensee authorized by you to work (use) this patent.
b. Date of license agreement.
c. Expiration date of license agreement.
d. List each brand which was covered by the patent and which was marketed by each licensee during the period 1956 to 1971, inclusive.
e. For the period 1956 to 1971, list the years in which each licensee's brand, named in response to question 8-d, was marketed.

Patent (Pending Patent)
Number _____

Patent and Pending Patent Questionnaire
Page 3

Table I: Drug Licensees

(a) Names of licensees	(b) Date of License Agreement	(c) Expiration date	(d) Licensee's brands marketed from 1956 to 1971	(e) Years brand was marketed during 1956 to 1971

6. Quantity figures should be reported as follows:
a. Where products are marketed in tablet or capsule form, report quantities in 1,000s of tablets or capsules.
b. Where products are marketed in liquid or ampule form, report quantities in liters.
c. Where products are marketed in suppository form, report quantities in 1,000s of suppositories.
d. Where products are marketed in ointment form, report quantities in pounds.
7. Exports and transfers to foreign affiliates should not be included.
8. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data, use the following symbol:

NM = not marketed during the year

If records are not available, and the product was marketed, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the brand name of the product to which such enclosure refers.

Table III-1
Sales and Quantities sold of Antianginal Products

Brand Name _____
U.S. P. or N.F. Generic Name _____
_____
Dosage Form _____
Dosage Strength _____
Units in which Quantities are reported* _____

Year	(a) Direct to Federal Government		(b) All Other		(c) Total	
	Sales ($)	Quantity	Sales ($)	Quantity	Sales ($)	Quantity
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

* See instruction 6 page xiv

Section III

Sales and Quantity Information

Tables III-1 and III-2, respectively, provide space for submission of sales and quantity data related to: 1) each dosage strength of each dosage form of your brands of antianginal drugs; 2) each dosage strength of each dosage form of your brands of diuretic and combination diuretic-antihypertensive drugs. Using one page for each dosage strength of each dosage form of each brand which you marketed at any time during the period 1956 to 1971, inclusive, please provide annual sales and quantity information as follows:

Columns

(a) Net domestic sales (to the nearest dollar) and quantities made directly to the Federal Government. Include only sales and quantities of products packaged under your own labels for human use.

(b) All other net domestic sales (to the nearest dollar) and quantities. Include only sales and quantities of products packaged under your own labels for human use.

(c) Total net domestic sales (to the nearest dollar) and quantities. Include only sales and quantities of products packaged under your own labels for human use. For each year, the sum of sales and quantities in columns (a) and (b) should equal the total sales and quantities given in column (c).

Instructions.

1. Where a product is promoted or marketed solely under its generic name, treat that product as a brand.
2. Sales and quantities of each dosage strength (i.e. 5 mg. and 10 mg.) of each dosage form (i.e. oral vs. oral timed-release vs. sublingual vs. injectable) of a brand are to be given separately.
3. Sales made under labels of others, and sales made unlabeled, should not be included.
4. Sales of products for veterinary use should not be included.
5. Sales figures should be reported net of all returns, allowances, and trade discounts. Quantity figures should be reported net of all returns.

Patent Number _____

License Questionnaire
Page 2

8. List the licensor's brands covered by the patent named in response to question 1 of this section _____

Section II

License Agreements

A. Section II is concerned with license agreements that you have held and which relate in any way to any antianginal, diuretic, or combination diuretic-antihypertensive drugs that you marketed at any time during the period 1956 to 1971. For each such license obtained from domestic or foreign firms, please complete a copy of the following two-page license questionnaire.

B. Submit copies of all license agreements listed in response to part A of this section.

x

License Questionnaire
Page 1

1. United States Patent Number _____

Instruction: Write this patent number in the space provided in the upper right hand corner of page 2 of this license questionnaire.

2. Type of patent (check one)

a. Pertains to product ☐

b. Pertains to process ☐

c. Pertains to both a and b ☐

3. Name of licensor (if foreign, indicate country) _____

4. Date of license agreement _____

5. Expiration date of license agreement _____

6. List the generic ingredient(s) covered by the license agreement _____

_____

_____

7. List your brands covered by the license agreement _____

_____

_____

_____

_____

_____

_____

_____

Table III-2
Sales and Quantities sold of Diuretic and
Combination Diuretic-Antihypertensive Products

Brand Name _____
U.S. P. or N.F. Generic Name _____
_____
Dosage Form _____
Dosage Strength _____
Units in which Quantities are reported* _____

Year	(a) Direct to Federal Government		(b) All Other		(c) Total	
	Sales ($)	Quantity	Sales ($)	Quantity	Sales ($)	Quantity
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

* See instruction 6 page xiv

Table III-3 provides space for the submission of total net domestic sales aggregated over all dosage-form prescription drugs, including so-called over-the-counter ethical preparations, sold by your firm during the period 1956 to 1971, inclusive. Please provide annual sales information as follows:

Column

(a) Total net domestic sales (to the nearest dollar) made directly to the Federal Government.

(b) Total all other net domestic sales (to the nearest dollar). Include only sales of products packaged under your own labels for human use.

(c) Total net domestic sales (to the nearest dollar) of all prescription drugs. Include only sales of products packaged under your own labels for human use. The sum of columns (a) (b) should equal the total reported in column (c).

Instructions:

1. Sales made under labels of others, and sales made unlabeled should not be included.
2. Sales of products for veterinary use should not be included.
3. Sales figures should be reported net of all returns, allowances, and trade discounts.
4. Exports and transfers to foreign affiliates should not be included.
5. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data, use the following symbol:

   NM = Not marketed during the year

   If records are not available, and prescription drugs were marketed, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the year and column to which it responds.

Table III-3

Sales of All Prescription-Drug Products

NOTE: NO DATA CELL SHOULD BE LEFT BLANK. SEE INSTRUCTION 5, PAGE XVII.

Year	Net Domestic Sales		
	(a) Direct to Federal Government ($)	(b) All Other ($)	(c) Total ($)
1956			
1957			
1958			
1959			
1960			
1961			
1962			
1963			
1964			
1965			
1966			
1967			
1968			
1969			
1970			
1971			

Section IV

Promotional Expenditures

Tables IV-1 and IV-2, respectively, provide space for submission of *dosage form* promotional expenses related to: (1) your brands of antianginal drugs; and (2) your brands of diuretic and combination diuretic-antihypertensive drugs. Using one page for each dosage form of a brand, please provide annual promotional expense information (to the nearest dollar) for each such dosage form which you marketed at any time during the period 1956 to 1971, as follows:

Column

(a) Dollar expenditure for detail or field representative effort. Include salaries, benefits, travel allowances, etc.

(b) Dollar expenditure for advertising in periodicals, including medical journals. Include cost of creative effort.

(c) Dollar expenditure for direct-mail promotion, including pamphlets, brochures, and package inserts. Include costs of printing, mailing, creative effort, etc.

(d) Dollar expenditure for free samples distributed.

(e) Dollar expenditure for other promotional effort.

(f) Total dollars of promotion expenditure (the sum of columns *a* through *e*).

Instructions:

1. Promotional expenditures of different dosage forms of a brand (i.e. oral vs. oral timed-release vs. sublingual vs. injectable) are to be given separately.
2. Where promotional expenditures cannot be allocated among different dosage forms of a particular brand, please so indicate and provide data which include promotion for all dosage forms of that brand.
3. If your accounting records do not provide a basis for allocation of promotional expense by individual brands, please base your data submission upon marketing-management or other managerial documents used by you to evaluate the effectiveness of promotional effort. Please indicate from what source your promotion data are derived.

4. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data use the following symbols:

NM = Not Marketed during the year, and no promotional expense.

O = Marketed, but no promotional expenditure.

If records are not available, and prescription drugs were marketed and promoted, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the brand-name of the product to which such enclosure refers.

XX

Table IV-1
Promotion of Antianginal Products

Brand Name _____ Dosage Form _____

NOTE: NO DATA CELL SHOULD BE LEFT BLANK. SEE INSTRUCTION 4, PAGE XX.

Year	(a) Expenditures for detailing effort ($)	(b) Expenditures for periodical advertising ($)	(c) Expenditures for direct-mail promotion ($)	(d) Expenditures for free samples ($)	(e) Other promotional expenditures ($)	(f) Total promotional expenditures ($)
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

Table IV-2

Promotion of Diuretic and Combination Diuretic-Antihypertensive Products

Brand Name _____ Dosage Form _____

NOTE: NO DATA CELL SHOULD BE LEFT BLANK. SEE INSTRUCTION 4, PAGE XX.

Year	(a) Expenditures for detailing effort ($)	(b) Expenditures for periodical advertising ($)	(c) Expenditures for direct-mail. promotion ($)	(d) Expenditures for free samples ($)	(e) Other promotional expenditures ($)	(f) Total promotional expenditures ($)
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

Table IV-3 provides space for submission of dosage-form promotional expenses aggregated over all *dosage-form* prescription-drug products, including so-called over-the-counter ethical preparations, which you marketed at any time during the period 1956 to 1971. Please provide annual promotional expense information (to the nearest dollar) as follows:

Column

(a) Dollar expenditure for detail or field representative effort. Include salaries, benefits, travel allowances, etc.

(b) Dollar expenditure for advertising in periodicals, including medical journals. Include cost of creative effort.

(c) Dollar expenditure for direct-mail promotion, including pamphlets, brochures, and package inserts. Include costs of printing, mailing, creative effort, etc.

(d) Dollar expenditure for free samples distributed.

(e) Dollar expenditure for other promotional effort.

(f) Total dollars of promotion expenditure (the sum of columns *a* through *e*).

Instructions:

1. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data use the following symbols:

   NM = Prescription drugs not marketed, and no promotional expense.

   O = Prescription drugs marketed, and no promotional expense.

   If records are not available, and prescription drugs were marketed and promoted, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the year and column to which it responds.

Table IV-3
Promotion of All Dosage-Form Prescription Drugs

Brand Name _____ Dosage Form _____

NOTE: NO DATA CELL SHOULD BE LEFT BLANK. SEE INSTRUCTION 1, PAGE XXIII.

Year	(a) Expenditures for detailing effort ($)	(b) Expenditures for periodical advertising ($)	(c) Expenditures for direct-mail promotion ($)	(d) Expenditures for free samples ($)	(e) Other promotional expenditures ($)	(f) Total promotional expenditures ($)
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

Section V

Sources of Supply

Do you manufacture or purchase bulk generic ingredients used in any of the brands indicated in response to Sections III and IV of this Report? Check appropriate box.

Yes ☐ ☐ No

If yes, then complete the remainder of this section.

Tables V-1 and V-2, respectively, provide space for submission of generic-ingredient supply data related to: (1) your brands of antianginal drugs; and (2) your brands of diuretic and combination diuretic-antihypertensive drugs, indicated in Section III and IV of this Report. Using one page for each such brand, regardless of dosage form, furnish the following information:

Column

(a) The U.S.P. or N.F. generic ingredients.

(b) For each ingredient, state the names of the supplying firms. If you or any of your subsidiaries manufacture the listed ingredients, state your name and, where applicable, the name of the subsidiary.

(c) For the period 1956 to 1971, state the years during which each supply relationship was in effect.

Table V-1
Sources of Supply:
Antianginal Drugs

Brand Name _____

(a) Names of generic ingredients	(b) Names of suppliers	(c) Dates of supply relationship

Table V-2
Sources of Supply:
Diuretic & Combination Diuretic Antihypertensive Drugs
Brand Name _____

(a) Names of generic ingredients	(b) Names of suppliers	(c) Dates of supply relationship

Section VI

Miscellaneous

Submit copies of marketing plans, reports, or analyses that pertain to the sale, promotion, or distribution of the brands listed in Section III of this Report, and which have been submitted to officers or directors of your company.

THIS REPORT IS DUE WITHIN 60 DAYS OF RECEIPT

OMB No. *56–S73020*
Expires *December 31, 1974*

FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

Prescription Drug Survey

SPECIAL REPORT II

PATENT AND LICENSE STATUS SALES AND PROMOTIONAL EXPENDITURES OF PRODUCTS IN SELECTED PRESCRIPTION DRUG MARKETS

THIS REPORT IS REQUIRED BY LAW. It is mandatory under the authotity of the Federal Trade Commission (15 U.S.C. 46).

REPORTING DATE. Within 60 days following receipt of this Report, complete and return one notarized copy of the reporting company's response with a certification attached thereto.

This Report is intended for parent companies. Efforts have been made to establish the identities of parent companies. If, however, recipient is controlled by a parent organization, this Report should be forwarded to such parent for completion and submission. If the parent is not a domestic company, this Report should be completed and submitted by its controlling domestic subsidiary.

Each parent company should include the requested information for its own operations as well as for the operations of subsidiaries which it controls. (Control for the purpose of this Report is ordinarily based upon the ownership of a majority of stock interest; that is, more than 50 percent. Control means the determination of basic business policies such as investment in plant and equipment, price policies, and product development and can also be based upon ownership of a less than majority stock interest).

Return all Special Reports and direct any written inquiries to:

Chief, Division of Industry Analysis
Bureau of Economics
Federal Trade Commission
Washington, D.C. 20580

Telephone inquiries may be directed to Dr. David F. Lean or Dr. Ronald S. Bond, telephone 202–254–7690.

State name and address of parent company responding to this Report:

Name _____

Address _____

_____

_____

_____

State name, address, and basis of control of each subsidiary engaged at any time from 1956 to 1971, inclusive, in the sale of drugs defined in this Report. If control over any subsidiary was assumed or relinquished at any time during the above period, state in a separate enclosure: (a) the name(s) of any predecessor(s) or successor(s) in interest and (b) the dates on which control was assumed or relinquished.

Name _____

Address _____

_____

Basis of Control _____

Name _____

Address _____

_____

Basis of Control _____

Name _____

Address _____

_____

Basis of Control _____

State number of *Patent and Pending Patent Questionnaires* filed in this Report. ____
State number of *License Questionnaires* filed in this Report. ____
State number of brands for which sales and quantities, promotion, and ingredient supply data were submitted.
Sales and Quantities ____
Promotion ____
Ingredient Supply ____

CERTIFICATION

This Special Report has been prepared by me or under my personal supervision from records of:

(Name of parent company)
and is correct to the best of my knowledge and belief.

_____ _____
(Signature of official) (Title)

_____ _____
(Typed signature of above official) (Office telephone number)

Date _____
Subscribed and sworn to before me this ___ day of _____, 197___

_____
Notary Public

My commission expires _____

INSTRUCTIONS

1. This Report requests information related to the drug metronidazole for the period 1956 to 1971.

2. Answers to specific questions should be derived from company books and records. If records are not available, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to reference such enclosure with the number of the question to which it responds.

3. When an item is not applicable, so indicate with the letters "NA".

4. All references to year refer to calendar year. However, if calendar year information is unavailable, then estimate calendar year and furnish fiscal-year data as well, indicating the 12-month period covered.

5. Additional copies of this Special Report may be reproduced from this copy or may be obtained by writing to: Chief, Division of Industry Analysis, Bureau of Economics, Federal Trade Commission, Washington, D.C. 20580.

Section I

Patents and Pending Patents

A. Section I is concerned with patents and pending patents that you have owned or controlled and which relate in any way to the drug metronidazole for the period 1956 to 1971. For each such patent and pending patent, please complete a copy of the following three-page questionnaire.

B. Submit copies of all patents and applications for pending patents listed in response to part A.

C. Submit copies of any agreements entered into in connection with the settlement of interference proceedings instituted by the U.S. Patent Office, in consequence of which you were a successful applicant for the patent.

D. Submit copies of all license agreements for patents listed under Part A of this section, without regard to their dates and regardless whether the licensor was your company or a predecessor in interest.

Patent and Pending Patent Questionnaire
Page 1

1. United States Patent (Pending Patent) Number _____
☐ Check if pending patent
Instruction: Write the above patent (pending patent) number in the appropriate spaces in the upper right-hand corners of pages 2 and 3 of this questionnaire.
2. Type of patent (check one)
a. Pertains to product ☐
b. Pertains to process ☐
c. Pertains to both a and b ☐
3. In the Table below, provide the following information:
a. In column (a), list the generic ingredient(s) covered by the above patent.
b. For *each* generic ingredient listed, write, in column (b), your brands in which the ingredient is incorporated.

(a) Generic Ingredient(s)	(b) Brands

Patent (Pending Patent)
Number _____

Patent and Pending Patent Questionnaire
Page 2

4. Date of patent issuance (application date for pending patent) _____
5. Expiration date of patent _____
6. Calendar years in which patent (pending patent) was worked (used) by you _____
☐ Check if never worked (used)
7. If patent was acquired from another firm, then state:
a. Name of firm from which patent was acquired _____
_____
b. Date of patent acquisition _____
8. In Table I. submit the following information
Column
a. list the name of each licensee authorized by you to work (use) this patent.
b. Date of license agreement.
c. Expiration date of license agreement.
d. List each brand which was covered by the patent and which was marketed by each licensee during the period 1956 to 1971, inclusive.
e. For the period 1956 to 1971, list the years in which each licensee's brand, named in response to question 8-d, was marketed.

Patent (Pending Patent)
Number _____

Patent and Pending Patent Questionnaire
Page 3

Table I: Drug Licensees

(a) Names of licensees	(b) Date of License Agreement	(c) Expiration date	(d) Licensee's brands marketed from 1956 to 1971	(e) Years brand was marketed during 1956 to 1971

Section II

License Agreements

A. Section II is concerned with license agreements that you have held and which relate in any way to the drug metronidazole for the period 1956 to 1971. For each such license obtained from domestic or foreign firms, please complete a copy of the following two-page license questionnaire.

B. Submit copies of all license agreements listed in response to part A of this section.

License Questionnaire
Page 1

1. United States Patent Number _____

Instruction: Write this patent number in the space provided in the upper right hand corner of page 2 of this license questionnaire.

2. Type of patent (check one)
a. Pertains to product ☐
b. Pertains to process ☐
c. Pertains to both a and b ☐

3. Name of licensor (if foreign, indicate country) _____

4. Date of license agreement _____

5. Expiration date of license agreement _____

6. List the generic ingredient(s) covered by the license agreement _____

7. List your brands covered by the license agreement _____

Patent Number _____

License Questionnaire
Page 2

8. List the licensor's brands covered by the patent named in response to question 1 of this section _____

_____

_____

_____

_____

_____

_____

Section III

Sales and Quantity Information

Table III provide space for submission of sales and quantity data related to each dosage strength of each dosage form of your brands of metronidazole. Using one page for each dosage strength of each dosage form of each such brand which you marketed at any time during the period 1956 to 1971, inclusive, please provide annual sales and quantity information as follows:

Columns

(a) Net domestic sales (to the nearest dollar) and quantities made directly to the Federal Government. Include only sales and quantities of products packaged under your own labels for human use.

(b) All other net domestic sales (to the nearest dollar) and quantities. Include only sales and quantities of products packaged under your own labels for human use.

(c) Total net domestic sales (to the nearest dollar) and quantities. Include only sales and quantities of products packaged under your own labels for human use. For each year, the sum of sales and quantities in columns (a) and (b) should equal the total sales and quantities given in column (c).

Instructions.

1. Where a product is promoted or marketed solely under its generic name, treat that product as a brand.
2. Sales and quantities of each dosage strength (i.e. 5 mg. and 10 mg.) of each dosage form (i.e. oral vs. oral timed-release vs. sublingual vs. injectable) of a brand are to be given separately.
3. Sales made under labels of others, and sales made unlabeled, should not be included.
4. Sales of products for veterinary use should not be included.
5. Sales figures should be reported net of all returns, allowances, and trade discounts. Quantity figures should be reported net of all returns.

6. Quantity figures should be reported as follows:

a. Where products are marketed in tablet or capsule form, report quantities in 1,000s of tablets or capsules.

b. Where products are marketed in liquid or ampule form, report quantities in liters.

c. Where products are marketed in suppository form, report quantities in 1,000s of suppositories.

d. Where products are marketed in ointment form, report quantities in pounds.

7. Exports and transfers to foreign affiliates should not be included.

8. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data, use the following symbol:

NM = not marketed during the year

If records are not available, and the product was marketed, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the brand name of the product to which such enclosure refers.

Table III
Sales and Quantities sold of Metronidazole

Brand Name _____
U.S. P. or N.F. Generic Name _____
_____
Dosage Form _____
Dosage Strength _____
Units in which Quantities are reported* _____

Year	(a) Direct to Federal Government		(b) All Other		(c) Total	
	Sales ($)	Quantity	Sales ($)	Quantity	Sales ($)	Quantity
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

* See instruction 6 page xiii

Section IV

Promotional Expenditures

Table IV provides space for submission of *dosage form* promotional expenses related to your brands of the drug metronidazole. Using one page for each dosage form of a brand, please provide annual promotional expense information (to the nearest dollar) for each such dosage form which you marketed at any time during the period 1956 to 1971, as follows:

Column

(a) Dollar expenditure for detail or field representative effort. Include salaries, benefits, travel allowances, etc.

(b) Dollar expenditure for advertising in periodicals, including medical journals. Include cost of creative effort.

(c) Dollar expenditure for direct-mail promotion, including pamphlets, brochures, and package inserts. Include costs of printing, mailing, creative effort, etc.

(d) Dollar expenditure for free samples distributed.

(e) Dollar expenditure for other promotional effort.

(f) Total dollars of promotion expenditure (the sum of columns *a* through *e*).

Instructions:

1. Promotional expenditures of different dosage forms of a brand (i.e. oral vs. oral timed-release vs. sublingual vs. injectable) are to be given separately.
2. Where promotional expenditures cannot be allocated among different dosage forms of a particular brand, please so indicate and provide data which include promotion for all dosage forms of that brand.
3. If your accounting records do not provide a basis for allocation of promotional expense by individual brands, please base your data submission upon marketing-management or other managerial documents used by you to evaluate the effectiveness of promotional effort. Please indicate from what source your promotion data are derived.

4. NO DATA CELL SHOULD BE LEFT BLANK. In the absence of data use the following symbols:

NM = Not Marketed during the year, and no promotional expense.

O = Marketed, but no promotional expenditure.

If records are not available, and prescription drugs were marketed and promoted, then enter your best estimate and designate that estimate with an asterisk (*), stating in a separate enclosure the basis upon which such estimate was made. Be sure to preface each enclosure with the brand-name of the product to which such enclosure refers.

Table IV
Promotion of Metronidazole

Brand Name _____ Dosage Form _____

NOTE: NO DATA CELL SHOULD BE LEFT BLANK. SEE INSTRUCTION 4, PAGE XVI.

Year	(a) Expenditures for detailing effort ($)	(b) Expenditures for periodical advertising ($)	(c) Expenditures for direct-mail promotion ($)	(d) Expenditures for free samples ($)	(e) Other promotional expenditures ($)	(f) Total promotional expenditures ($)
1956						
1957						
1958						
1959						
1960						
1961						
1962						
1963						
1964						
1965						
1966						
1967						
1968						
1969						
1970						
1971						

Section V

Sources of Supply

Do you manufacture or purchase bulk generic ingredients used in any of the brands indicated in response to Sections III and IV of this Report? Check appropriate box.

Yes ☐ ☐ No

If yes, then complete the remainder of this section.

Tables V-1 and V-2, respectively, provide space for submission of generic-ingredient supply data related to: (1) your brands of antianginal drugs; and (2) your brands of diuretic and combination diuretic-antihypertensive drugs, indicated in Section III and IV of this Report. Using one page for each such brand, regardless of dosage form, furnish the following information:

Column

(a) The U.S.P. or N.F. generic ingredients.

(b) For each ingredient, state the names of the supplying firms. If you or any of your subsidiaries manufacture the listed ingredients, state your name and, where applicable, the name of the subsidiary.

(c) For the period 1956 to 1971, state the years during which each supply relationship was in effect.

Sources of Supply:
Metronidazole

Brand Name _____

(a) Names of generic ingredients	(b) Names of suppliers	(c) Dates of supply relationship

Section VI

Miscellaneous

Submit copies of marketing plans, reports, or analyses that pertain to the sale, promotion, or distribution of the brands listed in Section III of this Report, and which have been submitted to officers or directors of your company.

xx

APPENDIX C

PATENTS AND LICENSES

Oral Diuretic Drug Patents

As shown in appendix Table C.1, ownership of important patents in the oral diuretic market is concentrated among relatively few firms. Concentration of patent ownership began in October 1957 when Merck obtained its first patent on chlorothiazide. For over a year Merck exercised complete control over the single-entity thiazide market, and Merck's long-term dominance was reinforced by a strong network of patents and a policy of non-licensing. From May 1956 through April 1961, Merck filed applications for six patents on chlorothiazide, covering both the product and processes of manufacture. Four of these patents were received by mid-1960, and they appear to have effectively prevented other firms from marketing generically identical substitutes for the original thiazide, chlorothiazide.

Merck apparently sought to protect its market position by attempting to patent other benzothiadiazine chemicals. Less than 13 months after its chlorothiazide patent application, Merck applied for an "intermediate"[1] patent on hydrocholothiazide (HCT). This patent was not awarded until December 1964. In July 1957, Merck applied for a patent on methyclothiazide. Though the patent was received in mid-1959, Merck never marketed a brand containing methyclothiazide. Finally, in August 1957, Merck applied for a multi-intermediates patent with claims useful to the manufacture of at least six of the thiazide chemicals: benzthiazide, cyclothiazide, hydrochlorothiazide, methyclothiazide, polythiazide, trichlormethiazide. This patent was received in December 1960.

Merck's success with chlorothiazide stimulated other firms to manipulate the chlorothiazide molecule. Accordingly, Merck was hardly the only firm applying for patents on thiazide chemicals. One of the earliest applications was by Squibb. Just 18 months after Merck applied for its first chlorothiazide patent (and less than one month after Merck received it), Squibb applied for a patent covering flumethiazide and intermediates for bendroflumethiazide. Although the application was involved in an interference proceeding that took nearly five years to resolve, Squibb

[1] An "intermediate" patent covers one or more claims to the product or process of manufacture of certain substances which themselves are not drugs or therapeutic compounds but are useful in the manufacture of certain benzothiadiazine chemicals.

began marketing Naturetin bendroflumethiazide in December 1959, using an exclusive U.S. license from SARATH,[2] which had acquired a patent from Loevens.[3]

While it was not the earliest, Ciba's application for the hydrochlorothiazide patent proved to be one of the most important and most disputed. Ciba's patent application, dated April 9, 1958, was followed within a few months by a similar application by Merck. Indeed, independent applications for HCT and HCT analogues were also filed by Abbott, Chinoin, Schering, and Loevens. Although Merck and Ciba settled their interference by exchanging royalty-free licenses, the Patent Office set up interference proceeding (*U.S.* v. *Ciba*, 1975, p. 15).

Prior to settlement of the interference, Ciba filed ten applications which were continuations-in-part of its original HCT patent application. Eight of the 11 patent applications, including the original, were abandoned by Ciba. It appears that with each new application the number of product and process claims was increased. When the patent was finally awarded to Ciba in December 1964, it covered 43 claims for its product and process of manufacture. (Only four other patents in our oral diuretic market cover 20 or more claims.) Though ownership of the patent was not determined until December 1964, three of the parties (Ciba, Merck, and Abbott) began marketing hydrochlorothiazide in 1959. The three competing brands were Ciba's Esidrix, Merck's Hydrodiuril, and Abbott's Oretic. Moreover, the Ciba patent became the basis for a complex series of licensing agreements involving a number of firms (see below).

From 1958 to 1961, a number of patent applications were filed on single-entity thiazides other than chlorothiazide and hydrochlorothiazide. In November 1958, Abbott applied for a patent on trichlormethiazide. The ownership of this patent was not determined until August 1968, nearly eight years later, and it appears that trichlormethiazide may also have been involved in an interference proceeding. Abbott never marketed trichlormethiazide, choosing instead to license Schering. Schering's Nagua trichlormethiazide was first marketed in March 1960.

In December 1958, Bristol applied for a patent on hydroflumethiazide, and began marketing Saluron hydroflumethiazide in July 1959. The patent application was abandoned by Bristol in May 1964, however.

The first applications for patents on bendroflumethiazide were filed by Bristol and Loevens in early 1959. In June of that year, American Cyanamid (Lederle) applied for a patent on quinethazone. The patent was awarded to American Cyanamid in March 1961. In August, Pfizer applied for a patent on benzthiazide, and although the patent was finally awarded in April 1969, Pfizer never marketed the drug under its own label.

[2] Societe Anonyme de Recherches pour Applications Therapeutiques, a Swiss company.

[3] Loevens is an American short form for Lovens Kemiske Fabrik ved. A. Kongsted, a Danish firm based in Ballerup, Denmark.

During the last quarter of 1960, Boehringer[4] applied for a patent on cyclothiazide, but the Patent Office declared interference between Boehringer and Eli Lilly. Though the patent was eventually awarded to Boehringer, Lilly received exclusive U.S. license rights to the patent in settlement of the interference and began marketing Anhydron cyclothiazide in 1963.

Also during the last quarter of 1960, three firms applied for patents on chemicals unrelated to the thiazide family: SKF for triamterine; Farbwerke Hoechst for furosemide; and Searle for spironolactone, a chemical Searle first patented in April 1955.

In January and February 1961, Pfizer applied for two non-intermediate patents on polythiazide. The first pertained to the product, and the second to the process of manufacture. In February of that year, Geigy (now Ciba–Geigy) applied for a patent on chlorthalidone. Finally, in December 1961, Merck applied for a patent on ethacrynic acid, another chemical unrelated to the thiazide family.

With the exception of a patent application in July 1965 by Schering for trichlormethiazide (received in June 1967), no new applications for single-entity thiazide patents were made after 1961. Perhaps the thiazide molecule, first introduced by Merck, had been thoroughly explored by this time. Furthermore, the significance of the single-entity thiazides was declining, being replaced gradually by products which combined an orally effective diuretic with a suitable antihypertensive agent. Consequently, few patent applications were filed after 1961 for drugs discussed in this study, and most of those filed were for drugs that combined two or more generic ingredients.[5]

In December 1962, Abbott applied for a process patent on methyclothiazide and pargyline HCL. The patent was issued to Abbott in November of 1964, and the patented process was used to manufacture Eutron (methyclothiazide and pargyline HCL), which was first marketed in 1965. In September 1963, Ciba applied for a patent covering hydroflumethiazide and reserpine, and received the patent in November 1966. In 1967, Ciba filed application for a patent which combined HCT with hydralazine and reserpine. The patent was received in 1970. Ciba had begun marketing the product in early 1960 under the brand name Ser-Ap-Es, one of the more successful combination brands. Finally, in June 1969, Ciba applied for another patent which omitted reserpine and simply combined HCT with hydralazine. The patent pertained to the product and was received in June

[4] Boehringer Ingelheim, G.m.b.H. is a firm based in Ingelheim am Rhein, Germany.

[5] Some patent applications for combination drugs were even earlier. In 1959, Bristol applied for a combination patent on hydroflumenthiazide, reserpine, and protoveratrine A, the first combination patent application in this matter. However, the application was abandoned by Bristol in January 1961. Following the Bristol combination patent application, five other combination thiazide-antihypertensive agent patent applications were filed. American Cyanamid filed an application for a patent covering a combination of quinethazone, reserpine, and acetazolamide in August 1960 and was awarded a patent pertaining to the product in July 1963. However, American Cyanamid never marketed such a product. The remaining combination patent applications (one by Abbott and three by Ciba) were filed in later years.

1970. The drug was marketed from 1959 to 1971 under the brand name Apresoline-Esidrix.

Oral Diuretic Drug Licenses

Early entry into the single-entity thiazide submarket was almost entirely dependent upon patent ownership or licenses received from the resolution of patent interferences. Therefore, entry into the thiazide market in the early years was limited to those firms capable of manipulating and inventing around the chlorothiazide molecule. Several firms were able to invent around the chlorothiazide patents, and the single-entity thiazide market was controlled by Merck and these firms for more than a decade. With the exception of hydrochlorothiazide and trichlormethiazide, each single-entity thiazide was marketed by only one firm: Abbott, methycloth-iazide; Bristol, hydroflumethiazide; Geigy, chlorthalidone; Lederle, quine-thazone; Lilly, cyclothiazide; Merck, chlorothiazide; Squibb, bendrofluo-methiazide (flumethiazide was never marketed as a single-entity thiazide); and Pfizer, polythiazide and (through Robins) benzthiazide. Hydrochlo-rothiazide was marketed by three firms, Merck, Ciba, and Abbott. Trichlormethiazide was marketed by two firms, Schering and (through Schering) Lakeside.[6]

As shown in Appendix C.2, some of the firms marketing particular single-entity thiazides do not own patents. Entry by such firms was the result of securing a license under several different circumstances: 1) licenses having patent interference as a basis; 2) licenses inferred from contracts entered into primarily for other purposes (implied licenses); 3) licenses which cover substances useful in preparing certain benzothiadiaz-ine chemicals (intermediate licenses).

Licenses are generally issued on patents which are not worked by the licensor, suggesting that firms may seek to avoid duplication of the product and, hence, avoid competition from identical generic ingredients.

Declarations of patent interference or infringement seem to result frequently in a license to the party not receiving the patent. Perhaps firms want to avoid the expensive and time-consuming process of litigation in settling not only an interference but also in prosecuting infringers. However, in the oral diuretic market there are only two instances in which more than one party to an interference actually began marketing the chemical. In the first instance, Bristol marketed Benuron bendroflumethia-zide nearly six years after the product was marketed by Squibb. Bristol received its own patent for bendroflumethiazide in January 1966. In the second instance, Ciba was joined by its licensees, Merck and Abbott, in

[6] An anomalous situation arose in 1961 when Western Research marketed HCT for three years based upon an implied license with Tru-Synthetics. Western Research abandoned marketing HCT, however, about the time that ownership of the patent was being determined.

marketing HCT. When it became apparent Ciba's HCT was not going to achieve the original sales goals, Ciba began to license other firms to sell hydrochlorothiazide and other chlorothiazide analogues under certain conditions (*U.S.* v. *Ciba*, 1975, p. 13). Thus, Merck's sales advantage may explain much of the post-1959 entry into the market.

Under certain contractural arrangements Ciba granted the following firms permission to market HCT in combination with other products: Carter-Wallace, Hoffmann-LaRoche, Lemmon, McNeil, Richardson-Merrell, Searle, SKF, and Warner-Lambert. All of the firms, except Lemmon, Searle, and LaRoche, had options to obtain licenses to manufacture their own HCT, but through 1971 none had exercised its option. Only five of the firms have been slccessful in marketing a Ciba-approved thiazide combination. Three of the firms, Lemmon, Hoffmann-LaRoche, and Richardson-Merrell, have never produced a product because they were unable to obtain FDA approval for their combinations.

Ciba's licensing policy permitted a few firms to gain entry. But single-entity thiazides would be available only from relatively large-firms for nearly a decade. Implied licences from Pfizer then permitted nine additional firms (including Lemmon) to market benzthiazide in what had become a declining submarket. All of these firms were relatively small, with little possibility of performing the R&D required to obtain or even possibly apply for a patent. All nine firms licensed directly and indirectly by Pfizer sell identical competing products. The impact of this entry, however, has been minute, as the combined 1971 market share of these firms' benzthiazide brands was less than one percent.

Although many of the firms listed in appendix table C.2. own one or more patents, most of them must also pay royalties to one or more other firms for use of a related, usually an intermediate, patent. Fourteen firms in the survey hold licenses from Ciba to manufacture their marketed brands. In addition, seven firms (including five of these 14) hold comparable licenses from Merck. In some cases, a firm's brand may make use of two or three different firms' patents, and to prevent royalties from being compounded to uneconomic levels, many of the licenses contain a "most favored licensee" clause that permits a reduction in the royalties payable to the licensor if the licenses must also pay royalties to a third party.

Oral Diuretic Drugs: Summary

In 1971, 25 firms marketed drugs in the oral diuretic market. Sixteen of these gained entry through implied licenses from firms owning patents on single-entity thiazides. Only 21 firms actually market a brand in the single-entity thiazide market; nine of which are patent holders. Fourteen firms in the oral diuretic market sell combination thiazide-antihypertensive agents,

TABLE C.1.—Oral Diuretic Patents and Licenses

Patent Application Date	Generic Ingredient	Patent Issue Date	Patent Holder	Patent No.	Patent Pertains to Product/Process	Licensee	License Issue Date
11-25-57	Bendroflumethiazide	06-19-62	Squibb[1]	3,040,042	Both	Ciba	02-01-61
						SKF	02-01-61
						Bristol	07-06-61
02-26-59	Bendroflumethiazide	01-18-66	Bristol	3,230,218	Process	None	
04-27-59	Bendroflumethiazide	07-09-65	SARATH[2]	3,392,168	Product	Squibb	12-01-59
08-04-59	Benzthiazide	04-22-69	Pfizer[3]	3,440,244	Product	Central	
						Lemmon	
						Mallard	
						North American	
						Pharmacal	
						Robins	
						Tutag	
						Western Research	
						Reid Provident	
						Pasadena Research	
05-02-56	Chlorothiazide	10-18-57	Merck	2,809,194	Both	None	
09-13-57	Chlorothiazide	10-27-59	Merck	2,910,475	Process	None	
09-13-57	Chlorothiazide	10-27-59	Merck	2,910,476	Process	None	
09-25-58	Chlorothiazide	05-17-60	Merck	2,937,169	Process	None	
04-07-61	Chlorothiazide	12-08-64	Merck	3,160,629	Process	None	
04-07-61	Chlorothiazide	01-08-65	Merck	3,164,589	Process	None	
02-17-61	Chlorthalidone	09-25-62	Geigy	3,055,904	Product	None	

08-06-57	Cyclothiazide	12-20-60	Merck	2,965,675	Product[4]	Lilly	01-01-68 01-30-79
11-23-59	Cyclothiazide	01-30-62	Merck	3,019,245	Product[4]	Lilly	01-01-68
10-31-60	Cyclothiazide	09-27-66	Boehringer[5]	3,275,625	Product	Lilly	09-30-63
09-25-64	Cyclothiazide	12-29-64	Ciba	3,163,645	Product	Lilly[6]	10-01-67
12-06-61	Ethacrynic acid	06-07-66	Merck	3,255,241	Product	None	
12-03-63	Ethacrynic acid	05-16-67	Merck	3,317,591	Process	None	
12-17-63	Ethacrynic acid	05-23-67	Merck	3,321,513	Process	None	
12-23-63	Ethacrynic acid	05-30-67	Merck	3,322,821	Process	None	
01-29-64	Ethacrynic acid	05-16-67	Merck	3,320,306	Process	None	
01-14-66	Ethacrynic acid	11-18-69	Merck	3,479,402	Process	None	
11-02-66	Ethacrynic acid	11-11-69	Merck	3,478,085	Process	None	
11-25-57	Flumethiazide	06-19-62	Squibb	3,040,042[7]	Both	None	
12-14-60	Furosemide	10-16-62	Fabwerke Hoechst	3,058,882	Product	American Hoechst	09-01-66
03-31-60	Guanethidine	10-23-62	Ciba	3,060,186	Product	None	
12-10-46	Hydralazine	10-11-49	Ciba	2,484,029	Product	None	
01-04-67	Hydralazine, reserpine and hydrochlorothiazide	03-03-70	Ciba	3,499,082	Product	None	

[1]Ciba, SKF, Bristol, and Squibb were parties to an interference, #90,041. This patent covers flumethiazide and intermediates for hydroflumethiazide and bendroflumethiazide.
[2]Society Anonyme de Recherches pour Applications Therapeutiques (Switzerland).
[3]All licensees are licensed directly or indirectly.
[4]An intermediates patent.
[5]A patent interference was declared between Boehringer and Lilly. Lilly filed an application for the patent on 01-23-61.
[6]The license pertains to intermediates.
[7]The patent was involved in an interference.

Table Continued

TABLE C.1.—Oral Diuretic Patents and Licenses—Continued

Patent Application Date	Generic Ingredient	Patent Issue Date	Patent Holder	Patent No.	Patent Pertains to Product/Process	Licensee	License Issue Date
06-02-69	Hydralazine and hydrochlorothiazide	06-02-70	Ciba	3,515,786	Product	None	
06-17-57	Hydrochlorothiazide (sulfanomide compounds)	12-15-64	Merck	3,161,675	Both	SKF[8]	09-20-66
08-06-57	Hydrochlorothiazide (intermediates)	12-20-60	Merck	2,965,675	Both	SKF[8]	09-20-66
04-09-58	Hydrochlorothiazide	12-29-64	Ciba[9]	3,163,645	Both	Merck	02-11-59
						Abbott	04-22-59
						Warner-Lambert[12]	08-27-59
						Schering	01-01-60
						Lakeside	07-08-60
						(See Table C.2, n.4)	
						SKF[12]	04-01-61
						Richardson-Merrell[12]	05-01-61
						McNeil[10]	07-01-61
						Wallace[12]	09-01-61
						Lilly[11]	10-01-67
						Searle[12]	03-21-60
						Lemmon[12]	10-01-61
						Hoffman-La Roche[12]	04-28-65

11-26-58	Hydrochlorothiazide	03-13-62	Merck	3,025,292	Process	None	
10-14-59	Hydrochlorothiazide	07-10-62	Merck	3,043,840	Process	None	
11-23-59	Hydrochlorothiazide	01-30-62	Merck	3,019,245	Both	SKF[13]	07-22-66
01-04-67	Hydrochlorothiazide, reserpine, and hydralazine (See also Hydralazine)	03-03-70	Ciba	3,499,082	Product	None	
06-02-69	Hydrochlorothiazide and hydralazine	06-02-70	Ciba	3,515,786	Product	None	
11-25-57	Hydroflumethiazide (intermediate)	06-19-62	Squibb (Olin Mathieson)	3,040,042	Product	Bristol	07-06-61 06-19-78
12-08-58	Hydroflumethiazide	Abandoned 05-10-64	Bristol	SN778,599[14]	Product		
02-16-59	Hydroflumethiazide, reserpine, and protoveratrine A	Abandoned 01-19-61	Bristol	SN793,295[14]	Product		
01-22-60	Hydroflumethiazide	05-31-66	Loevens[15]	3,254,076	Product	Bristol	10-03-66 05-31-83
09-12-63	Hydroflumethiazide and reserpine	11-29-66	Ciba	3,288,678	Product	Bristol	01-01-67 11-29-83

[8]Intermediates license to manufacture hydrochlorothiazide, but license is not being exercised.
[9]Merck and Ciba were parties to Interference no. 90,020.
[10]McNeil discontinued purchasing HCT in 1969.
[11]License relates to cyclothiazide.
[12]Implied license.
[13]The license has not been exercised.
[14]SN refers to the patent application serial number.
[15]Lovens Kemiske Fabrik ved. A. Kongsted (Denmark).

Table Continued

TABLE C.1.—Oral Diuretic Patents and Licenses—Continued

Patent Application Date	Generic Ingredient	Patent Issue Date	Patent Holder	Patent No.	Patent Pertains to Product/Process	Licensee	License Issue Date
07-30-57	Methyclothiazide	05-12-59	Merck	2,886,566	Process	Abbott[16]	06-08-65
						Neisler	10-06-60
08-06-57	Methyclothiazide (intermediate)	12-20-60	Merck	2,965,675	Both	Abbott[16]	06-08-68
						Neisler	10-06-60
10-16-59	Methyclothiazide	12-29-64	Ciba	3,163,644	Product	Abbott	05-09-66
						Neisler	10-06-60
11-23-59	Methyclothiazide (intermediate)	01-30-62	Merck	3,019,245	Both	Abbott[16]	06-08-68
						Neisler	10-06-60
05-31-63	Methyclothiazide and Pargyline HCL	06-21-66	Abbott	3,257,277	Both	None	
12-15-53	Methyldopa	01-13-59	Merck	2,868,818	Product	None	
04-09-62	Methyldopa	11-24-64	Merck	3,158,648	Process	None	
09-19-63	Methyldopa	01-30-68	Merck	3,366,679	Process	None	
12-01-63	Methyldopa	09-26-67	Merck	3,344,023	Process	None	
04-20-64	Methyldopa	12-06-66	Merck	3,290,225	Process	None	
08-19-64	Methyldopa	10-22-68	Merck	3,407,226	Both	None	
11-17-64	Methyldopa	10-08-68	Merck	3,405,159	Process	None	
03-26-65	Methyldopa	10-17-67	Merck	3,347,752	Process	None	
05-14-65	Methyldopa	01-18-66	Merck	3,230,143	Process	None	
10-22-65	Methyldopa	08-27-68	Merck	3,399,226	Process	None	
10-22-65	Methyldopa	01-06-70	Merck	3,488,363	Process	None	
09-21-67	Methyldopa	06-23-70	Merck	3,517,057	Process	None	
02-06-69	Methyldopa	07-13-71	Merck	3,592,844	Process	None	
10-22-69	Methyldopa	01-30-73	Merck	3,714,241	Process	None	
12-03-62	Pargyline HCL	11-03-64	Abbott	3,155,584	Process	None	

08-06-57	Polythiazide (intermediate)	12-20-60	Merck	2,965,675	Both	Pfizer[17]	04-03-64
11-23-59	Polythiazide (intermediate)	01-30-62	Merck	3,019,245	Both	Pfizer[17]	04-03-64
01-04-61	Polythiazide	11-21-61	Pfizer	3,009,911	Product	None	
02-01-61	Polythiazide	05-12-64	Pfizer	3,133,060	Process	None	
06-30-59	Quinethazone	03-21-61	American Cyanamid	2,976,289	Product	None	
08-25-60	Quinethazone, reserpine and acetazolamide	07-16-63	American Cyanamid	3,098,009	Product	None	
01-18-61	Quinethazone (intermediate)	03-21-61	American Cyanamid	3,092,631	Product	None	
09-21-53	Spironolactone	04-05-55	Searle	2,705,712	Product	None	
12-22-60	Spironolactone	12-12-61	Searle	3,013,012	Product	None	
10-01-63	Spironolactone	08-30-66	Searle	3,270,008	Process	None	
10-08-65	Spironolactone	10-18-66	Searle	3,280,116	Both	None	
09-08-60	Triamterine	03-12-63	SKF	3,081,230	Both	None	
08-06-57	Trichlormethiazide (intermediate)	12-12-60	Merck	2,965,675	Product	Schering Lakeside	12-19-67 07-08-60
04-09-58	Trichlormethiazide	12-29-64	Ciba	3,163,645	Both	Schering Lakeside	01-01-60 07-08-60
11-03-58	Trichlormethiazide	08-02-66	Abbott	3,264,292	Product	Schering Lakeside	06-27-67 07-08-60
11-23-59	Trichlormethiazide (intermediate)	01-30-62	Merck	3,019,245	Product	Schering Lakeside	12-19-67 07-08-60
04-25-60	Trichlormethiazide (intermediate)	09-04-65	Schering	3,206,507	Both	None	
07-06-65	Trichlormethiazide	06-30-67	Schering	3,326,908	Process	None	

[16]The license was amended and re-issued 07-11-68.

[17]The license was amended 01-01-68.

Source: Federal Trade Commission, Bureau of Economics, Prescription Drug Survey.

many of which are combined with reserpine. But only three firms hold patents on the separate elements as well as the combinations.

TABLE C.2—Firms Holding Patents or Licenses

I. Single-Entity Thiazides

Firm	Number of Patents	Licenses Held From:
Abbott	2	Ciba, Merck
Bristol	1	Ciba, Loevens,[1] Squibb[2]
Central	0	Pfizer[5]
Ciba	2	Squibb[2]
Geigy[3]	1	.....
Lakeside	0	Ciba,[4] Merck[4]
Lederle	3	.....
Lemmon	0	Ciba,[5] Pfizer[5]
Lilly	0	Boehringer,[2] Ciba, Merck
LaRoche	0	Ciba[5]
McNeil	0	Ciba[5]
Mallard	0	Pfizer[5]
Mallinckrodt (Neilser)[6]	0	Merck
Merck	15	Ciba[2]
North American	0	Pfizer[5]
Pasadena Research	0	Pfizer[5]
Pfizer	3	Merck
Reid Provident	0	Pfizer[5]
Richardson-Merrell	0	Ciba[5]
Robins	0	Pfizer[5]
Schering-Plough	2	Abbott, Ciba, Merck
Searle	0	Ciba[5]
SKF	0	Ciba[5] Merck, Squibb[2]
Squibb	1	SARATH[7]
Tutag	0	Pfizer[5]
Wallace	0	Ciba[5]
Warner-Lambert	0	Ciba[5]
Western Research	0	Pfizer,[5] Tru-Synthetics
	30	

II. The Combination of a Thiazide and an Antihypertensive

Firm	Number of Patents	Licenses Held From:
Abbott	1	.....
Ciba	3	.....
Lederle	1	.....

III. Potassium-Sparing Entities

Firm	Number of Patents	Licenses Held From:
SKF	1	.....
Searle	4	.....

IV. Loop Diuretics

Firm	Number of Patents	Licenses Held From:
American Hoechst	0	Farbwerke Hoechst
Merck	7	.....

[1]Loevens is an American short form for Lovens Kemiske Fabrik ved A. Kongsted, a Danish firm based in Ballerup, Denmark.

[2]License was issued in settlement of an interference.

[3]Patent rights were sold to U.S. Vitamin upon the merger of Ciba and Geigy.

[4]For licensing purposes, Schering was given permission by Ciba and Merck to treat Lakeside as an affiliate. Hence, Lakeside has implied licenses from Schering to patents belonging to Ciba and Merck but which are licensed to Schering.

[5]An implied license.

[6]Neisler has a sub-license to all of Abbott's patents and licenses on methyclothiazide to manufacture and sell methyclothiazide in combination form only. This requirement was modified in January 1971 to allow sales of the compound as a single entity.

[7]Societe Anonyme de Recherches pour Applications Therapeutiques.

Antianginal Drug Patents

Patents and licenses have not been important features of the structure of the antianginal market. Brands with the largest share of the market are not protected by patents and, as shown in Table C.3, the list of patented products or processes is quite short. Eli Lilly held a product patent on Paveril Phosphate (dioxyline phosphate) from 1955 to 1972, but the drug's share declined from 9 percent in 1956 to 0.4 percent in 1971. Warner-Lambert's Parke, Davis division introduced Nitrostat, a new supposedly more stable form of nitroglycerin, in 1971, the last year of the study period, but the patent covering both the product and the process was issued only in 1974. Two firms, Key Pharmaceuticals, Inc. and U.S. Ethicals, Inc. hold patents on new sustained-action dosage forms of nitroglycerin. Key's patent pertains to Nitroglyn, relates to the process of making the sustained-action dosage form, and expires in 1980. Nitroglyn's peak share was 4.6 percent in 1958. U.S. Ethical's patent pertains to Nitrong, covers the product and the process, and expires in 1984. Marion Laboratories unpatented sustained-action dosage form of nitroglycerin (Nitrobid) has done reasonably well, achieving a peak share of 5.7 percent of the market by 1971.

Antianginal Drug Licenses

Only five products were marketed under patent licenses in the 1956 to 1971 period, and no license was critical for entry. These products are listed in Table C.4.

Pfizer held a non-exclusive non-assignable license from Astra Pharmaceutical Products, Inc. that applied to a process for making a sustained-action dosage form tablet. Pfizer utilized this process for the drug Metamine (trolnitrate phosphate). Introduced in 1953, Metamin's share of the market remained below 2 percent from 1964 to 1971, the only years for which data were provided. Pfizer also had an exclusive license from Union Chimique Belge S.A. (Belgium) that pertained to the tranquilizing agent hydroxyquin hydrochloride used by Pfizer in combination with PETN in the drug Cartrax. Cartrax held only 3.6 percent of the market in 1956, its best share year.

Key Pharmaceuticals, in addition to holding a patent on a method of making a sustained-action dosage form tablet, also held a license from

Hans Lowey that related to a method of making a sustained-action dosage form. The license agreement with Lowey was utilized with respect to Nitroglyn (sustained–action nitroglycerin).

Persantine was introduced by Geigy Pharmaceuticals, Inc. under an exclusive non-transferable license from Boehringer. With an option to continue the agreement until 1976, Geigy ended the agreement in 1971 following a period of declining sales.

Finally, Warner-Lambert held a license from Ciba to use hydrochlorothiazide in combination with the leading antianginal product, Peritrate (PETN). Marketed under the brand name Perithiazide from 1961 to 1970, this combination drug achieved a peak share of 2 percent in its first year.

TABLE C.3—Antianginal Patents

Patent Holder	U.S. Patent No.	Patent Pertains to Product/Process	Brands Covered	Generic Ingredient	Patent Issue Date	Licensee
Key Pharmaceuticals	3,080,294	Process	Nitroglyn	nitroglycerin (sustained action)	03–05–63	none
U.S. Ethicals	3,344,029	Both	Nitrong	nitroglycerin (sustained action)	09–26–67	none
Warner-Lambert (Parke, Davis)	3,789,119	Both	Nitrostat	nitroglycerin	01–29–74	none
Eli Lilly	2,728,769	Product	Paveril Phosphate	dioxyline phosphate	12–27–55	none

TABLE C.4—Antianginal Licenses

Licensee	U.S. Patent No. to which License Pertains	Patent Pertains to Product/Process	Licensor	License Issue Date	Generic Ingredient	Licensee's Brand
Geigy Pharmaceuticals	3,031,450	Both	Boehringer-Ingelheim, G.m.b.H.[1]	01–01–63	dipyridamole	Persantine
Key Pharmaceuticals	2,853,420	Process	H. Lowey	05–18–53	nitroglycerin[2] (sustained action)	Nitroglyn
Pfizer, Inc.	3,317,394	Both	Astra	05–03–65	trolnitrate phosphate[2]	Metamine
	2,899,436	Product	Union Chimique Belge, S.A. (Belgium)	01–18–65	hydroxyzine	Cartrax
Warner-Lambert	3,163,645	Both	Ciba	08–27–59	hydrochloro-thiazide	Perithiazide

[1]U.S. Patent No. 3,031,450 was issued April 24, 1962 to Dr. Karl Thomae G.m.b.H., Biberach (Riss), Germany. Rights to this patent were apparently acquired by Boehringer-Ingelheim.
[2]The license does not pertain to the generic ingredient, but covers the method for making a sustained-action dosage form.

REFERENCES

American Medical Association, (1960). Council on Drugs. *New and Non-Official Drugs.*

——— (1971). *AMA Drug Evaluations.* Chicago.

——— (1973). *AMA Drug Evaluations.* 2nd ed. Acton, Mass.: Publishing Sciences Group.

Aviado, D.M. (1972). *Krantz and Carr's Pharmacologic Principles of Medical Practice.* 8th. ed. Baltimore: The Williams and Wilkins Company.

Bain, J.S. (1956). *Barriers to New Competition.* Cambridge: Harvard University Press.

Bass, Frank M., and Parsons, Leonard J. (1969). "Simultaneous-Equation Regression Analysis of Sales and Advertising," *Applied Economics,* 1 (May): 103–124.

Bloch, Harry (1974). "Advertising and Profitability: A Reappraisal," *Journal of Political Economy,* Vol. 82, No. 2 (March/April): 267–286.

Burack, Richard (1970) *The New Handbook on Prescription Drugs.* New York: Pantheon Books.

Charlier, R. (1961). *Coronary Vasodilators.* New York: Pergamon Press.

Comanor, William S., and Wilson, Thomas A. (1967). "Advertising, Market Structure, and Performance," *The Review of Economics and Statistics,* Vol. XLIX, No. 4 (November): 423–440.

——— (1974). *Advertising and Market Power.* Cambridge: Harvard University Press.

Cowling, Keith, and Rayner, A.J. (1970). "Price, Quality, and Market Share," *Journal of Political Economy,* Vol. 78, No. 6 (November/December): 1292–1309.

Cowling, Keith, and Cubbin, John (1971). "Price, Quality, and Advertising Competition: An Econometric Investigation of the United Kingdom Car Market," *Economica: New Series,* Vol. XXXVIII, No. 152 (November): 378–394.

Cowling, Keith (1972). "Optimality in Firm's Advertising Policies: An Empirical Analysis," in Cowling, Keith, ed. *Market Structure and Corporate Behavior: Theory and Empirical Analysis of the Firm.* London: Gray-Mills Publishing Ltd.: 85–104.

Ehrenberg, A.S.C. (1972). *Repeat-Buying: Theory and Applications.* Amsterdam: North-Holland Publishing Company.

FDA Bulletin (1974). January.

FDC Reports (1974). August 26, pp. B–6–14.

Fein, Rashi (1967). *The Doctor Shortage: An Economic Diagnosis.* Washington, D.C.: The Brookings Institution.

Feldstein, Martin S. (1970). "The Rising Price of Physicians' Services," *Review of Economics and Statistics,* Vol. LII, (May): 121–133.

Ferguson, James M. (1974). *Advertising and Competition; Theory, Measurement, Fact.* Cambridge, Mass.: Ballinger Publishing Company.

Friedberg, Charles K. (1966). *Diseases of the Heart.* 3rd. ed. Philadelphia: W.B. Saunders Company.

Gaskins, Darius W.,Jr. (1970). "Optimal Pricing by Dominant Firms." Unpublished Ph.D. Dissertation, The University of Michigan.

_____ (1971). "Dynamic Limit Pricing: Optimal Pricing Under Threat of Entry." *Journal of Economic Theory*, Vol. 3, No. 3 (September). 306–322.

"Generics Pose No Threat to Big Drug Firms" (1974). *Chemical and Engineering News*, November 11; p. 71.

Goodman, Louis S., and Gilman, Alfred, (1941). *The Pharmacological Basis of Therapeutics.* New York: The MacMillan Company.

_____ eds. (1955). *The Pharmocological Basis of Therapeutics*, 2nd. ed. New York: The MacMillan Company.

_____ (1965). *The Pharmacological Basis of Therapeutics*, 3rd. ed. New York: The MacMillan Company.

Green, James R. (1972). "Welfare Losses from Monopoly in the Drug Industry: The Oklahoma 'Antisubstitution Law,' *Antitrust Law and Economics Review*, Vol. 5, No. 3 (Spring, 1972). 97–119.

Ireland, N.J. (1972). "Concentration and the Growth of Market Demand: A Comment on Gaskins Limit Pricing Model," *Journal of Economic Theory*, Vol. 5, No. 2 (October): 303–305.

Kessel, Reuben A. (1958). "Price Discrimination in Medicine," *Journal of Law and Economics*, Vol. I (October): 20–53.

Krantz, Jr., John C. (1974). *Historical Medical Classics Involving New Drugs.* Baltimore: The Williams and Wilkins Company.

Mann, H. Michael (1974). "Advertising, Concentration, and Profitability: The State of Knowledge and Directions for Public Policy," in Goldschmidt, Harvey J., Mann, H. Michael, and Weston, J. Fred. *Industrial Concentration: The New Learning.* Boston: Little, Brown and Company: 137–161.

Melville, Kenneth I. (1954). "Nitrites, Nitrates, and Miscellaneous Drugs, " in Drill, Victor A. ed. *Pharmacology in Medicine.* New York: McGraw-Hill Book Company, Inc.

Modell, Walter, ed. (1970). *Drugs of Choice 1970–1971.* Saint Louis: C.V. Mosby Company.

Peles, Yoram (1971). "Rates of Amortization of Advertising Expenditures," *Journal of Political Economy*, Vol. 79, No. 5 (September/October): 1032–1058.

Report of the National Advisory Commission on Health Manpower (1967). Volume II, November.

Scherer, F.M. (1970). *Industrial Market Structure and Economic Performance.* Chicago: Rand McNally & Company.

Schmalensee, R. (1972). *The Economics of Advertising.* Amsterdam: North-Holland Publishing Company.

Simon, Julian L. (1970). *Issues in the Economics of Advertising.* Urbana: The University of Illinois Press.

Sollman, Torald (1957). *A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology.* 8th. ed. Philadelphia: W.B. Saunders Company.

Taber, C.W. (1970). *Taber's Cyclopedic Medical Dictionary.* Philadelphia, Pa.

Telser, L.G. (1962). "Advertising and Cigarettes," *Journal of Political Economy*, Vol. 72, No. 5 (October): 471–499.

——— (1975). "The Supply Response to Shifting Demand in the Pharmaceutical Industry," in Robert B. Helms, ed. *Drug Development and Marketing*, American Enterprise Institute, Washington, D.C. 2077–223.

U.S. vs. Bristol-Myers Company, et al. (1970). "Complaint for Declaratory and Injunctive Relief and Damages," Civil No. 822–70, March 19.

U.S. vs. Ciba Corporation (1975). "Government's Pretrial Brief on the Merits." U.S. District Court, N.J. Civil Action No. 791–69. March 27.

U.S. Fact Book (1975). New York: Grosset & Dunlap

U.S. Federal Trade Commission (1975). "Prescription Drug Price Disclosures," Staff Report to the Federal Trade Commission, January 28.

U.S. Senate, Select Committee on Small Business, Subcommittee on Monopoly (1972). *Hearings on Competitive Problems in the Drug Industry*: Summary and Analysis.

Virginia State Board of Pharmacy v. *Virginia Citizens Consumer Council*, 425 U.S. 748 (1976).