AN ECONOMIC ANALYSIS OF THE NET RATE OF ENTRY IN PRESCRIPTION DRUG MARKETS

By

SHIU-FANG YU

Bachelor of Arts
National Taiwan University
Taipei, Taiwan
1971

Master of Science
Oklahoma State University
Stillwater, Oklahoma
1973

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
DOCTOR OF PHILOSOPHY
May, 1981

AN ECONOMIC ANALYSIS OF THE NET RATE OF ENTRY

IN PRESCRIPTION DRUG MARKETS

Thesis Approved:

Joseph M. Dadlow
Thesis Adviser

Joseph Sloan

Stephen J. Miller

John D. Reed

Norman N. Durham
Dean of the Graduate College

ACKNOWLEDGMENTS

I wish to express my appreciation to the chairman of my graduate committee, Dr. Joseph M. Jadlow, for his interest, guidance, and assistance during the course of this study. Appreciation is also extended to the other members of my committee: Dr. John D. Rea, Dr. Joseph Shaanan, and Dr. Stephen J. Miller, for their valuable suggestions and assistance.

I would also like to thank the faculty of the Department of Economics for making my graduate education a rewarding and stimulating experience. I am especially grateful to Dr. Richard H. Leftwich whose advice and encouragement were indispensable to the completion of this study. My appreciation is also extended to the Pharmaceutical Manufacturers Association whose Doctoral Dissertation Research Grant made this study possible. In addition, thanks are extended to Sandi Ireland for her excellent typing of this thesis.

Finally, I wish to express my deepest appreciation and gratitude to my parents, Mr. and Mrs. C. J. Yu, for their understanding, encouragement, and many sacrifices.

TABLE OF CONTENTS

Chapter Page

LIST OF TABLES

Table Page

FIGURE

CHAPTER I

INTRODUCTION

A. Purpose of the Study

The rapid surge in the costs of health care has become of pressing national concern. In 1965 the nation spend $38.9 billion in health care, amounting to 5.9 percent of the GNP. In 1977 total national health expenditures reached $163 billion, or 8.8 percent of the GNP.[1] While drugs are an indispensable component of the health care system as a whole, the costs of drugs have accounted for not only a relatively small but also a declining share of total health costs. As shown in Table I, drugs and drug sundries accounted for $12.6 billion, or 7.7 percent of total national health care expenditures in 1977, in comparison with 11.9 percent in 1965.

It is clear that drugs present a relatively inexpensive form of therapy. Drug therapy often provides an alternative to more expensive means of treatment such as surgery, hospital care, and radiology. The substitution of low-cost drug therapy for other more costly types of therapy can greatly reduce medical costs. In view of the rapidly rising costs of health care, the production of new and existing drugs may

---

[1]Trends in "total national health expenditures" and in "drugs and drug sundries" are presented in Table I, p. 11.

provide large benefits to consumers. Rates of output in the pharmaceutical industry, however, will in fact depend largely on conditions of entry.

Theoretical work in the past 20 years by Sylos [59], Bain [3], and Modigliani [38] has suggested that firms considering entry into an existing market may face a disadvantage relative to firms already established in that market. Despite the theoretical importance of entry conditions, however, little empirical research has been done on the determinants of and effects of entry.

The purpose of this study is to develop a theoretical model of entry conditions into the pharmaceutical industry, and using data for prescription drug markets, to investigate empirically the determinants of the rate of entry and the effects of entry on market structure. An important feature of the study is an examination of the role of technological innovation in the entry process in therapeutic drug markets. In previously published papers, some economists have argued that research and development (R & D) activities in the pharmaceutical industry may tend to reduce competition [11]. The present study investigates whether R & D resulting in new drug introductions facilitates or impedes competition in drug markets.

B. Methodology of the Study

Much of the research for the present study is concerned with the development and quantification of a measure of the rate of entry and of various alternative market structure variables which seem likely to affect the rate of entry. The study employs proprietary data for thousands of prescription drug products sold in the United States during

the period 1964-1974. A sample of 20 therapeutic drug markets is used in the study. In general, these markets are more well-defined--according to economic substitutability criteria--than have been the samples of markets employed in most of the previous empirical studies of entry.

A number of empirical studies of entry have regressed the profit rate, rather than entry, on various structural characteristics considered to be entry barriers [12, 37]. As pointed out by Orr [43, p. 58] in his study, this specification is an indirect rather than a direct test of "the propensity of these factors to deter entrants." In addition, measurement errors in the profit rate may distort the true condition of entry [43, p. 58]. The present study regresses the rate of entry on variables designed to measure entry barriers and entry incentives. More specifically, the rate of entry into drug markets is expected to be determined by factors such as demand growth, technological innovation, product differentiation and seller concentration. Ordinary least squares techniques are employed in the study to estimate the parameters for various alternative versions of a model which is hypothesized to explain the rate of entry into drug markets.

C. Organization of the Study

The chapters of this study are organized as follows. Chapter II presents important background information about the economics of the pharmaceutical industry in the United States. Chapter III develops a theoretical model of entry along with a brief review of previous studies of entry. Chapter IV presents the hypotheses and the empirical results of the study; it also includes a description of data source, the sample,

and variables used in the study. Chapter V provides a brief summary and conclusions for the study.

CHAPTER II

THE U.S. PHARMACEUTICAL INDUSTRY

The main objective of this chapter is to provide background information for the theoretical and empirical analysis of the pharmaceutical industry presented later in the study. The chapter consists of four sections. The first section gives an overview of the pharmaceutical industry in the United States. The next two sections focus on the characteristics of demand for and supply of pharmaceutical drugs. The last section deals with major governmental policies concerning the pharmaceutical industry.

A. Overview of the Industry

1. Definition of the Industry

The pharmaceutical drug industry is defined to include those firms that manufacture and distribute pharmaceutical preparations available to consumers only by medical prescription. Prescription drugs are potent chemotherapeutic agents, frequently with unwanted side effects, and require the supervision of a physician. Pharmacists dispense these products only to patients who present a physician's prescription. Thus, producers of prescription drugs promote their products primarily to the medical professions licensed by law to prescribe and dispense them. Consequently, the industry is often referred to as the ethical drug

industry, as opposed to the proprietary drug industry whose products are safe for self-medication and promoted primarily to the general public [64, p. 4].

2. Drug Names

Each drug may be identified by three names: (1) chemical name, (2) generic name, and (3) brand name. Most drugs are synthesized from chemical substances and have chemical names to describe the molecular structure of the principal ingredient(s). They are often complex. For example, the chemical name of a widely prescribed antibiotic is:

4-Dimethylemino-1,4,4a,5,5a,6,11,12a-Octahydro-3,6,10,12,12a-Pentahydroxy-6-Methyl-1,11-Dioxo-2-Naphthacenecar-Boxamide-Hydrochloride

A new drug is assigned a generic name which supposedly indicates the general pharmaceutical properties of its substance [57, p. 36]. The generic name of the above chemical substance is tetracycline hydrochloride.

A firm may choose to market the drug under its generic name. However, a firm often assigns it a brand name, which is usually short, simple and easy to remember. Thus, generically similar drugs are frequently available under different brand names. Achromycin (Lederle), Panmycin (Upjohn), Robitet (Robins), and Sumycin (Squibb) are examples of branded tetracyclines [50].

3. Development of the Industry[1]

The discovery of sulfa drugs in the 1930's and the commercial success

---

[1]Materials presented here are primarily from Measday [36, pp. 250-255].

of penicillin during World War II have drastically changed the outlook of the ethical drug industry. Before World War II there were relatively few drugs available to the physician. Most of them were of natural substance. The ethical drug industry primarily supplied active drug ingredients in bulk form to the pharmacist, who then compounded them as prescribed by the physician into dosage forms for the patient's consumption. Little effort was devoted to the research and development of new drugs. The promotional efforts of drug companies were minimal because a large proportion of their products were relatively standardized medicinal chemicals.

The advent of sulfa drugs stimulated the research interest in drug therapy and eventually led to a revolution in chemotherapy. Leadership in pharmaceutical innovation shifted from Europe to the United States during World War II. Since then, most new drugs have been discovered in the U.S. World War II not only had a profound impact on the research and development of antibiotics and other drugs, it also changed other important aspects of the industry. Today almost all prescription drugs are provided in final dosage form, ready for administration to the patient. That is, the compounding function of the retail pharmacist is displaced by the mass production of drug manufacturers. Accordingly, the drug companies have since launched large promotional campaigns directed to the medical profession. As a result, product differentiation achieved through research and development of new drugs and accompanying intensive promotion has become the vehicle of competition among the leading pharmaceutical firms.

The persistently high profitability for the pharmaceutical industry has attracted a number of new firms since World War II. One route of

entry has been by firms that were originally chemical companies. Firms such as Merck and Pfizer started as major suppliers of drug products in finished form during World War II. A more recent example is the Dow Chemical Company moving into the pharmaceutical field.

Another route of entry has been the expansion of proprietory manufacturers. American Home Products acquired Wyeth and Ayerst to enter the race in the ethical sector. Bristol Laboratories was established by Bristol-Myers. Norwich Pharmacal Company set up Eaton Laboratories.

Hoffman-LaRoche, Ciba-Geigy and a host of others form another distinct group of entrants. They are subsidiaries of foreign pharmaceutical manufactuers. In 1977 there were 36 subsidiaries owned by 20 foreign pharmaceutical manufacturers as opposed to 12 manufacturers owned abroad in 1963 [45, p. 73].

B. Demand for Prescription Drugs

1. The Nature of Demand for Prescription Drugs

A distinct characteristic of demand for prescription drugs can be summarized in the words of the late Senator Kefauver [30, p. 8], "The man who orders does not pay, the man who pays does not order." Unlike most consumer goods, the ultimate consumer of a prescription drug is not the same person making the decision as to the product choice and the amount to be consumed. The decision is made for the consumer by his physician due to the fact a medical prescription is required to purchase any prescription drug. In writing a prescription, the physician not only decides on the appropriate drug therapy for his patient, he also determines the quantity to be taken by his patient. In addition, the choice of firm manufacturing the drug is often specified on a

prescription. The physician may explicitly specify the manufacturer of the prescribed drug product or he may implicitly identify the manufacturer by the use of its brand name. Thus, the physician acts as the purchasing agent for the patient who is then responsible for paying all or part of the drug bills.

2. Price Elasticity of Demand

The price inelasticity of demand for prescription drugs is, in large part, the result of the unique relationship between the physician and the patient as mentioned above. The drug selection is made not by the patient but by the physician who is not spending his own money. Hence, physicians may not be as price conscious as patients. In addition, the physician may be concerned more with the appropriateness of drug therapy for his patient than with the costs involved [36, p. 258; 56, pp. 108-109; 58, p. 133]. Moreover, most physicians do not have adequate knowledge of price or price alternatives due to the lack of such information in drug advertisements [36, p. 258; 64, p. 31]. Therefore, the price of a drug may not be considered as an important factor in the physician's prescribing decision.

Neither does the patient tend to consider the price as an important factor in his buying decision [36, p. 258; 58, p. 133]. Drugs may be concerned with life and health, patients will have prescriptions filled independently of price. In many cases, the patient is unlikely to buy larger quantities of a particular drug than those recommended by his physician, even if its price declines substantially. Thus, in general, price changes are expected to have insignificant effects on quantity taken. Estimates of price elasticity of demand for prescription drugs

range from 0.07 to 0.15 [68], indicating the demand for prescription drugs is relatively inelastic with respect to price.

While the demand for prescription drugs as a whole is relatively inelastic, the demand for many individual drugs, particularly for different brands of the same drug may exhibit considerable elasticity. The existence of substitutability among different brands tends to make demand for multi-source drugs more elastic. In addition, substitution among alternative brands has been facilitated by the repeal of state anti-substitution laws. Many states have passed laws permitting the pharmacist to substitute a generic equivalent for the drug prescribed by the physician [15, p. 7]. Hence, with the aid of state substitution laws, demand for a multi-source drug may become relatively elastic, compared with demand for a single-source drug for which there are no good substitutes.

3. Increases in Demand Over Time

a. Measures of Demand Increases

As shown in Table I, expenditures for "drugs and drug sundries" in the United States have grown spectacularly from $601 million in 1929 to $12.5 billion in 1977. It should be pointed out that these expenditures includes "only spending for outpatient drugs and appliances and exclude those provided to hospital inpatients, nursing home patients, and through physicians' offices" [17, p. 18]. It has been estimated that expenditures for outpatient prescription drugs were $7 billion, and accounted for 56 percent of total spending for drugs and drug sundries in 1977 [17, p. 4]. Drugs administered in hospitals are included in the costs of hospital care. According to American Hospital Association Surveys,

TABLE I

NATIONAL HEALTH EXPENDITURES, 1929-1977

Year	Total National Health Expenditures* $ million	Total National Health Expenditures* Percent of GNP	Drugs and Drug Sundries** $ million	Drugs and Drug Sundries** Percent of Total National Health Expenditures
Ending June:				
1929	3,589	3.5	601	16.7
1935	2,846	4.1	471	16.5
1940	3,883	4.1	624	16.1
1950	12,027	4.5	1,642	13.7
1955	17,330	4.5	2,282	13.2
1960	25,856	5.2	3,591	13.9
1965	38,892	5.9	4,647	11.9
1966	42,109	5.8	5,032	11.9
1967	47,897	6.2	5,480	10.4
1968	53,765	6.5	5,865	10.9
1969	60,617	6.7	6,482	10.7
1970	69,201	7.2	7,114	10.3
1971	77,162	7.6	7,626	9.9
1972	86,687	7.8	8,233	9.5
1973	95,383	7.7	8,942	9.5
1974	106,321	7.8	9,695	9.3
1975	132,716	8.5	10,357	8.4
Ending September:				
1975*	127,719	8.6	10,582	8.3
1976*	145,102	8.7	11,472	7.9
1977*	162,627	8.8	12,516	7.7

Sources: *Robert M. Gibson and Charles R. Fisher, "National Health Expenditures, Fiscal Year 1977," Social Security Bulletin, Vol. 41 (July, 1978), pp. 3-20.

**Nancy L. Worthington, "National Health Expenditures, 1929-1974," Social Security Bulletin, Vol. 38 (February, 1975), pp. 1-20.

hospital expenditures for drugs amounted to less than 4 percent of total hospital costs [49, p. 66]. Thus, the nation spent approximately $10 billion for drugs administered in and out of the hospital in 1977.

Drug utilization measured in terms of number of prescriptions dispensed also increased rapidly since 1967. Table II shows the number and percentage distribution of prescriptions dispensed by type of vendor. In 1967, the total prescriptions dispensed in this nation were 1.6 billion. By 1974, there were 2.7 billion prescriptions written and filled, an increase of 70 percent over the period of seven years. Total outpatient prescriptions rose steadily from 1.1 billion in 1967 to 1.8 billion in 1974. Table II also indicates that prescriptions dispensed to ambulatory patients are the most important segment of prescription market, accounted for more than 65 percent of total prescriptions dispensed during 1967-1974. On the other hand, hospital inpatients' prescriptions showed a gradual increase in market share from 28.9 percent in 1967 to 35.0 percent in 1974.

b. Causes of Demand Increases

These phenomenal growth trends in drug use have been influenced by several factors over the years. These factors include population growth, the development of new drugs, increase in income, and third party health care finance.

(1) Population Growth. Total population in the United States grew steadily from 133 million in 1940 to 217 million in 1977 [67, p. 6]. In general, the larger the number of people, the larger quantity of pharmaceuticals that are demanded. More importantly, changes in the composition

of the population are expected to exert even greater influence on drug utilization. The elderly tend to use drugs more frequently than other groups. Total population for the aged increased from 16.7 million in 1960 to 23.5 million in 1977 [67, p. 8]. As the population grows older, an increasing share of drug expenditures is for the old. In 1977, about 23 percent of total drug expenditures was spent by the elderly who comprised about 11 percent of the population [18, p. 3].

TABLE II

NUMBER AND PERCENTAGE DISTRIBUTION OF PRESCRIPTIONS DISPENSED, BY TYPE OF VENDOR, 1967-1974

Year	Total Rx's (million)	Hospital Inpatient Rx's (million)	Hospital Inpatient Percent of Total	Outpatient Rx's (million)	Outpatient Percent of Total
1967	1,593	461	28.9	1,132	71.0
1968	1,756	513	29.2	1,243	70.7
1969	1,878	568	30.2	1,310	69.7
1970	2,000	630	31.5	1,370	68.5
1971	2,142	699	32.6	1,443	67.3
1972	2,296	769	33.4	1,527	66.5
1973	2,446	853	34.9	1,593	65.3
1974	2,704	946	35.0	1,758	65.0

Source: U.S. Department of Health, Education and Welfare, Social Security Administration, Office of Research and Statistics, Prescription Drug Data Summary, 1974, p. 35.

(2) Development of New Drugs. Advances in medical technology have greatly helped scientists to discover and develop new and/or improved

drugs. As indicated in Table III, large numbers of new and improved drugs have been invented since World War II. The rate of drug use tends to increase as a result of the development of more effective drugs. There may be no drug yet available to treat some diseases. Some existing drugs may have important limitations, therapeutically or administratively, which tend to discourage patients from consuming them. New drugs may not be merely good substitutes for previously existing drugs; they may eventually replace old drugs. In addition, new effective drugs may even replace other means of treatment such as surgery and radiology. Hence, demand for pharmaceuticals in general appears to depend largely on the number of effective drugs available.

(3) Increases in Incomes. Per capita income has been steadily increasing over the past three decades. Rising per capita income tends to increase demand for prescription drugs. The number of unfilled prescriptions tends to decline as a result of growth in income. More importantly, increases in income has encouraged consumers to seek more medical advice from their doctors which in turn has led to more drugs prescribed.

(4) Third Party Health Care Finance. Americans are provided more access to medical care through private health insurance programs and Medicaid and Medicare since 1967. The expansion of third-party financing system has helped to remove financial barriers to medical care, especially for the elderly and the poor. Consumers have come to bear much less than the full costs of health services. In 1977, total third-party payments accounted for 70 percent of the outlays for personal health care [17, p. 5], compared with 31.7 percent in 1950 and 44.7

TABLE III

NEW PRODUCT INTRODUCTIONS IN THE ETHICAL PHARMACEUTICAL INDUSTRY, 1950-1974

Year	New Single Chemicals	Duplicate Products	Compounded Products	New Dosage Forms
1950	28	100	198	118
1951	35	74	212	120
1952	35	77	202	170
1953	48	79	226	97
1954	38	87	255	108
1955	31	90	282	96
1956	42	79	280	66
1957	51	88	261	96
1958	44	73	253	109
1959	63	49	203	104
1960	45	62	199	98
1961	39	32	189	106
1962	27	43	180	84
1963	16	34	149	52
1964	17	29	111	41
1965	23	18	71	22
1966	12	15	53	26
1967	25	25	32	14
1968	11	26	50	21
1969	9	22	31	12
1970	16	50	39	23
1971	14	40	29	30
1972	11	35	18	30
1973	19	37	18	17
1974	18	42	23	26
Total	717	1,306	3,564	1,686

Source: Paul de Haen, Ten Year New Product Survey, 1950-1960, Non-Proprietary Name Index, Vol. VI (New York: Paul de Haen, Inc., 1967); New Products Parade, 1973-1974 (New York: Paul de Haen, Inc., 1975).

percent in 1960 [19, p. 18]. The impact of these third-party payments is to increase the demand for medical services which leads to an increase in demand for pharmaceuticals. In addition, prescription drugs financed by third parties have represented a rising proportion of total prescriptions. It is estimated that the ratio doubled in five years, from 11.9 percent in 1969 to 23.7 percent in 1974 [49, p. 58].

C. Supply of Prescription Drugs

The characteristics of pharmaceutical manufacturers is discussed in this section. It should be noted that some of the data presented here include both prescription and non-prescription drugs. No attempt is made here to separate these two components since non-prescription drugs comprise a small proportion of the "pharmaceutical" industry. In addition, today the same pharmaceutical manufacturers often participate in production in both areas.

1. Size and Distribution of Sales

Table IV shows in current and constant dollars the growth in ethical pharmaceuticals in final dosage form for human use since 1955. Over the period of 20 years, the total sales in current dollars have grown almost 318 percent from over $1.5 billion in 1955 to $6.1 billion in 1974, even though the wholesale prices for ethical pharmaceuticals remained relatively stable over these years. Prices of drugs in fact declines for the decade of the 60's as shown in Table IV. The growth in constant-dollar sales was 311 percent between 1955 and 1974, which is equivalent to an average rate of growth of 7.7 percent. On the average, the industry grew more rapidly than GNP for those years with real GNP averaging 3.3 percent growth per year [67, p. 439].

TABLE IV

THE GROWTH OF U.S. ETHICAL PHARMACEUTICAL SALES, 1955-1974

Year	Current Dollar Sales* ($ millions)	Wholesale Price Index**	Constant-Dollar Sales
1955	1,457	107.7	1,353
1956	1,676	107.2	1,563
1957	1,742	108.7	1,603
1958	1,802	109.1	1,652
1959	1,850	108.8	1,700
1960	1,905	108.4	1,757
1961	1,954	105.2	1,857
1962	2,199	102.2	2,152
1963	2,317	101.2	2,290
1964	2,479	100.8	2,459
1965	2,779	101.2	2,746
1966	3,011	100.8	2,987
1967	3,226	100.0	3,227
1968	3,655	99.1	3,688
1969	4,008	100.1	4,004
1970	4,322	101.0	4,279
1971	4,667	102.9	4,535
1972	5,018	102.4	4,900
1973	5,507	102.7	5,362
1974	6,083	109.3	5,565

Sources: * PMA Annual Survey Report; Also reprinted in Medical Marketing and Media, March 1978, p. 18.

** John M. Firestone, Index of Manufacturer's Prices to Retailers for Ethical Pharmaceuticals, 1976.

A distribution of sales by therapeutic category is presented in Table V. In 1972, antibiotics and ataraxics (including major and minor tranquilizers) constituted the two largest classes, with shares of 13.2 percent and 11.0 percent respectively. Hormonal drugs (including contraceptives) was in third place with 8.7 percent of total sales, followed by drugs for cardiovascular purposes with a share of 7.4 percent. Considerable increases in relative shares since 1957 were noted for antiathritics, ataraxics, cardiovascular, and diuretic drugs. There were decreases in relative shares of antibiotics, and antiinfectives. All therapeutic classes show growing trends in terms of dollar sales.

The Pharmaceutical Manufacturers Association estimated that there were about 750 manufacturers of prescription drugs in 1974. Approximately 80 percent of these firms were small, with less than $50 million in annual sales [49, p. 37]. According to the Internal Revenue Service, almost two thirds of 1,139 "drug" manufacturers in 1971 were small, with less than $100,000 in assets. Only 24 had assets of $100 million or more [49, p. 40]. The U.S. Bureau of the Census compiles data on the concentration ratios for the largest 4, 8, and 20 firms in the "pharmaceutical preparations" industry (SIC 2834). These concentration data are presented in Table VI. The overall industry concentration ratios have reamined remarkably stable between 1947 and 1972. The 4 largest firms account for about 25 percent, the largest 8 firms for about 45 percent, and the largest 20 firms for about 75 percent of total shipments. Thus, the remaining 25 percent of the industry's shipments accounted for by a large number of small firms. The market share held by the leading firms has in fact declined from 12.7 percent in 1951 to 7.6 percent in 1974 [49, p. 38].

TABLE V

U.S. WHOLESALE SALES OF ETHICAL DRUGS, BY THERPEUTIC CATEGORY ($ MILLIONS)

	1957		1960		1965		1972	
	$	%	$	%	$	%	$	%
Analgesics	65.2	3.9	76.8	4.0	129.8	4.8	256.3	5.4
Anesthetics	15.8	0.9	16.9	0.9	36.1	1.3	55.1	1.2
Antiarthritics		0	15.8	0.8	35.8	1.3	100.0	2.1
Antiinfectives* and anthelminthics	42.3	2.5	40.6	2.1	65.0	2.4	108.0	2.3
Antibiotics and sulfonamides	335.2	20.2	335.5	17.4	418.2	15.5	625.2	13.2
Antiobesity	6.8	0.4	63.7	3.3	94.4	3.5	71.8	1.5
Ataraxics	111.1	6.7	144.2	7.5	253.0	9.4	520.2	11.0
Bronchodilators	7.9	0.5	17.1	0.9	40.8	1.5	69.2	1.5
Cardiovasculars**	82.9	5.0	103.3	5.3	175.7	6.5	346.3	7.3
Dermatologicals		0	49.3	2.5	52.6	1.9	108.7	2.3
Diabetic therapy	28.1	1.7	55.2	2.9	79.8	4.0	126.6	2.7
Diuretics	17.5	1.1	47.6	2.5	79.7	2.9	163.6	3.5
Gastrointertinal drugs***	125.5	7.6	147.5	7.6	201.6	7.5	350.8	7.4
Hormones	124.6	7.5	147.0	7.6	237.4	8.8	411.3	8.7
Muscle relaxants****	8.6	0.5	21.5	1.1	26.1	1.0	54.6	1.2
Psychostimulants	4.2	0.3	13.4	0.7	42.9	1.6	73.3	1.6
Sedatives	31.1	1.9	36.3	1.9	49.5	1.8	61.0	1.3
All Others	651.5	39.3	599.8	31.0	685.1	25.3	1,217.0	25.8
Total Ethical Market	1,658.1	100.0	1,931.5	100.0	2,703.4	100.0	4,718.8	100.0

*Antibacterials and antimalarials. Excludes antibiotics and sulfonamides.
**Also includes digitalis preparations and vasopressors.
***Includes antacids, antidiarrheals, antinauseants, antispasm, and laxatives.
****Surgical and nonsurgical.

Source: IMS America, Ltd., U. S. Pharmaceutical Market, Drug Stores and Hospitals, various years. Reprinted in David Schwartzman, Innovation in the Pharmaceutical Industry, Baltimore: The Johns Hopkins University Press, 1976, p. 27.

TABLE VI

PHARMACEUTICAL PREPARATIONS INDUSTRY (SIC 2834), CONCENTRATION RATIOS, 1947-1972

Year	Percentage Accounted for by the Largest		
	4 Firms	8 Firms	20 Firms
1947	28	44	64
1954	25	44	68
1958	27	45	73
1963	22	38	72
1967	24	40	73
1970	26	43	NA
1972	26	44	75

Source: U.S. Department of Commerce, Bureau of the Census, Census of Manufacturers, 1972 (Washington, D.C.: U.S. Government Printing Office, 1975).

While the entire industry exhibits relatively moderate concentration ratios, concentration in specific therapeutic categories is considerably higher. Table VII presents average concentration ratios in 17 therapeutically important categories for the period 1956-1965. The top four products had market share of 50 percent or higher in 15 classes. The top eight products had more than two-thirds of the market in all 17 classes.

Table VIII presents the 4-firm concentration ratios measured in terms of number of prescriptions written and filled in 1964 and 1974 for 20 relevant markets. As shown in Table VIII, there is considerable concentration in each therapeutic market. Some markets registered a moderate gain in concentration while others have shown a substantial decline in concentration over the period 1964-1974.

TABLE VII

CONCENTRATION RATIOS IN 1956-1965, 17 THERAPEUTIC CATEGORIES

Therapeutic Category	Average Percent Share of Market by Dollar Volume 1956-1965 Top Four Products	Average Percent Share of Market by Dollar Volume 1956-1965 Top Eight Products
Analgesic, nonnarcotic	55.9	73.9
Antiarthritics, nonsteroidal	69.5	84.1
Antibiotics, broad and medium specturm	48.0	67.7
Antibiotics, penicillins	61.3	78.6
Antihistamines	66.7	85.4
Antiobesity, amphetamines	68.5	79.1
Ataraxics	71.1	88.6
Rauwolfia-diuretic combintaion	73.4	92.2
Coronary vasodilators	64.3	74.8
Diabetic therapy, other*	99.4	99.8
Diuretics**	69.6	80.0
Hormones, corticoids	52.4	68.5
Corticoids with antiinfectives	48.6	66.6
Oral muscle relaxants	53.2	71.8
Psychostimulants	69.2	82.7
Sedatives, barbiturate	62.6	70.8
Sulfonamides	57.4	68.7

*Covers the period 1957-1965.
**Covers the period 1959-1965.

Source: Arthur D. Little, Inc., "Trends in Market Shares for Ethical Pharmaceutical Products," reprinted in U.S. Senate Select Committee on Small Business, Subcommittee on Monopoly, Hearings on Competitive Problems in the Drug Industry, Part 5, 90th Congress, 1st Session (1968), pp. 1,788-1,805.

TABLE VIII

4-FIRM CONCENTRATION RATIO BY PRESCRIPTION VOLUME, 20 RELEVANT MARKETS

Market*	Index of Firms Turnover 1964-1974** (%)	Market Share of Top 4 Firms in 1964 (%)	Market Share of Top 4 Firms in 1974 (%)
1	25	58	34
2	25	66	66
3	50	53	69
4	25	66	62
5	0	58	55
6	25	87	94
7	0	48	42
8	25	70	62
9	25	87	77
10	0	77	85
11	25	61	55
12	50	43	53
13	50	71	70
14	50	45	42
15	50	39	39
16	25	98	87
17	25	60	64
18	75	69	69
19	25	98	69
20	25	72	78

*The numbers in this column refer to the listing of relevant markets presented in Table XIV (p. 61).

**Number of firms appearing among the 4 largest in each therapeutic market in 1964 that did not appear among the 4 largest in 1974, expressed as a percentage.

Source: IMS America, Ltd., National Prescription Audits, 1964-1974. Ratios were compiled by the author.

Although the commonly used measure of the degree of monopoly power is the concentration ratio, and as indicated above, the levels of 4-firm concentration ratios within the therapeutic markets run relatively high, they provide no information on the turnover of leading firms. In the 20 relevant markets, the identity of the top 4 firms remained the same in only 3 markets. In 6 of the 20 at least 2 of the largest 4 firms in 1964 had been displaced by other firms by 1974. Markham [35, pp. 169-170], Comanor [11, pp. 376-377], and Schwartzman [56, pp. 127-128] attribute this phenomenon of instability of leadership within therapeutic markets to innovative competition in the form of new product development and to a rapid rate of product obsolescence in the pharmaceutical industry.

2. Cost Structure

Developments since World War II have correspondingly changed the cost structure of the pharmaceutical industry. Variable costs on materials, labor, supplies, containers, and other necessary items involved in the production process of finished drugs account for a relatively low portion of total costs. As shown in Table IX, variable costs amounted to only 43 percent of total costs for 22 large pharmaceutical firms in 1958. More than half of total costs were expenditures on drug research and development, sales promotion, and general administration. In addition to relatively low variable costs, the economies of size in the production process tend to be of negligible importance [58, pp. 134-135; 64, pp. 36-37]. The most important economy of size seems to be in research for and development of new drugs and sales promotion. Another important characteristic concerns the relatively high mobility of resources employed within the areas of manufacturing, R & D, and marketing [9, pp. 235-238]. The degree of resource flexibility may be

manifested in the number of therapeutic categories in which an individual firm has products for sale. On the basis of the leading 21 drug firms, Cocks [9, p. 236] concludes that "the average firm has products for sale in approximately 60 percent of the available therapeutic categories" in years of 1962 and 1972, indicating a high degree of manufacturing, R & D and marketing resource mobility possible within these firms.

TABLE IX

COSTS DISTRIBUTION FOR 22 LEADING DRUG COMPANIES, 1958

Costs*	Percent of Sales*	Percent of Total Costs
Cost of Goods	32.1	43.3
Research and Development Expenditures	6.3	8.5
General and Administrative Expenditures	10.9	14.7
Selling and Promotional Outlays	24.8	33.5
Total Costs	74.1	100.0

*Sales and expenditures relating to drug operations only.

Source: United States Senate Subcommittee on Antitrust and Monopoly, Report of the Study on Administered Prices in the Drug Industry, 87th Congress, 1st Session, 1961, p. 31.

In an attempt to differentiate their products from rivals', drug manufacturers have spent large sums on research and development and sales promotion. The following section deals with the nature and the costs of product differentiation activities pursued by drug manufacturers.

3. Product Differentiation

Since World War II, product differentiation has become a far more important means of competition than the prices of drugs in the pharmaceutical industry [11, p. 373; 55, p. 897; 58, p. 148]. Research and development activities and sales promotion activities are the major strategies pursued by a drug manufacturer for differentiating its products from rivals either physically or conceptually. The efforts directed at new drug research and development are mainly conducted by larger drug firms. The product differentiation efforts of smaller drug firms tend to be limited largely to sales promotion.

Extensive product differentiation may have the important effect of preventing the entry of firms into therapeutic markets in which profits are made [11, p. 373; 55, p. 899]. On the other hand, product differentiation in the form of breakthrough products may provide an effective weapon to new firms of all sizes for surmounting barriers to entry into a drug field from which they would otherwise be foreclosed [54, p. 230].

a. Research and Development

The health and welfare of human beings have been significantly enhanced by a flow of new drug products and processes as a result of firms' efforts to differentiate their products through R & D activities [56, 57]. Meanwhile, the market position and the profitability of individual drug firms depend to a large extent on the results of their research efforts. Many wonder drugs introduced in the past have significantly improved the market position and the financial health of the innovating firms. The important relationship of innovative efforts to financial success was soon recognized and the innovative strategy

which calls for investment in R & D has been the prevailing competitive strategy of large pharmaceutical manufacturers since World War II [11, 36, 57].

(1) Motivations. Drug firms recognize that the way to achieve the greatest financial success is through significant breakthroughs in drug therapy. Successful drugs introduced in the 1950's and 1960's made investment in pharmaceutical R & D very attractive. Drugs with outstanding therapeutic value such as Valium, Keflin, Indocin, and Aldomet continue to generate large sales and make a significant contribution to the innovating firm's profits. In 1975, Indocin and Aldomet accounted for more than 25 percent of Merck's $1.5 billion in sales and for more than 40 percent of its $229 million in profits [51, p. 135]. It is this profit incentive that stimulates drug firms to engage in pharmaceutical research.

The incentive to innovate is further strengthened by the current patent system. Patents create a barrier to entry by making it difficult for other firms to imitate the patented drug product. The original innovator is more likely to recoup what it has invested in R & D than is possible without patent protection.

(2) New Product Introduction. The pharmaceutical industry's research effort is primarily devoted to the search for and development of new and improved drugs. As a result, a number of new drug products are introduced into the U.S. market each year. Table III (p. 15) lists the annual number of new drug products available in the U.S. during the period of 1950-1974.

Types of new products in the pharmaceutical industry include new chemical entities (NCE's), duplicates, new combination products, and new

dosage forms [44]. New chemical entities represent the most innovative output of pharmaceutical research since they are unique compounds not previously known and frequently represent significant new therapeutic advances. More than half of the total NCE's were introduced during the 1950's, the golden era of drug therapy. In 1959, the largest number (63) of new single chemicals ever recorded in one year were introduced. Since then, the number has been declining.

Duplicates of previously marketed chemical entities are usually manufactured by new firms and marketed under new brand names. New combinations of drugs are products having more than one active (previously introduced) ingredient. Table III reveals a sharp decline in the number of combination products over the time period. New dosage forms for drugs are developed in attempts to ease drug administration and to improve patient's compliance in drug therapy. For instance, if a product has originally been marketed in ampules, new dosage forms might include tablets, capsules, suppositories, etc.

(3) R & D Expenditures. Table X lists total R & D expenditures for human pharmaceuticals spend by the U.S. pharmaceutical industry from 1951-1974. Total R & D expenditures have substnatially increased from $50 million in 1951 to $859 million in 1974, an average rate of 13 percent of growth per year.

Unlike other industries, government funds play a minor role in financing pharmaceutical R & D. The largest portion of R & D projects conducted by drug manufacturers is financed through their own internal funds. In 1974, the Federal Government provided $8.6 million to the pharmaceutical industry in R & D contracts, representing less than 1 percent of total R & D expenditures for pharmaceuticals [49, p. 3].

This is in sharp contrast to an average rate of 37 percent for all industry as a whole [40, p. 2].

TABLE X

R & D EXPENDITURES FOR HUMAN ETHICAL DRUGS

Year	Global R & D Expenditures ($ million)	Domestic R & D Expenditures ($ million)	Domestic Sales Human Ethicals ($ million)	R & D/ Sales Ratio
1951	$ 50			
1953	67			
1955	91			
1957	127			
1959	197			
1961	227			
1963	267			
1965	328	$304	$2,940	10.3%
1966	374	344	3,178	10.8
1967	412	378	3,393	11.1
1968	472	410	3,808	10.8
1969	506	464	4,135	11.2
1970	566	519	4,444	11.7
1971	629	577	4,796	12.0
1972	667	601	5,136	11.7
1973	753	644	5,644	11.4
1974	859	726	6,273	11.6

Source: Pharmaceutical Manufacturers Association, Annual Survey Report, various issues; domestic R & D expenditures and sales also appear in Grabowski [22, p. 43].

The pharmaceutical industry's strong commitment to research is reflected in its relatively high ratio of R & D to sales. Pharmaceutical

R & D expenditures in the U.S. have remained around 11-12 percent of domestic sales during 1965-1974, and reached a peak of 12.0 percent in 1971 (see Table X). These relatively stable ratios indicate that R & D outlays for pharmaceutical research have kept pace with pharmaceutical sales volume.

According to a PMA survey, more R & D funds are allocated to the search for drugs to treat central nervous system diseases, infections, neoplasms, and cardiovascular disorders. These four categories have accounted for approximately two-thirds of applied R & D expenditures over the 1965-1974 period.

The industry R & D allocation data presented in Table XI shows a rather stable pattern of R & D funds allocation among therapeutic classes. Caglorcan, Faust and Schnee [6] further examine the pattern of allocation among drug manufacturers. They conclude that larger firms tend to have more stable patterns of R & D funds allocation than smaller firms [6, pp. 340-343].

b. Sales Promotion

As a result of the proliferation of drug products, sales promotion becomes an important tool to a firm to penetrate a market initially and to maintain its market position later on. Therefore, research efforts are frequently accompanied by sales promotion efforts in order to achieve effective product differentiation [11, 36, 56, 57]. That is why drug companies with intensive R & D efforts tend to incur large sums of promotional expenditures.

(1) Promotional Intensity. The pharmaceutical industry is characterized as one of high promotional intensity as reflected in its

TABLE XI

ALLOCATION OF R & D EXPENDITURES BY THERAPEUTIC CLASSES

Therapeutic Class	Percentage of Total U.S. R & D Funds*							
	1965	1966	1967	1968	1971	1972	1973	1974
Central Nervous System	20.3	17.6	17.8	16.9	17.0	19.9	17.4	18.5
Parasitic and Infective Diseases	18.6	20.0	20.0	20.7	21.5	18.1	15.8	17.8
Neoplasms, Endocrine System, and Metabolic Diseases	18.0	17.9	19.5	17.4	16.6	17.1	15.4	14.0
Cardiovascular System	10.4	11.0	11.0	11.7	12.2	13.6	12.8	15.1
Digestive and Genitourinary Systems	8.3	7.6	6.7	6.1	7.1	6.0	6.0	6.2
Biologicals	4.6	4.8	7.8	5.5	5.0	5.6	4.0	4.5
Respiratory System	3.0	3.7	3.2	3.4	3.7	4.1	3.9	4.8
Dermatologicals	1.8	2.0	2.6	4.5	2.1	3.6	4.1	3.5
Diagnostics	2.3	2.3	2.2	2.0	4.1	2.9	5.1	**
Vitamins	2.6	2.6	2.1	1.9	3.0	2.4	2.0	2.1
Other	10.1	10.5	7.1	9.9	7.7	6.7	5.8	6.1
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

*Data for 1969 and 1970 not available.

**Omitted in the 1974 survey.

Source: Pharmaceutical Manufacturers Association, Annual Survey Report, various issues.

ratio of promotional expenditures to sales. The estimates of promotion/sales ratios for the pharmaceutical industry vary. Most authors estimate that between 20 to 30 percent of the sales dollar is accounted for by drug promotion activities. Bond and Lean [5, p. 1] estimated that in 1970 the 30 largest drug manufacturers spent $682 million on promotion, or 21 percent of their sales dollar. A 25 percent of sales figure for drug promotion appeared in Congressional Hearings in 1961 [69, p. 157].

In comparison to other industries, the drug industry spends relatively more on advertising than most other industries [7, p. 60]. Based on Comanor and Wilson's [12, p. 439] estimates for 41 consumer goods industries during 1954-1957, the pharmaceutical industry was placed third after perfumes and cereals.

It is clear that the pharmaceutical industry has allocated a considerably larger proportion of its sales revenues to promotion activities than to research and development. For the industry as a whole, the promotion expenditures appear to be at least twice as large as R & D expenditures.

(2) Promotion Activities. A pharmaceutical firm engages in extensive promotional activities to differentiate its products from others [11, 36, 56, 57]. The promotional efforts of drug firms are directed not toward the consumer but primarily toward the medical profession which makes drug selections for the consumer. In general, promotional media employed by drug firms include detailing, journal advertising, direct mails [28, 36, 56, 57]. The pharmaceutical industry uses substantial numbers of sales representatives to call on physicians and pharmacists in person. Data compiled by IMS indicate that more than two-third of total promotional expenditures were accounted for by

detailing during 1972-1978 [28]. Detailmen inform doctors and pharmacists of the availability, the effects and the appropriate use of the company's new products. They also remind doctors and pharmacists of the company's older drugs. They persuade the doctors to prescribe a company's products by stressing both brand names and company name, in hopes that sales will be expanded and that brand loyalties for the company's products will provide insulation from competition.

Advertising in professional and trade journals is the second most important element in the promotion budget. It is estimated that approximately 23 percent of promotional expenditures were spend on journal advertising [28].

Direct-mail promotion accounts for less than 10 percent of total promotion spending [28]. The doctor receives thousands of promotional pieces a year. Drug promotion activities also include drug samples distributed free to physicians, the support of scientific or medical conferences or symposia and exhibits at medical conventions.

4. Price Competition

Non-price competition as discussed above tends to overshadow price competition in the pharmaceutical industry. During the Kefauver hearings, it was charged that manufacturers of pharmaceuticals frequently were able to "administer" prices of their drug products and refrain from price competition [70]. Since the Kefauver hearings, however, the conditions of competition in the pharmaceutical industry have markedly changed, and the use of price as a competitive strategy has become increasingly important.

The evidence of price inflexibility in antibiotics and corticosteroid hormones was presented during the Kefauver hearings. In another study Markham [35] observed prices for 308 individual products for the 10-year period 1949-1959. He concluded that more than 50 percent of products observed did not change price at all during the 10-year period [p. 170].

More recent studies of drug prices provide the evidence that there has been a great deal of price competition in the pharmaceutical industry [10, pp. 349-362; 56, pp. 251-299]. Cocks and Virts [10] analyzed the price movement of 107 leading products in 10 therapeutic classes. In Table XII, the price trends of leading products in 10 therapeutic products sets are shown. Through 1967, prices in each of the 10 product sets had declined from their 1962 levels. Despite general inflation in the U.S. since 1966, only 2 of 10 product sets exhibited upward price trends, being above the 1962 levels by 5 percent and 8 percent respectively. In 5 product sets, prices declined between 1962 and 1971. Substnatial price decline is noticed in the antiinfectives, oral contraceptives, and diabetic therapy, by 32, 23, and 19 percent respectively.

Schwartzman [56] confined his price study to multiple source products. He observed that "during the 1960's and early 1970's, manufacturers of large-selling multiple-source drugs engaged in severe price competition, especially in antibiotics" [p. 252]. Manufacturers of multiple source products were, evidently, seeking a sales edge through price cutting. In antibiotic markets, Schwartzman has observed that firms with smaller market shares were aggressive price cutters while firms with larger market shares tended to delay their price cuts.

TABLE XII

PRICE INDEXES IN THE DRUG INDUSTRY, TEN ETHICAL DRUG PRODUCT SETS, 1962-1971

Product Set	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
1. Vitamin and hematinic	100	100.3	98.5	97.4	97.4	97.2	97.1	100.4	101.3	101.3
2. Antiinfective	100	92.8	90.4	87.9	84.9	77.6	74.8	73.7	71.3	68.2
3. Cough and cold	100	107.0	101.6	99.9	99.7	99.5	99.9	104.5	105.7	108.3
4. Analgesic and antiinflammatory	100	100.7	100.0	103.0	99.0	97.5	95.7	96.3	95.6	98.0
5. Antihypertensive and diuretic	100	98.4	97.4	97.2	96.1	95.8	93.1	91.4	92.3	93.4
6. Psychopharmaceutical	100	99.4	97.7	96.3	95.3	94.8	91.6	93.4	92.2	91.7
7. Antiobesity	100	103.1	101.4	100.8	99.2	99.7	98.6	100.2	101.3	105.1
8. Oral contraceptive	100	85.9	79.7	76.3	75.5	70.6	69.1	73.0	75.3	77.0
9. Anticholinergic and antispasmodic	100	101.2	99.8	99.8	99.9	98.8	99.0	99.1	101.0	100.7
10. Diabetic therapy*	100	95.7	89.0	87.1	83.8	81.7	82.3	81.6	80.3	81.0
BLS consumer price index for prescriptions	100	97.6	96.3	95.2	95.1	93.4	91.3	93.0	94.5	94.6

* In the diabetic set the pricing data for the products of the company with whom the authors are associated was not complete. These numbers were directly obtained from the company.

Source: Douglas L. Cocks and John R. Virts, "Pricing Behavior of the Ethical Pharmaceutical Industry," Journal of Business, Vol. 47 (July, 1974), pp. 355-358.

In the face of shrinking market shares, larger firms may be forced to cut their prices eventually [p. 298].

Schwartzman [56, pp. 255-271] considered a number of factors that facilitate price competition. One is the ease of entry into the production of duplicates. The costs of entry are within the reach of even small firms. The excess of average costs over marginal cost also permits firms which enter into a market late to undercut prices. In addition, public policies have moved in the direction of encouraging price competition in the industry [p. 299]. The repeal of anti-substitution laws and the Maximum Allowable Cost (MAC) program are examples.

5. Profitability

The pharmaceutical industry has long been known for its persistently high rate of return on investment. Table XIII shows the average rate of return on net worth for the pharmaceutical industry and for all manufacturing during the period of 1958-1975. The average rate of return in the pharmaceutical industry was 1.63 times the average rate of return for all manufacturing.

The rates of return on net worth as shown in Table XIII represent accounting rates of return. Expenditures on R & D and sales promotion are treated as a current expense rather than an asset. Thus, the accounting rates of return may tend to overstate the true economic rate of return for those industries with a high rate of intangible investment in R & D and/or sales promotion. Clarkson [7] and Grabowski and Mueller [23] have made attempts to correct the accounting rates of return for the pharmaceutical industry by capitalizing the intangible investments in R & D and sales promotion. Both studies reached essentially similar

conclusions that the expensing of R & D and sales promotion overstate the rate of return on net worth in the pharmaceutical industry by 3-5 percent [7, p. 64; 23, p. 332]. Even after appropriate adjustments of assets were made, the pharmaceutical industry was still a relatively profitable industry.

TABLE XIII

RATES OF RETURN ON AVERAGE STOCKHOLDER'S INVESTMENT,* PHARMACEUTICAL INDUSTRY AND ALL MANUFACTURING, 1958-1975

Year	Drug Industry	All Manufacturing
1958	17.7	8.6
1959	17.8	10.4
1960	16.8	9.2
1961	16.7	8.8
1962	16.8	9.8
1963	16.8	10.3
1964	18.2	11.6
1965	20.3	13.0
1966	20.3	13.4
1967	18.7	11.7
1968	18.3	12.1
1969	18.4	11.5
1970	17.6	9.3
1971	17.9	9.7
1972	18.6	10.6
1973	19.0	12.8
1974	18.8	14.9
1975	17.8	11.6

*Net Profit as a percent of the average of net worth at the beginning and end of each year.

Source: FTC, Rates of Return for Identical Companies in Selected Manufacturing Industries (Washington, D.C.: U.S. Government Printing Office, annual).

D. Public Policy

The structural behavior and performance of the pharmaceutical industry have been increasingly influenced by a number of governmental policies. Two major policies concerning the pharmaceutical industry will be presented in this section. They are policies with regard to patents and new drug approvals. The emphasis will be primarily on changes in policies and their impacts on pharmaceutical innovation.

1. Patents

In order to protect the results of their research and development efforts, drug manufacturers increasingly seek protection primarily in the form of product patents. In the U.S., patents on pharmaceuticals may be granted for new products as well as for new processes. Process patents are numerically less important than product patents in the U.S. pharmaceutical industry. It was estimated that in 1961 nearly 80 percent of patents relating to medicine were used for new drug products rather than for new processes [11, p. 379]. In addition, patents on manufacturing processes tend to offer weaker protection to the inventor than patents on new drugs because a product like drugs may be synthesized by alternative processes.

The following data reveal the important role that patent rights play in the pharmaceutical industry. A large share of prescription drugs are single-source drugs under patent protection.

Walker [64, p. 48] estimated that approximately 54 percent of the pharmaceutical industry sales in 1961 were accounted for by patented drugs which were available from a single supplier. In 1972, drugs which were protected by patents accounted for 65 percent of total drug sales

[56, p. 107]. This implies that approximately 56 percent of total prescriptions were filled with patented drugs [56, p. 108]. In 1974, the 200 most frequently prescribed drugs accounted for more than two-thirds of private prescription costs. Of these 200 leading drugs, at least 90 percent were still under patent protection and were produced by only one firm [36, p. 264]. In addition, many less frequently prescribed drugs are also patented.

It is interesting to note that the definition of a patentable product has been broadened since 1946. No product patent was available for penicillin on the ground that it was obtained from naturally occurring molds. Neither cortisone nor hydrocortisone was granted a product patent. In 1946, however, a patent was obtained on the new antibiotic streptomycin and in 1955 a patent was issued on another antibiotic tetracycline despite the fact that both were natural products [58, p. 136]. The broadening of the definition of patentability has profoundly affected the pharmaceutical industry's research interest in such areas as antibiotics, hormones and the like. In June 1980 the Supreme Court ruled that new forms of life created in the laboratory could be patented [62]. This decision is expected to influence the direction of pharmaceutical research. Already it is technically possible to produce on a large scale human insulin and human interferon, the antiviral substance that is being tested against cancer. In the future, pharmaceutical researchers should be able to develop new drug therapies to meet other medical needs through the new technology of gene transplantation.

Due to the nature of drug products which are chemically synthesized, the patent system plays a dual role in the pharmaceutical industry. Drug

patents are employed to limit competition by impeding imitations. On the other hand, drug patents encourage competition in the form of product variations by allowing other firms to "invent around" the patented drug.

A drug product is relatively easy to imitate. With patent protection, the inventor of the drug can be insulated from outside competition and obtain monopoly power in that market. Therefore, patents are frequently considered as an entry barrier. By restricting competition, a patent can prevent the innovator's return to R & D from being eroded by competition and, hence, provides drug manufacturers with incentives to invest even in difficult research. Walker [64, pp. 49-50] has demonstrated that patents indeed confer some monopoly power and that entry into a drug market has been limited by patent protection.

However, patent rights do not prevent other firms from "inventing around" the original patent [4, pp. 185-186]. The product patent of a drug reveals the molecular structure of the drug. This helps other scientists search for a useful product by manipulating the molecule of the existing product. Marck's success with chlorothiazide (Diuril), which was introduced in late 1957, has encouraged other firms to enter the diuretics market. At least nine thiazide diuretics have been patented and marketed in the U.S. [4, p. 186]. Most molecular manipulations have resulted in new drugs with therapeutic value similar to the original drug. Yet they may be different enough to obtain a patent. Sometimes, molecular manipulations have yielded breakthrough products which possess other attributes different from the existing drugs. In spite of its success with Diuril, Merck could not rest on its laurels. A threat of drug obsolescence and diminishing monopoly position forced Merck to engage in further research. In 1959 Merck introduced hydrochlorothiazide

(HydroDiuril), which is a derivative of Diuril and yet is a breakthrough drug to treat hypertension [4, p. 186].

Thus, the patent can encourage competition on the basis of product variations. As a result, monopoly power of the original innovating firm may be eroded even during the life of the patent. In short, while entry barriers may be created by patents, these can be surmounted in the drug field, and, in fact, the opportunity to patent provides strong incentives to engage in research and development for newer drugs.

2. New Drug Approval

In an attempt to protect consumers' health, the federal government has imposed increasingly strict regulations on the development and marketing of drugs. In 1938, the Food, Drug and Cosmetic Act was enacted in response to the tradegy caused by unsafe sulfanilamide [28, p. 6]. Before marketing any new drug, drug manufacturers were required by the 1938 law to submit a New Drug Application (NDA) and prove to the Food and Drug Administration (FDA) that the drug was "safe" for the use suggested on the label. Under this law, the FDA was required to reject an NDA within a period of 180 days or the new drug was automatically approved for marketing [48, p. 6].

The most sweeping changes that took place in FDA regulation came with the 1962 amendments to the 1938 law. Revelations that the tranquilizer thalidomide had caused thousands of deformed babies was the main force in getting Congress to pass the 1962 amendments [48, p. 8]. With regard to premarket approval, a proof-of-efficacy requirement was added to the proof-of-safety requirement of the 1938 law [48, p. 9]. No new drug may now be marketed unless and until the FDA determines that

there is substantial evidence of safety and effectiveness in its intended use.

The FDA was also given discretionary power over premarket testing procedures [48, p. 9]. Prior to filing an NDA the drug manufacturer must now submit to the FDA a plan of investigations of the new drug (IND) for clinical testing along with information from pre-clinical toxicity testing. The FDA may, at any point, terminate or modify clinical investigations on the basis of its evaluation of the IND and subsequent progress reports of clinical research. In addition, the 1962 amendments remove the time constraint on FDA action on NDA's.

Several studies were conducted to assess the impacts of the 1962 amendments on the pharmaceutical industry [2, 47, 56]. Despite their methodological differences, many authors reached the same conclusion that the more stringent regulations for drug safety and efficacy has had a significant adverse side effect on pharmaceutical innovation. First, it now costs considerably more to develop a new drug than it did before 1962. Schwartzman [56, pp. 69-70] estimated that the R & D cost of a new chemical entity was $1.3 million in 1960 and the corresponding estimate for 1973 was $24.4 million. Studies by Baily [2, p. 78] and by Peltzman [47, p. 1097] also provide estimates of the effect of the 1962 amendments on R & D costs. Baily estimated that the 1962 amendments have increased the cost of an NCE by 131 percent, while Peltzman estimated that they have doubled the constant-dollar cost of an NCE.

Second, the 1962 amendments have lengthened the gestation times for new drugs reaching the market. Sarett [52, pp. 18-19] estimated that the total development and clearance time (exclusive of the discovery stage) has increased from 2.5 years in 1960 to 7.5 to 10 years in the

period 1968-1972. The lengthening product development time has shortened the effective life of a patent. Although the nominal patent life is 17 years, the effective patent life declined from 13.9 years for drugs introduced in 1966-1969 to 12.4 years for those introduced in 1970-1973 [56, p. 180]; the effective patent life of those NCE's approved in 1977 further declined to 9 years [65, p. 10].

Third, there appears to have been an increase in the risks of pharmaceutical innovation in the post-1962 period. Clymer [8] estimated that prior to 1962, one out of every three new compounds that entered human testing became commercially available drugs. A higher attrition rate at the stages of IND and NDA submission was observed by Wardell [65] since the passage of the 1962 amendments:

> For every 10 that reach the stage of an IND filing in the U.S., five are dropped by the firm by 15 months into human testing. Nine out of the 10 have been dropped by the stage of NDA submission, but the one survivor that reaches an NDA submission has 90% chance of being approved by the FDA [p. 10].

Studies by Baily [2], Peltzman [48], and Grabowski, Vernon, and Thomas [24] all found that increased regulatory control in ethical drugs has been a major cause of the declining rate of innovation. As shown in Table III (see p. 15), in the decade before the amendments (1952-1961) an average of 44 NCE's were introduced annually while in the subsequent decade it had fallen to 17.

Consequently, higher costs and risks precipitated by the 1962 drug amendments seem to have made it difficult or impossible for small drug firms to conduct research. Innovational output has become more and more concentrated in fewer and larger drug firms [22, pp. 55-63]. In fact, the number of firms in the U.S. introducing new pharmaceutical products has dropped markedly from 89 in 1963 to 33 in 1972 [44].

E. Summary

This chapter provides the background information necessary to understand the theoretical and empirical analysis of conditions of entry into the pharmaceutical industry presented in Chapters III and IV. Demand for pharmaceutical products has grown rapidly since World War II. Several factors have contributed to this growth. These factors include the growth of population, the development of new drugs, the rise in income and the expansion of third party health care finance. On the supply side, the pharmaceutical industry is moderately concentrated, with a significant number of smaller firms. Meanwhile, concentration ratios for specific therapeutic categories are considerably high. The available evidence suggests that there seem to be no economies of size in the production of pharmaceutical drugs. Product differentiation through R & D and sales promotion is considered an important entry barrier. Another important entry barrier is created by the increased government regulation of drug quality as a result of 1962 Drug Amendments.

CHAPTER III

ENTRY CONDITION MODELS

This chapter contains three sections. The first discusses the important role of entry conditions in explaining the relationship between market structure and performance. The next section develops a theoretical model for explaining the phenomenon of entry in a profit-maximization framework. The last section of the chapter reviews selected previous literature pertaining to entry.

A. The Importance of Entry Conditions

The role of entry is of great importance in the process of adjustment of the productive capacity of an economic system to dynamic change. In the perfectly competitive model entry is assumed to be free and easy; consequently, adjustments of productive capacity in response to profits and losses are thought to proceed smoothly and completely. Long-run adjustments in the size of plant by individual firms, and the entrance or exit of firms to and from the industry tend to eliminate the profits or losses made in the industry. Prices of products are equal to their marginal and average costs in the long run.

In the pure monopoly model, entry is assumed to be completely blocked, and adjustments to demand or cost changes--to the extent that they occur--are very incomplete. Adjustments in the monopolized industry's productive capacity are limited to the changes in the size of

plant that the monopolist is able and willing to make, together with variations in the output rate of any given size of plant. Since the monopolist faces a less than perfectly elastic demand curve, the monopoly price exceeds marginal revenue and, consequently, price is greater than marginal cost. The monopolist's output is less than that at which marginal cost equals price. At the same time, blocked entry may keep price above average costs in the long run so that the profits persist. For both of these reasons monopolistic output tends to be below what the competitive output would be.

In oligopoly models the assumed entry conditions range all the way from completely open to completely blocked. However, much oligopoly analysis is based on an implicit assumption that entry is blocked; that is, it leaves the potential competition of entrants out of consideration, concentrating on the relationships among existing firms [3, p. 1]. Actually, a wide range of adjustments to changes in demand or costs is possible in an oligopolistic industry depending on whether entry is partially or completely blocked. With partially blocked entry the time period over which price may exceed average costs will be longer than would be the case with completely open entry, but it is possible that profits could be eroded away over time. In other words, in the long run it may be possible for entry or exit of firms to occur. Whether or not the industry remains oligopolistic depends to a large extent on the condition of entry into that industry.

In summary, entry conditions are an aspect of industrial structure which may be very useful in explaining market performance. Further, the conditions of entry tend to place a limit or ceiling on the degree

to which established firms can raise their prices above a competitive level without inducing entry [3, p. 3].

B. A Theoretical Model of Entry

In building a theoretical model of entry, the premises underlying the theory should be stated explicitly. The fundamental premise used in this study is that firms attempt to maximize profits. The profit-maximizing premise implies a firm will produce the output at which marginal cost is equal to marginal revenue. The same rules in profit maximization apply to the firms of particular oligopolistic industries in which nonprice competition through product differentiation (such as advertising and variation in product characteristics) is frequently used.[1] That is, the firm seeking to maximize profits will carry out each activity to the point at which the marginal revenue from it equals its marginal cost [31, p. 319].

It is useful to start with a theory that is based on pure competition. This will help reveal what generates incentives for entry, how and why barriers to entry are erected, and what the impact of entry, if effected and to the degree it is effected, will be.

In a purely competitive industry, entry is assumed to be easy and free. There are no barriers to entry. Assume that a purely competitive industry is initially in the long-run equilibrium situation as designated by point R_1 in Figure 1. Now suppose that a disequilibriating force such as an increase in demand for the product occurs. Given the number

---

[1] Profit maximization rules do not apply to the firms that practice limit pricing policies.

of firms operating in the industry, the price of that product will move upwards along the initial supply curve S_1S_1 to P_1' and existing firms make profits. The existence of profits provides incentives for entry. Since there are no barriers, entry will take place until profits are aqueezed out. As shown in Figure 1, the expansion of capacity by existing firms, and the participation of new firms in the industry, shift the industry supply curve to S_2S_2. The industry output increases from Q_1 to Q_2, and all firms earn zero profit in the long run.

When entry into an industry is partially or completely blocked, however, the rate of entry will not only be determined by the profitability of existing firms, it will also be affected by the existence and height of entry barriers. Some entry barriers are of an absolute nature, for example, a government license may be needed to enter and the license may be unobtainable by potential entrants. Other barriers--the ones that seem most important in this study--take the form of explicit or implicit entry costs imposed on potential entrants because of disadvantages which they have compared to firms already in the industry. Incentives to enter an industry vary directly with the amount of profits that are being made in it. On the other hand, entry incentives vary inversely with the expected entry costs imposed by entry barriers. In making its entry decision, each potential entrant must consider the expected post-entry price level of its product and the expected cost conditions which it will have. The profits being earned by the existing firms may not induce the potential competitor to enter if the cost disadvantages imposed by entry barriers outweigh those profit incentives. In short, while profitability of existing firms will encourage new firms to enter, entry occurs only if a prospective entrant anticipates that post-entry profits will be realized.

Thus, the long-run adjustments in an industry characterized with entry barriers fall short of that illustrated in the purely competitive model. In terms of Figure 1, in response to an increase in demand the industry supply curve will shift to the right, to say S_3S_3, but not as far to the right as it would in the case of free entry.

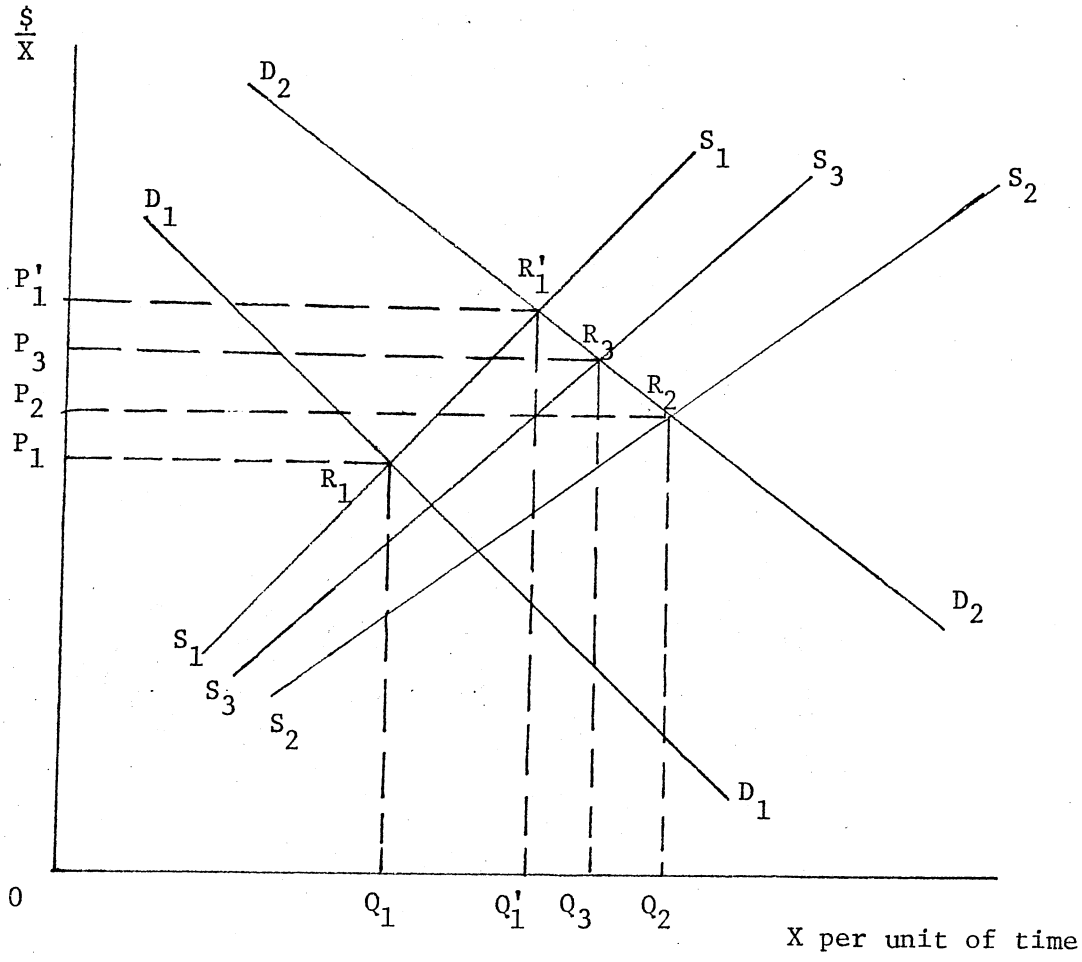

Figure 1. Supply Response to Shifting Demand

Obviously the disturbing force need not be an increase in product demand. It could as well be a decrease in costs for firms in the industry brought about by decreases in resource prices and/or improvements in technology. The entry rate response to the resulting increase in profits would be no different than in the theory discussed above. Neither would the entry rate response to entry barriers be different.

Accordingly, the general form of a theoretical model can be expressed by the following two equations:

$$E = f(\pi^*) \tag{1}$$

$$\pi^* = g(X_1, X_2, \ldots, X_n, Y_1, Y_2, \ldots, Y_m) \tag{2}$$

where

E is the actual rate of entry,

π^* is the expected profit rate of the entering firm,

X_i represents variables which provide incentives to entry, and

Y_j represents variables which measure entry barriers.

Therefore,

$$E = h(X_1, \ldots, X_n, Y_1, \ldots, Y_m) \text{ and } \frac{\partial E}{\partial X_i} > 0, \frac{\partial E}{\partial Y_i} < 0. \tag{3}$$

That is, entry is a function of the incentives to enter relative to the level of entry barriers.

The following additive regression equation is used in Chapter IV to investigate empirically the determinants of the rate of entry for a sample of 20 therapeutic markets in the pharmaceutical industry:

$$E_i = a + b(DG_i) + c(I_i) + d(PD_i) + e(CR_i) + u_i \tag{4}$$

where

E_i is the rate of entry to market i,

DG_i is the rate of demand growth in market i,

I_i is the rate of innovation in market i,

PD_i is the measure of product differentiation entry barrier for market i,

CR_i is the measure of concentration for market i, and

u_i is a random error term.

The variables will be specified in Chapter IV. Ordinary least squares techniques will be employed to estimate equation (4). The empirical results will be presented in Chapter IV.

It should be recognized that not all variables affecting entry are included in the present study. As mentioned in Chapter II, for the pharmaceutical industry, the capital investment outlay for a potential entrant seems to be relatively low [49] and the economies of size in the production process do not appear to be of importance [58, 64]. On the other hand, the economies of size in R & D and in sales promotion seem to be large enough to deter entry [11, 55, 56, 58]. However, the difficulty of obtaining data which measure these economies for 20 therapeutic drug markets has prevented this study from examining these variables.[2]

C. Selected Review of Previous Studies

Although the conditions of entry have been recognized as one of the dimensions of market structure, direct measures of the rate of

---

[2]The exclusion of the economies of size in R & D and in sales promotion from the regression equation may lead to biasedness of the least squares estimators [63], especially the estimated regression coefficient of concentration. If these variables were included in the equation, a negative sign would be expected on their coefficients. Furthermore, the correlation between these omitted variables and the measure of concentration (for example, the four-firm concentration ratio or the Herfindahl Index) is expected to be positive. Thus, the estimated coefficient of concentration is expected to be biased downward.

entry were not used as dependent variables to study the relative importance of the various entry barriers until Mansfield introduced them in 1961 [33]. Alternative measures of the rate of entry will be discussed first. Then a number of previous studies of the determinants of entry will be reviewed.

1. Measures of Entry

There is considerable disagreement among economists about how the rate of entry should be measured. McGuckin [32] and Duetsch [14] argue in separate studies that the "net rate of entry" is the proper measure to be used. They measure this net rate by the percentage change in the actual number of firms operating in a market over a given period. This measure ignores "firm turnover" (i.e., offsetting entries and exits of firms) during the time period and treats exits from an industry as negative entries; thus, the measure will have a negative value if the number of firms in the market declines over the time period. In addition, the measure does not take into account the sizes of individual entrants. As a result, it gives considerable weight to the changing number of very small firms. McGuckin and Duetsch each seem to think that this is an advantage of the measure because all entrants are potentially strong competitors in a market and, consequently, regardless of their sizes, they all may have important effects upon a market's performance.

In another recent study, Telser [61] develops a somewhat different measure of "net entry". While his measure also ignores firm turnover, it does take the size of entrants into consideration. He measures the net rate of entry in a market by the proportion of the market's sales (in dollars) in a terminal year by companies who were absent from the

market in some specified base year. It measures successful "net" entry, not "gross" entry. It can be seen that this measure does not explicitly take into account the actual number of entrants within the time period studied. If the arguments of McGuckin and Duetsch are valid, Telser's measure suffers from the shortcoming that it dismisses the fact that small entrants may represent important sources of potential competition.

An alternative measure of successful net entry is developed by Mansfield [33]. He measures the rate of entry in a market by the number of successful firms during the period (i.e., firms that entered and were still in operation) as a proportion of the original number of firms. The advantage of this measure over Telser's is that it takes into account the number of successful entrants in a market.

Still another view about the proper way to measure entry in empirical studies is provided by Orr [43]. He contends that: "Gross entry is the appropriate measure of entry since we expect total entrants to be determined by the incentives and barriers to entry" [p. 59]. Orr measures the gross rate of entry by calculating the average annual number of new corporations in an industry during a given time period. He defines this measure in a way so that it must be either positive or equal to zero; it cannot be negative.

The measure of entry used in this study follows closely that of Mansfield. It intends to measure the relative importance of successful entrants. It will be specified in Chapter V.

2. Determinants of Entry

Past studies of entry conditions have examined several determinants of entry. These are described below. The determinants used in this study will be specified in Chapter IV.

a. Expected Rate of Return. In testing the theoretical profit-entry relationship, Orr [43, pp. 63-64] and Duetsch [14, p. 454] found that observed industry profitability measured by either the past profit rates or price-cost margins had a positive but weak impact on entry into manufacturing industries. A potential entrant bases its decision about whether to enter an industry not only on the past and current profitability of the industry, but also on expected rate of return on its investment. The expected, not the observed rate of return on investment, is an important determinant of the actual entry rate. The higher the expected rate of return, other things being equal, the more strongly the potential entrants will be attracted into the industry.

b. Demand Growth. Published studies by Gort [21] and Duetsch [14] have suggested that rapid growth in demand for products is likely to be a disequilibriating force that results in profits in the short run. Increases in the level of market demand for products, other things being equal, could raise profits of existing firms in the short run and thereby attract the entry of new firms to the industry in the long run.

c. Technological Innovation. The impact of technological innovation on the rate of entry depends to a large extent on whether control over technology is in the hands of established firms or potential entrants [42, p. 174; 71, p. 252]. It is necessary, therefore, to resort to empirical evidence in order to determine whether technological innovation deters entry or facilitates it.

d. Economies of Large Size in Production. The presence of significant size economies tends to provide an impediment to entry. If the

firms of an industry are characterized by declining long-run average cost curves and an appreciable fraction of industry output is accounted for by firms of minimum efficient size[3], small-sized potential entrants would be forestalled due to the higher costs of production at outputs less than those of minimum efficient size. Further, the presence of significant size economies tends to build progressively higher barriers to entry as further entry occurs. The larger the fraction of industry output accounted for by a minimum efficient firm size, the more an entrant's output will depress industry price. Thus, the "supply effect" [43, p. 61] of economies of size tends to increase the ability of existing firms to raise the price without making entry profitable. Sylos [59] and Modigliani [38] considered this as a fundamental barrier to entry. Barriers to entry resting on large size economies may be measured by minimum efficient firm size divided by total market size. The higher the height of size economy barriers to entry, the fewer the new firms that are likely to enter the market.

e. Capital Investment. The establishment of a new firm is an investment of new capital in the industry. Entry can be treated as a form of capital investment [46]. The investment required to establish a firm of minimum efficient size may be an entry barrier. Mansfield [33] estimated the effect of an industry's capital requirements on its entry rate. His study revealed a strong negative relationship between capital requirements and the rate of entry. In Orr's [43, p. 63] analysis of the determinants of entry, capital requirements also seemed to create a significant barrier to entry.

---

[3]Minimum efficient size is defined as the smallest size at which all economies of size are realized.

f. Product Differentiation. Bain [3] found that product differentiation was the most important barrier to entry in 20 manufacturing industries. Product differentiation barriers to entry result from the preferences of buyers for established products. Advertising is an important method of establishing brand loyalties. Thus strong product differentiation is usually expected to result from large advertising expenditures and this differentiation seems likely to discourage the entry of new firms. Even if new or improved products are invented, the entrants must allocate large sums to promote them. The costs of promotion may constitute one of the main elements in the cost of entry. Advertising intensity (advertising expenditures of established firms in an industry divided by the industry's total sales) has been used to measure the height of product-differentiation barriers to entry. An inverse relation between promotion intensity and the rate of entry was supported by the statistical studies of Orr [43, p. 63] and Duetsch [14, p. 455].

This widely held view that high promotional outlays create a barrier to entry has been reexamined by Telser [61]. His empirical results evidenced the contrary result of a positive relationship between advertising intensity and the rate of entry. In other words, promotional outlays may represent a means of competition [pp. 473-477]. They constitute an avenue of entry, especially for large firms in developing new products. Well-established marketing channels as well as advantages of certain economies of size in promotion and physical distribution often permit large firms to gain market penetration more rapidly with new products.

g. Research and Development. Research and development projects are risky as well as expensive. Conceptual materialization, technical possibility and the extent of commercial utilization are uncertain when research projects are initiated. Some projects may be spectacularly costly and require a significant investment of resources. The view that research and development costs act as a barrier to entry has been carefully examined by Mueller and Tilton [39]. There may be some technical and financial economies of size in the performance of research and development. Several statistical analyses suggest that there may be increasing returns to R & D achievements when firms' sales levels range roughly from $75 million to $200 million (at the 1955 price level) in most industries. But beyond the "threshold" further increases in R & D activities are likely to have diminishing returns [34, 53].

h. Concentration. High short-run profits in an industry may eventually attract new firms which, in turn, would depress the post-entry profits of established firms. Established firms may refrain from setting high prices and deliberately produce outputs greater than those that maximize profits in the short run, lowering price sufficiently so that it is not profitable for potential entrants to enter [13, pp. 114-119, 141-151; 54, pp. 219-234]. Therefore, firms with large market shares may engage in limit pricing to forestall entry and enjoy their profits over the long run.

Alternative measures of concentration have been employed in different studies. These include the 4-firm concentration ratio, a "dynamic" measure of concentration originated by Grossack [25], the Herfindahl Index and a "numbers equivalent" derived from it. None of these measures of concentration, however, is completely satisfactory.

D. Summary

This chapter developed a theoretical model of entry which assumes entry is a function of the incentives to entry relative to the level of entry barriers. This model will be used in the next chapter to evaluate the condition of entry into the pharmaceutical industry.

CHAPTER IV

EMPIRICAL RESULTS

This chapter is divided into five sections. The first three sections describe data sources, the sample, and the variables used in the study. The fourth section contains the hypotheses to be tested. Finally, the empirical results of the study are presented.

A. Data Sources

The principal source of data for this study is the National Prescription Audit (NPA), which is compiled by IMS America, Ltd. The NPA is designed to measure the rate that prescription drugs move from retail pharmacies to consumers. IMS audits a sample of 800 retail pharmacies stratefied by geographic location and store type.[1] Individual pharmacies are also selected on the basis of prescription files representing a wide cross-section of different prescribers. The prescription information obtained from the sample is then projected to national levels.[2] Prescription drugs dispensed in the institutional setting such as hospitals, nursing homes, or government agencies are not considered in the NPA. Nevertheless, the NPA represents prescription drug consumption

---

[1]The number of sampled retail pharmacies has increased from 400 to 800 since 1973, according to IMS Pharmaceutical Services Reference File, 1978.

[2]Starting in 1964, both new and refilled prescriptions have been collected. Prior to 1964, only new prescriptions were available.

and also reflects prescribing activity in the most important retail segment of the pharmaceutical industry.

Data on drug product innovations were obtained from the Food and Drug Administration's report [16], "Yearly Introduction of New Drug Products, 1950-1973". Each newly introduced drug was rated by personnel in the FDA's Bureau of Drugs on the basis of its "degree of therapeutic gain". New drugs were rated "A", "B", or no rating according to the following criteria.

> "A" Important Therapeutic Gain--Drug may provide effective therapy or diagnosis (by virtue of greatly increased efficacy or safety) for a disease not adequately treated or diagnosed by any marketed drug, or provide markedly improved treatment of a disease through improved efficacy or safety (including decreased abuse potential).
>
> "B" Modest Therapeutic Gain--Drug has a modest, but real advantage over other available marketed drugs; e.g., somewhat greater effectiveness, decreased adverse reactions, less frequent dosing in situations where frequent dosage is a problem, etc. [16, p. 1].

Not all of the new drug products listed by the FDA are very original. That is, some of the new drug products are new salts or esters of previously marketed drugs. Thus, the definition of drug innovations for this study includes all new products rated A or B less any salts or esters of drugs already on the market.[3]

B. The Sample

The importance of determining well-defined markets within the pharmaceutical industry has been stressed in several previous studies [26, 29, 61]. This stems from the fact that drug manufacturers do not

---

[3]Detailed information on drug innovation for the time period 1963-1973 is presented in Jadlow [29, pp. 49-67].

compete on an industry-wide basis [11, p. 377]. In addition, inappropriate market definitions tend to distort the results of empirical studies [29, p. 37].

Theoretically, an economically meaningful market should be defined to include all those products which are close substitutes in both consumption and production [41, pp. 17-22]. However, in defining empirical drug markets, much emphasis is usually given to substitutability in consumption [10, pp. 349-351; 26, pp. 19-22; 60, pp. 211-212].

The pharmaceutical industry is grouped into 20 therapeutic drug markets as a basis for the empirical analysis of the present study. These 20 drug markets used in this study are the same as those developed by Jadlow [29] and are presented in Table XIV.

In defining these markets, Jadlow [29] relied heavily upon substitutability in drug usage. The data from National Disease and Therapeutic Index (NDTI)[4] on physicians' prescribing patterns for individual drug products were employed to group National Prescription Audit therapeutic classes into 20 relevant markets. This was accomplished by first identifying the therapeutic classes of drugs prescribed to treat similar broad diagnoses and then, from these groupings, sorting out the classes which had similar desired therapeutic actions. Finally, drug classes prescribed for more specific diagnoses were grouped together [29, pp. 40-48].

---

[4]NDTI is compiled by IMS America, Ltd.

TABLE XIV

THERAPEUTIC CLASSES GROUPED AS TWENTY ECONOMIC MARKETS (MARKET/THERAPEUTIC CLASSES)

1. Antibiotics
   a. Broad and medium spectrum antibiotics
   b. Penicillins
   c. Other antibiotics
2. Sulfonamides and Antibacterials
   a. Urinary antibacterials
   b. Antibiotics with sulfas
   c. Sulfonamides
3. General antibacterials
4. Analgesics
   a. Narcotic analgesics
   b. Nonnarcotic analgesics
5. Local and Topical Anesthetics
6. Antiarthritics
7. Hormones
   a. ACTH
   b. Corticoids
   c. Corticoids with analgesics
   d. Corticoids with antiinfectives
8. Oral Muscle Relaxants
9. Ataraxics
10. Psychostimulants
11. Sedatives
   a. Barbiturate sedatives
   b. Nonbarbiturate sedatives
12. Cough and Cold Preparations
13. Antihypertensives and Diuretics
   a. Rauwolfias
   b. Rauwolfias-Diuretic combinations
   c. Non-Rauwolfia hypotensives
   d. Diuretics
14. Hematinics

TABLE XIV (Continued)

15. Vitamins

16. Oral Contraceptives

17. Anticholinergics and Antispasmodics

18. Antiobesity Preparations
    a. Amphetamines
    b. Nonamphetamines

19. Diabetes Therapy
    a. Insulins
    b. Others

20. Antihistamines

Source: Joseph M. Jadlow, An Empirical Study of the Relationship Between Market Structure and Innovation in Therapeutic Drug Markets, 1976.

C. The Variables

The dependent and indiependent variables which are employed for the empirical analysis of the present study are discussed below. The values of these variables for each of the 20 drug markets are presented in Table XV. A correlation matrix of the independent variables is listed in Table XVI. As can be seen, no serious linear dependence exists between the explanatory variables.

1. The Rate of Entry (E)

In this study, the rate of entry is measured by computing the number of new firms operating in a market as a percentage of the total number of firms in that market. Specifically, for each of 20 markets,

$$E = \frac{\text{The number of firms in 1974 that had not been in the market in 1964}}{\text{The average of the total number of existing firms in 1964 and 1974}}$$

2. The Rate of Demand Growth (DG)

The rate of demand growth for each market is measured by the rate of growth in the number of prescriptions in that market between 1964 and 1974. DG can be expressed as follows:

$$DG = \frac{\text{Change in number of prescriptions between 1964 and 1974}}{\text{Total number of prescriptions in 1964}}$$

3. The Rate of Innovation (I)

The rate of innovation is defined as the ratio of the value of new products relative to the size of the market. In this study, the value of each new product is measured by the product's dollar sales in its

TABLE XV

VALUES OF VARIABLES USED FOR THE EMPIRICAL ANALYSIS

Market*	E	DG	I	PD	CR4	HI	NE	DYN
1	82.667%	99.938%	26.995%	26.67%	57.689%	11.457%	9	0.223
2	39.456	-1.713	23.504	40.48	65.611	23.338	4	0.849
3	46.512	63.388	4.031	37.19	52.555	11.892	8	0.820
4	60.987	117.936	1.398	21.54	65.877	18.254	5	0.786
5	57.143	30.981	0.000	6.38	57.654	11.184	9	0.826
6	40.000	242.652	232.710	45.03	86.822	35.902	3	0.732
7	45.752	65.102	0.000	27.59	47.705	8.231	12	0.592
8	45.283	51.115	0.000	32.80	69.585	14.993	7	0.667
9	71.642	125.611	0.437	14.69	86.735	24.113	4	1.069
10	22.727	54.635	0.000	100.00	77.452	16.256	6	1.196
11	46.269	-8.645	8.195	27.27	60.906	10.800	9	0.513
12	71.161	100.259	0.000	33.63	42.794	7.462	13	0.727
13	49.524	107.100	7.822	41.38	71.292	19.535	5	0.858
14	54.971	13.769	0.000	31.40	44.888	8.500	12	0.471
15	55.870	31.491	0.000	42.78	38.471	6.110	16	0.618
16	54.545	269.243	0.000	100.00	97.883	49.001	2	0.288
17	53.691	40.849	0.000	51.90	60.105	13.056	8	0.995
18	41.667	-40.537	10.845	39.69	69.313	19.920	5	0.279
19	16.667	147.866	29.007	56.60	97.737	54.335	2	0.229
20	64.789	28.644	0.000	0.00**	71.792	17.071	6	1.173

*The numbers in this column refer to the listing of revelant markets presented in Table XIV.

**Based on the National Prescription Audit, the calculated value of PD was equal to -22.64%. A negative PD may be due to rounding errors since numbers less than 1,000 were not registered in the NPA. Since a negative PD does not make sense on theoretical grounds, it was replaced with zero.

second calendar year on the market[5], and the size of a market is measured by its total number of prescriptions in 1964. Therefore, for each market, I is calculated as follows:

$$I = \frac{\text{The dollar sales of new products during their second calendar year on the market}}{\text{The total number of prescriptions in 1964}}$$

TABLE XVI

CORRELATION MATRIX

	DG	I	PD	CR4	HI	NE	DYN
DG	1.00						
I	0.49	1.00					
PD	0.39	0.06	1.00				
CR4	0.60	0.33	0.41	1.00			
HI	0.69	0.37	0.47	0.89	1.00		
NE	-0.46	-0.32	-0.29	-0.92	-0.81	1.00	
DYN	-0.16	-0.06	-0.15	-0.03	-0.30	-0.04	1.00

4. Measure of Product Differentiation (PD)

Product differentiation cannot be achieved without costs. As discussed in the previous chapter, large drug firms tend to spend large sums on new product introduction and sales promotion in an attempt to

[5]The second year is used instead of the first year because the sales data available are for calendar years and because the sales in the first year are likely to provide distorted weights. By doing so, an indication of the economic importance of each new drug is obtained [29].

establish effective product differentiation. Thus, investment in R & D and sales promotion may be regarded as the costs of product differentiation. They are often beyond the reach of small firms and may constitute an important barrier to entry to a drug market. Moreover, expenditures on sales promotion often have a "cumulative effect, so that newcomers starting from scratch face a dilemma: They either have to spend large amounts on promotion per unit of output to overcome their disadvantage, or they must accept a lower unit price for products of comparable quality" [54, p. 230].

Since expenditures on R & D and sales promotion for individual drug markets are not available for this study, a proxy for product differentiation has been developed. The wholesale prices of generic drug products in a given therapeutic class have frequently been far below those of the brand-name products [56, p. 315]. The disparities in price may reflect the higher level of product differentiation efforts in behalf of established drug products. Hence, the relative wholesale price differentials between brand-name prescriptions[6] and generic prescriptions[7] should provide a crude measure of product differentiation (PD). For each market, PD is calculated as below:

$$PD = \frac{P_b - P_g}{P_b}$$

where P_b = the average wholesale price of brand-name prescriptions in 1964, and

P_g = the average wholesale price of generic prescriptions in 1964.

---

[6]Brand-name prescriptions are those prescriptions which specify brand names or designate manufacturers of the prescribed drugs.

[7]Generic prescriptions are those prescriptions which are prescribed by generic names only.

5. Measure of Concentration (CR)

Four alternative measures of concentration are employed in this study. These are (1) the 4-firm concentration ratio (CR4), (2) the Herfindahl Index (HI), (3) the numbers-equivalent (NE), and (4) the "dynamic" measure of concentration (DYN).

a. Four-Firm Concentration Ratio. The 4-firm concentration ratio (CR4) is the well-known static measure of market power and is measured in this study as the percentage of a market's total prescriptions contributed by the largest 4 firms in that market.

b. Herfindahl Index. The Herfindahl Index (HI) is a summary measure of concentration which takes into account absolute sizes of sellers and the dispersion of seller sizes; it is measured by the sum of the squared percentage market shares of all sellers in a market. In the present study, a technique suggested by Adelman [1, p. 101] is used to calculate the HI. For each market, the HI is estimated on the basis of the respective market shares of the 8 largest firms in that market and the shares of the smaller firms, where the latter are assumed to share equally the remainder of the market.

c. Numbers-Equivalent. The numbers-equivalent (NE) is equal to the reciprocal of the Herfindahl Index [1]. The NE can be interpreted as "the number of equal-sized firms" in a market which would generate the observed value of the Herfindahl Index [1, p. 100].

d. Dynamic Measure of Concentration. The "dynamic" measure of concentration (DYN) is the regression coefficient that is estimated by regressing individual firms' market shares in 1974 on their 1964 market

shares [25]. The DYN measures market share stability over the time period studied. The larger firms in 1964, on the average, gained market shares when the value of DYN is greater than one and lose market shares when the value of DYN is less than one [25, p. 303]. In the present study, DYN is estimated by using the respective market shares of the 7 largest firms either in 1964 or in 1974 and the shares of the smaller firms, which were assumed to share equally the remainder of the market. It should be noted that these regression results for DYN are the same as those which appeared in the study by Jadlow [29].

D. Hypotheses About the Signs of the Regression Coefficients

As discussed in Chapter III, the entry rate is expected to respond positively to variables which may increase the rate of profits and negatively to the extent and height of entry barriers. In order to assess the relationship between the rate of entry and the condition of entry into drug markets, the following equation will be estimated:

$$E_i = a + b(DG_i) + c(I_i) + d(PD_i) + e(CR_i) + u_i$$

The rapid growth in demand for products is likely to be a disequilibrating force that results in supranormal profits of existing firms in the short run [21, pp. 54-55] and thereby attracts the entry of new firms in the long run. Therefore, a positive sign is expected on the coefficient of DG.

Technological innovation may foreclose or facilitate entry, depending largely on whether established firms or potential entrants control the technology necessary for producing products [42, p. 174; 71, p. 252]. Therefore, the sign for the coefficient of I could be positive or negative.

Product differentiation cannot be accomplished without costs. Costs of product differentiation such as expenditures on R & D and/or sales promotion may be sufficiently large so that it is not profitable for potential firms to enter [3, 39]. Thus, a negative sign is expected on the coefficient of PD.

Firms with high monopoly power may practice limit pricing to discourage entry [13, pp. 114-119, 141-151; 54, pp. 219-234]. Thus, a negative sign is expected on the coefficient of concentration measured alternatively by CR4, HI, and DYN. Since the numbers-equivalent is the reciprocal of the Herfindahl Index [1], a positive sign is expected on the coefficient of NE.

E. The Empirical Results

Table XVII summarizes the empirical results of the multiple regression equations based upon the model specified in Chapter III. The regression results with E (the number of new firms operating in a market as a percentage of the total number of firms in that market) as the dependent variable are presented in Table XVII. To estimate each of the equations, the same independent variables are employed with the exception of the measure of concentration. Concentration is measured by the 4-firm concentration ratio in equation 1; the Herfindahl Index in equation 2; the numbers-equivalent in equation 3; and the dynamic measure of concentration in equation 4.

For each equation, the estimated regression coefficients of the variables are listed in the table along with the coefficient of multiple determination (R^2) and the value of the F-ratio. In the parentheses below each coefficient is the valur of the t-statistic for that

TABLE XVII

DETERMINANTS OF THE RATE OF ENTRY, E AS THE DEPENDENT VARIABLE, 1964-1974

Equation	Inter-cept	DG	I	PD	Concentration				R^2	F-value
					CR4	HI	NE	DYN		
1	83.072*	0.145*	-0.115****	-0.379*	-0.400***				.588	5.34*
	(7.37)	(3.10)	(-1.96)	(-3.22)	(-2.04)					
2	67.149*	0.171*	-0.109****	-0.339*		-0.746**			.662	7.34*
	(14.28)	(3.83)	(-2.05)	(-3.12)		(-2.89)				
3	48.782*	0.129**	-0.110****	-0.405*			1.411****		.563	4.83*
	(5.31)	(2.79)	(-1.81)	(-3.41)			(1.75)			
4	62.492*	0.103***	-0.125****	-0.438*				-0.223	.473	3.37***
	(6.56)	(2.16)	(-1.90)	(-3.39)				(-0.02)		

Note: The t-statistics are in parentheses below their corresponding regression coefficients.

*Significant at the .01 level.

**Significant at the .02 level.

***Significant at the .05 level.

****Significant at the .10 level.

coefficient. Significance tests have been performed on individual regression coefficients. One asterisk indicates the coefficient is significantly different from zero at the 0.01 level; two, the 0.02 level; three, the 0.05 level; and four, the 0.10 level. F-tests are made to determine the overall significance of estimated equations. One, two, or three asterisks attached to the value of the F-ratio indicate alternative levels of significance as described earlier.

When the dependent variable (i.e., the rate of entry) was measured by E, the overall regression was significant at the 0.01 level for equations 1 through 3 and at the 0.05 level for equation 4. The coefficient of multiple determination (R^2) measures the proportion of variation in the rate of entry explained by the set of independent variables. Hence, the closer R^2 is to 1, the higher the explanatory power of independent variables. As can be seen in Table XVII, regression equation 1 explains nearly 59 percent of the variation in E among the 20 relevant markets; equation 2, 66 percent; equation 3, 56 percent; and equation 4, 47 percent.

While R^2 measures the degree to which the variation of the dependent variable is accounted for by the explanatory variables, it does not show the importance of the individual explanatory variable in explaining the dependent variable. Neither does the magnitude of the regression coefficient measure the importance of each explanatory variable. In fact, the magnitude of the coefficient can be changed by changing the units of measurement of the variable [20, p. 197].

As suggested by Goldberger [20, pp. 167-187] and Theil [63, pp. 197-200], the "marginal' or "incremental" contributions of individual variables to the explanation of the rate of entry (E) are calculated

and presented in Table XIX. With the exception of equation 2, product differentiation was the most important explanatory variable, followed by the demand growth variable. The third most important explanatory variable was the measure of concentration (CR4, HI, or NE) for equations 1, 2, and 3, and it was drug innovation for equation 4. The least important explanatory variable was drug innovation for all but equation 4.

TABLE XVIII

INCREMENTAL CONTRIBUTIONS OF EXPLANATORY VARIABLES

Equation	Variable	Incremental Contribution	Incremental Contribution as a Percentage of Total Contribution (%)
1	DG	.265	34.4
	I	.105	13.7
	PD	.286	37.1
	CR4	.114	14.8
2	DG	.331	39.7
	I	.095	11.4
	PD	.220	26.3
	HI	.189	22.6
3	DG	.227	30.2
	I	.095	12.7
	PD	.340	45.2
	NE	.090	11.9
4	DG	.164	23.6
	I	.126	18.2
	PD	.404	58.2
	DYN	.000	0.0

a. The Effect of Market Growth. In each of the four equations, the regression coefficient for the demand growth rate was positive and significantly different from zero. This result is similar to what earlier studies have found [14, 32] and confirms the theoretical importance of demand growth in determining the rate of entry. It suggests that among markets with the same entry barriers, rapidly growing markets are more likely to encourage entry than are less rapidly growing ones.

b. The Effect of Drug Innovation. In each of the four equations, the regression coefficients for the rate of innovation was negative and significantly different from zero at the .10 level. This inverse relationship implies that new drug innovation serves as a deterrent to entry [71]. This result seems consistent with the thesis that in markets with rapid rates of innovation, there is less chance for smaller firms to enter the market.

The result is not surprising. As pointed out in Chapter II, all new drug compounds must pass an extensive premarket regulatory review process since the passage of the 1962 Drug Amendments. As a result, the drug research and development has become more expensive and riskier. Consequently, the development and introduction of new chemical entities in the United States has increasingly become the domain of fewer and larger drug firms. New chemical entities available in the United States during the period of 1963-1973 were, in fact, introduced by the largest 25 drug firms [29, pp. 47-69]. In other words, nearly all new drugs were introduced into a market by firms already in the market, rather than by new firms.

Moreover, new drugs and patent protection usually go hand in hand. Patent rights make it more difficult for other firms to imitate new products. Because of patent barriers, firms seem more likely to enter into a market where a substantial proportion of drugs being sold are "old" drugs.

Therefore, it may not be surprising that in markets where there is a high rate of innovation, the net rate of entry has been relatively low while the entry rate has been high in markets where there has been a low rate of innovation. In the case of the pharmaceutical industry, the rate of innovation may be considered as an approximation to entry barriers associated with R & D and/or patent protection.

c. The Effect of Price Differentials. In each of the four equations, the regression coefficient for the price differentials was negative and significantly different from zero at the .01 level. This result supports the proposition that product differentiation constitutes a barrier to the entry of new firms.

In the pharmaceutical industry, it is a well-known practice that drug manufacturers who market branded drugs spend large sums to promote their products to the medical profession and hence establish strong brand loyalties. This places new entrants in a disadvantageous position because they must spend heavily on product promotion and/or set their prices perceptibly lower than those of established products in order to overcome brand loyalties. In fact, little promotional effort is made by many smaller firms that enter into the production and sale of drugs on which the patents have expired. These firms primarily market drugs under generic names and place their products at a price substantially

below existing drug firms. Therefore, significant differences in promotion strategies may in large part explain the wide differences in prices of branded and unbranded products.

In short, entry appears to be more difficult and hence less frequent in markets characterized by substantial product differentiation entry barriers created through product promotion.[8] The result of the present study supports the view that high promotional outlays may serve as an impediment to entry.

d. The Effects of Concentration. Four alternative measures of concentration were employed to estimate their effects on the rate of entry. When the level of concentration was measured by the market shares held by the largest four firms in 1964, the rate of entry and the 4-firm concentration ratio were found to be inversely related. The regression coefficient of CR4 was significantly different from zero at the .05 level.

When the Herfindahl Index was substituted for the CR4, the inverse relation remained and the coefficient for HI was significantly different from zero at the .02 level. It has been argued that on theoretical grounds the Herfindahl Index is the best measure of market power [66]. The suitability of HI over other measures of concentration is supported here by the fact that the R^2 turned out to be the highest when concentration was measured by HI.

When concentration was measured by the numbers-equivalent, the regression coefficient was positive and significantly different from zero at the .10 level. Since the NE is equal to the reciprocal of the

---

[8]Product differentiation through R & D has been taken into account by including the rate of innovation in the regression as discussed earlier.

estimated value of HI, a negative relation between the HI and the net entry rate would imply a positive relation between the NE and entry.

When the dynamic measure of concentration was substituted for the static measure of concentration, the regression coefficient was negative. However, the statistical testing shows that coefficient is not significantly different from zero.

The statistical evidence reveals that entry into a highly concentrated market is more difficult than entry into a less concentrated market. This result would be consistent with the use of limit pricing to deter entry in highly concentrated markets. Alternatively, the inverse relationship between the entry and the level of concentration described here could be explained by the presence of barriers to entry in a concentrated market. Thus, concentration may serve as a proxy for other unmeasured entry barriers. The finding that concentration is inversely related to entry is consistent with that of Orr [43] and Hornbrook [27].

F. Summary

In this chapter, an empirical model developed in the previous chapter is estimated along with a discussion of data and hypotheses. The major empirical findings of the study may be summarized as follows:

1. Product differentiation, concentration, and drug innovation were found to be inversely related to the rate of entry into drug markets, and
2. the growth rate of demand for pharmaceuticals was found to be positively related to the rate of entry.

CHAPTER V

SUMMARY AND CONCLUSIONS

This chapter summarizes the methodology and empirical results of the study. Also, based on the findings of this study, suggestions are made for further research.

A. Summary

Entry is of great importance in explaining relationships between industrial structure and performance. Despite its theoretical prominence, however, until recently there has been little empirical research on the factors that determine the rate of entry into any specific industry.

The present study has focused specifically on entry in the pharmaceutical industry. The main objective of the study has been to develop and test a model which describes the various determinants of entry into the pharmaceutical industry during the period 1964-1974.

In this study, the rate of enter (E) as the dependent variable was measured by the number of new firms operating in a market as a percentage of the total number of firms in that market. The variables used in this study to explain the variations in the rate of entry were market growth, drug innovation, product differentiation, and concentration. Market growth was measured by the percentage change in the size of the market over the time period studied. The value of new drug products relative to the size of the market was used as the measure of the rate of drug

innovation. Product differentiation was measured by the relative price disparities between branded and generic drugs. Concentration was measured alternatively by the 4-firm concentration ratio, the Herfindahl Index, the numbers-equivalent, and the dynamic measure of concentration. The difficulty of obtaining other data by therapeutic market has confined this study to the above variables.

All four of the alternative equations which were estimated were statistically significant. The statistical evidence revealed: (1) a positive and statistically significant relationship between the rate of entry and the rate of growth in demand; (2) a negative and statistically significant relationship between the rate of entry and product differentiation; (3) a negative and statistically significant relationship between the rate of entry and the rate of drug innovation; and (4) an inverse relationship between the rate of entry and the measure of concentration, regardless of which of the four measures of concentration was used; however, no statistical relationship was observed between the rate of entry and the dynamic measure of concentration.

Furthermore, this study has indicated that product differentiation is the most important factor in explaining the variations in the rates of entry. Demand growth was found to be the second most important factors, followed by concentration and drug innovation.

In sum, the statistical findings of the study were consistent with a prior expectations and the few previous studies which have been published [3, 14, 32, 43]. It is interesting to note that product differentiation tends to present a barrier to entry into drug markets, while Telser [60] has concluded that promotional outlays tend to serve as a means of entry. It should be noted, however, that price disparities

between branded and generic drugs were used as a proxy for product differentiation in this study. A more conventional measure of product differentiation (i.e., promotional intensity) was employed in Telser's study [60].

One of the unique features of the present study was to examine the role of technological innovation in the process of entry into therapeutic drug markets. In this regard, the focus of the study was on new drug innovation. The statistical evidence indicated that R & D resulting in new drug introductions serves as a barrier, not a means of entry as hypothesized by Comanor [11].

Still another feature of the study was to employ four alternative measures of concentration as explanatory variables for the rate of entry. Out of all the estimated equations, the equation employing the Herfindahl Index did the best job of explaining the rate of entry. This is not surprising because it is generally considered to be the best measure of market power on theoretical grounds [66].

B. Future Research

Lack of data precluded the analysis in this study of the impacts on entry of various other possible determinants of the rate of entry. It would be useful, for example, to incorporate such variables as economies of size in R & D and in sales promotion into the model in future studies.

As discussed in Chapter II, previous studies have suggested that the 1962 Drug Amendments heightened entry barriers to conduting R & D in the pharmaceutical industry. This subject seems important enough to warrant further study. It would be useful to estimate the model developed here for a period before 1962 and compare the results with those found

for the post-Amendments period to see if increased regulation has altered the determinants of the rate of entry.

Probably the most obvious extension of this study would be to obtain data for other industries and estimate entry models similar to those employed here. This could be useful, for example, in the formulation of public policy toward these industries in the antitrust area.

BIBLIOGRAPHY

[1] Adelman, M. A. "Comment on the 'H' Concentration Measure as a Numbers-Equivalent." Review of Economics and Statistics, Vol. 51 (February, 1969), pp. 99-101.

[2] Baily, Martin N. "Research and Development Cost and Returns: The U.S. Pharmaceutical Industry." Journal of Political Economy, Vol. 80 (January/ February, 1972), pp. 70-85.

[3] Bain, Joe S. Barriers to New Competition. Cambridge: Harvard University Press, 1956.

[4] Beyer, Karl H., Jr. Discovery, Development and Delivery of New Drugs. Jamaica, N.Y.: Spectrum Publications, Inc., 1978.

[5] Bond, Ronald and Lean, David. Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets. (Federal Trade Commission Staff Study.) Washington, D.C.: U.S. Government Printing Office, February 1977.

[6] Caglarcan, Erol, Faust, Richard E., and Schnee, Jeromee E. "Resource Allocation in Pharmaceutical Research and Development." Impact of Public Policy on Drug Innovation and Pricing. Samuel A. Mitchell and Emery A. Link (eds.). Washington, D.C.: The American University, 1976, pp. 331-348.

[7] Clarkson, K. W. Intangible Capital and Rates of Return: Effects of Research and Promotion on Profitability. Washington, D.C.: American Enterprise Institute, 1977.

[8] Clymer, Harold. "The Changing Costs and Risks of Pharmaceutical Innovation." The Economics of Drug Development. J. D. Cooper (ed.). Washington, D.C.: American University Press, 1970.

[9] Cocks, Douglas L. "Product Innovation and the Dynamic Elements of Competition in the Ethical Pharmaceutical Industry." Drug Development and Marketing. Robert B. Helms (ed.). Washington, D.C.: American Enterprise Institute, 1975, pp. 225-254.

[10] Cocks, Douglas L. and Virts, John R. "Pricing Behavior of the Ethical Pharmaceutical Industry." Journal of Business, Vol. 47 (July, 1974), pp. 349-362.

[11] Comanor, William S. "Research and Competitive Product Differentiation in the Pharmaceutical Industry." Economica, Vol. 31 (November, 1964), pp. 372-384.

[12] Comanor, W. M. and Wilson, T. A. "Advertising, Market Structure, and Performance." Review of Economics and Statistics, Vol. 49 (November, 1967), pp. 423-440.

[13] Dewey, Donald. Microeconomics. New York: Oxford University Press, 1975.

[14] Duetsch, Larry L. "Structure, Performance, and the Net Rate of Entry into Manufacturing Industries." Southern Economic Journal, Vol. 41 (January, 1975), pp. 450-456.

[15] Federal Trade Commission, Bureau of Consumer Protection. Drug Product Selection. Washington, D.C.: U.S. Government Printing Office, January, 1979.

[16] Food and Drug Administration. "Yearly Introduction of New Drug Products, 1950-1973." Mimeographed.

[17] Gibson, Robert M. and Fisher, Charles R. "National Health Expenditures, Fiscal Year 1977." Social Security Bulletin, Vol. 41 (July, 1978), pp. 3-20.

[18] _____. "Age Differences in Health Care Spending, Fiscal Year 1977." Social Security Bulletin, Vol. 42 (January, 1979), pp. 3-16.

[19] Gibson, Robert M. and Muller, Marjorie Smith. "National Health Exoenditures, Fiscal Year 1976." Social Security Bulletin, Vol. 40 (April, 1977), pp. 3-22.

[20] Goldberger, A. S. Econometric Theory. New York: John Wiley & Sons, Inc., 1964.

[21] Gort, Michael. "Analysis of Stability and Change in Market Shares." Journal of Political Economy, Vol. 71 (February, 1963), pp. 51-63.

[22] Grabowski, H. G. Drug Regulation and Innovation: Empirical Evidence and Policy Options. Washington, D.C.: American Enterprise Institute, 1976.

[23] Grabowski, H. G. and Mueller, D. C. "Industrial Research and Development, Intangible Capital Stocks, and Firm Profit Rates." Bell Journal of Economics, Vol. 9 (Autumn, 1978), pp. 328-343.

[24] Grabowski, H. G., Vernon, J. M. and Thomas, Lacy G. "Estimating the Effects of Regulation on Innovation: An International Comparative Analysis of the Pharmaceutical Industry." Journal of Law and Economics, Vol. 21 (April, 1978), pp. 133-163.

[25] Grossack, Irvin M. "The Concept and Measurement of Permanent Industrial Concentration." Journal of Political Economy, Vol. 80 (July/August, 1972), pp. 745-760.

[26] Hornbrook, Mark C. "Definition of Drug Markets: Theory and Procedures." Mimeographed.

[27] _____. "Market Structure and Advertising in the U.S. Pharmaceutical Industry: Some Implications for Public Policy." Medical Care, Vol. 16 (February, 1978), pp. 90-109.

[28] IMS America, Ltd. Promotional Audits. Ambler, PA, 1972-1978.

[29] Jadlow, Joseph M. An Empirical Study of the Relationship Between Market Structure and Innovation in Therapeutic Drug Markets. 1976. (The final report to the National Science Foundation under Grant No. RDA 75-21075.)

[30] Kefauver, Estes. In A Few Hands: Monopoly Power in America. New York: Pantheon Books, 1965.

[31] Leftwich, R. H. The Price System and Resource Allocation. 7th Ed. Hinsdale, IL: The Dryden Press, 1979.

[32] McGuckin, Robert. "Entry, Concentration Change, and Stability of Market Shares." Southern Economic Journal, Vol. 38 (January, 1972), pp. 363-370.

[33] Mansfield, E. "Entry, Gibrat's Law, Innovation and Growth of Firms." American Economic Review, Vol. 52 (December, 1962), pp. 1023-1050.

[34] _____. "Size of Firm, Market Structure, and Innovation." Journal of Political Economy, Vol. 71 (December, 1963), pp. 556-576.

[35] Markham, Jesse W. "Economic Incentives in the Drug Industry." Drugs in Our Society. Paul Talalay (ed.). Baltimore: The Johns Hopkins University Press, 1964, pp. 163-179.

[36] Measday, Walter S. "The Pharmaceutical Industry." The Structure of American Industry. 5th Ed. Walter Adams (ed.). New York: The Macmillan Company, 1977, pp. 250-284.

[37] Miller, R. A. "Market Structure and Industrial Performance: Relation of Profit Rates to Concentration, Advertising Intensity and Diversity." Journal of Industrial Economics, Vol. 17 (April, 1969), pp. 104-118.

[38] Modigliani, Franco. "New Developments on the Oligopoly Front." Journal of Political Economy, Vol. 66 (June, 1958), pp. 215-232.

[39] Mueller, D. C. and Tilton, J. E. "Research and Development Costs as a Barrier to Entry." Canadian Journal of Economics, Vol. 2 (November, 1969), pp. 570-579.

[40] National Science Foundation. Research and Development in Industry, 1975. Washington, D.C.: U.S. Government Printing Office, 1976.

[41] Needham, Douglas. Economic Analysis and Industrial Structure. New York: Holt, Rinehart and Winston, Inc., 1969.

[42] _____. The Economics of Industrial Structure, Conduct, and Performance. New York: St. Martin's Press, 1978.

[43] Orr, Dale. "The Determinants of Entry: A Study of the Canadian Manufacturing Industries." Review of Economics and Statistics, Vol. 56 (February, 1974), pp. 58-66.

[44] Paul de Haen, Inc. New Product Parade, 1972. New York, 1973.

[45] _____. "1973-1977: A Five Year Survey." de Haen New Drug Analysis, U.S.A., Vol. XIV, 1978.

[46] Peltzman, S. "Entry in Commercial Banking." Journal of Law and Economics, Vol. 8 (October, 1965), pp. 11-50.

[47] _____. "An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments." Journal of Political Economy, Vol. 81 (September/October, 1973), pp. 1049-1091.

[48] _____. Regulation of Pharmaceutical Innovation. Washington, D.C.: American Enterprise Institute, 1974.

[49] Pharmaceutical Manufacturers Association. Prescription Drug Industry Fact Book, 1976. Washington, D.C., 1977.

[50] Physicians' Desk Reference. 32nd Ed. Oradell, NJ: Medical Economics Company, 1978.

[51] Robertson, Wyndham. "Merck Strains to Keep the Pots Aboiling." Fortune, Vol. 93 (March, 1976).

[52] Sarett, L. H. "FDA Regulations and Their Influence on Future R & D." Research Management, Vol. 17 (March, 1974), pp. 18-20.

[53] Scherer, F. M. "Firm Size, Market Structure, Opportunity, and the Output of Patented Inventions." American Economic Review, Vol. 55 (December, 1965), pp. 1097-1125.

[54] _____. Industrial Market Structure and Economic Performance. Chicago: Rand McNally and Company, 1970.

[55] Schifrin, Leonard G. "Ethical Drug Industry: The Case for Compulsory Patent Licensing." Antitrust Bulletin, Vol. 12 (September, 1967), pp. 893-915.

[56] Schwartzman, David. Innovation in the Pharmaceutical Industry. Baltimore: The Johns Hopkins University Press, 1976.

[57] Silverman, Milton and Lee, Philip R. Pills, Profits, and Politics. Berkeley: University of California Press, 1974.

[58] Steele, Henry. "Monopoly and Competition in the Ethical Drugs Market." Journal of Law and Economics, Vol. 5 (October, 1962), pp. 131-163.

[59] Sylos-Labini, Paolo. Oligopolio e progress technico. Milan: Giuffrè, 1957.

[60] Telser, Lester G. "The Supply Response to Shifting Demand in the Ethical Pharmaceutical Industry." Drug Development and Marketing. Robert B. Helms (ed.). Washington, D.C.: American Enterprise Institute, 1975, pp. 207-223.

[61] Telser, Lester G. et al. "The Theory of Supply with Applications to the Ethical Pharmaceutical Industry." Journal of Law and Economics, Vol. 18 (October, 1975), pp. 449-478.

[62] "Test-Tube Life: Reg. U.S. Pat. Off." Time (June 30, 1980), pp. 52-53.

[63] Theil, H. Principles of Econometrics. New York: John Wiley & Sons, Inc., 1971.

[64] Walker, Hugh D. Market Power and Price Levels in the Ethical Drug Industry. Bloomington: Indiana University Press, 1971.

[65] Wardell, William M. "The History of Drug Discovery, Development and Regulation." Issues in Pharmaceutical Economics. Robert I. Chien (ed.). Lexington, Maine: D. C. Heath and Company, 1979, pp. 3-11.

[66] Weiss, L. W. "Quantitative Studies of Industrial Organization." Frontiers of Quantitative Economics. M. D. Intriligator (ed.). Amsterdam: North-Holland Publishing Company, 1971, pp. 362-403.

[67] U.S. Department of Commerce, Bureau of the Census. Statistical Abstract of the United States. Washington, D.C.: U.S. Government Printing Office, 1979.

[68] U.S. Department of Health, Education, and Welfare. The Impact of Comprehensive National Health Insurance on Demand for Health Manpower. Washington, D.C. U.S. Government Printing Office, July, 1976.

[69] U.S. Senate Committee on the Judiciary, Subcommittee on Antitrust and Monopoly. Report of the Study on Administered Prices in the Drug Industry. 87th Congress, 1st Session, 1961.

[70] _____. Hearings on Administered Prices. 86th Congress, 1st Session, 1960.

[71] Vernon, John M. "Concentration, Promotion, and Market Share Stability in the Pharmaceutical Industry." Journal of Industrial Economics, Vol. 19 (July, 1971), pp. 246-266.

VITA[2]

Shiu-fang Yu

Candidate for the Degree of

Doctor of Philosophy

Thesis: AN ECONOMIC ANALYSIS OF THE NET RATE OF ENTRY IN PRESCRIPTION DRUG MARKETS

Major Field: Economics

Biographical:

Personal Data: Born in Taiwan, Republic of China, March 21, 1949, the daughter of Mr. and Mrs. C. J. Yu.

Education: Received Bachelor of Arts degree in Economics from National Taiwan University in June, 1971; received Master of Science degree in Economics from Oklahoma State University in July, 1973; completed requirements for the Doctor of Philosophy degree in Economics at Oklahoma State University in May, 1981.

Professional Experience: Graduate assistant, Department of Economics, Oklahoma State University, 1972-1975; research associate, Department of Economics, Oklahoma State University, 1975-1976; part-time instructor, Department of Economics, Oklahoma State University, 1976-1977; marketing research analyst, Department of Marketing and Sales Research, Merck Sharp & Dohme, 1977-1979.