FOREIGN COMPETITION AND THE UK PHARMACEUTICAL INDUSTRY

Arthur W. Lake

Working Paper No. 155

NATIONAL BUREAU OF ECONOMIC RESEARCH, Inc.
261 Madison Avenue
New York, N.Y. 10016

November 1976

Preliminary; Not for Quotation

The research reported on in this paper was financed by a grant from the National Science Foundation to the National Bureau of Economic Research for a study of The Impact of Multinational Firms on Technology and Trade Flows. Any opinions, findings, conclusions, or recommendations expressed herein are those of the author and do not necessarily reflect the views of the National Science Foundation.

NBER working papers are distributed informally and in limited number for comments only. They should not be quoted without written permission.

This report has not undergone the review accorded official NBER publications; in particular, it has not yet been submitted for approval by the Board of Directors.

CONTENTS

FOREIGN COMPETITION AND THE UK PHARMACEUTICAL INDUSTRY

1. Introduction

a) Basic Issues and Approach. The British pharmaceutical industry has had an enviable record of innovation throughout the post-war period.[1] Nevertheless,

[1] A review of British innovative activity is contained in NEDO [1973, 1].

a substantial number of new ethical drugs issued in the United Kingdom have arisen from research of foreign companies who by their operations have influenced British firms.[2] The stimulating effects of transnational market-entry

[2] NEDO [1973, 1], p. 30.

activity on British companies in the industry have contributed substantially to its structural change and growth. It is thus of interest to economists to inquire how much competitive pressure is put on host-country firms, how they respond, and with what speed they can enter newly emerging markets. This paper, which seeks to identify factors contributing to the rate and character of technical transfer and to assess host-country research and development effort in response to foreign competition, is one of three examining the impact of technically-advanced companies, particularly American, on British industries.[3] Beginning first with an analysis of imitation cycles in

[3] In this connection, the reader may find it useful to read the first study of the series, which covers the British semiconductor industry, Lake [1976]. The paper by Cohen, Katz and Beck [1975] is also very relevant in this regard.

pharmaceuticals and making use of a model of these, the study proceeds to examine the transnational operations of American and other foreign companies, showing the connection between company size, sales and new product introductions.

The competition among firms selling ethical products, which form the most technically advanced part of the pharmaceuticals market, is based primarily on new product introductions consisting of new chemical entities and permutations of the specific qualities or combinations of drug components. Research activity in the post-war period appears to have concentrated primarily in the creation of new and substitute products with less attention devoted to the improvement of the economies of manufacture as through automation in order to reduce costs.[4] Manufacturing economies frequently have been achieved not so

---

[4]McDonald [1973], pp. 23-27. Only a few of the very major products are manufactured in bulk form, such as the antibiotics, penicillin, the tetracyclines, neomycin, and the cortisones. Thus among ethical products only a small percentage provide scope for substantial economies of scale. In the case of over-the-counter proprietary products the proportion of the total number is much larger.

---

much by mechanization or scaling-up production throughputs, but by the creation of new material sources for chemical entities or the replacement of natural sources with synthetics.[5] These technical advances in their final useful forms

---

[5]Many of the discoveries in pharmaceuticals of the post-war period are associated with the development of synthetic substitutes for natural products.

The synthetics permit greater control over quality and more easily lend themselves to the scaling up of production runs.

---

constitute new products. Our approach is to treat them individually, placing them within the time scale and competitive situation of the imitation cycle.

b) The Data. Considerable time has been spent in the collection and classification of data and information for the studies undertaken. The work was divided into four groups: 1) individual pharmaceutical products, over one thousand in all, 2) companies introducing pharmaceutical products into the UK, numbering in excess of one hundred and fifty over the twenty-three year period, 3) company patent rights over the sale of individual pharmaceutical products, including products patented before 1950, in order to ascertain how "new" the medicinal substances were, and 4) classifications of medicinal substances into therapeutic groups, into chemical-action groups, and into families of chemical substances. The data are employed to establish imitation cycles as outlined in Tables 1 and 2 and as described in the following section 2c. Table 4 gives the original therapeutic classes, used. Information on products introduced into the UK covered the period from January 1950 to December 1972. The study made use of standard references such as the Martindale Extra Pharmacopea, the Monthly Index of Medical Specialties (MIMS), the NEDO (Centre for the Study of Industrial Innovations, CSII) list of 466 new chemical substances 1958-70, journals such as the Pharmaceutical Journal, the Chemist and Druggist, and standard texts.[6] We also employed information for American products given in the

---

[6] See Wilson, Grisvold, and Doerge [1971].

TABLE 1

List of Imitation Cycles
(A)

Drug or Chemical Name	First Drug Introduced	First Date of Issue	First Company	Type[1]
Alimentary System				
1 Anticholinergics	procyclidine	(11/51)	Wellcome	II
2 Synthetic Cathartics	bisacodyl	(4/56	Lewis Labs	III
Cardiovascular System				
3 Vasodilators (Nitrates)	PETN	(6/53)	Bayer Winthrop	II
4 Vasodilators (Excl. Nitrates)	phentalamine	(7/54)	CIBA	III
5 Reserpine and Synthetics	alseroxylon	(11/53)	Riker	II
6 Adrenergic Sympathetic Amines	nylidrin	(9/54)	Smith & Nephew	II
7 Thiazides (i.e. Diuretics)	clorothiazide	(1/58)	Merck Sharp & Dohme	II
8 Non-Thiazide Hypertensives	hydrolazine	(10/53)	CIBA	III
Central Nervous System				
9 Analgesics (Non-Opiate)	nifenazone	(9/58)	Trommsdorf	III
10 Analgesics (Synthetic)	dipipamone	(11/55)	Burroughs Wellcome	III
11 Sedatives	promethazine	(11/52)	May & Baker	III
12 Phenothiazines (Alkyl, Piporidyl, and Propyl Piperazine	piperazine	(3/53)	British Drug Houses	II
13 Phenothiazines (Propyl Dialky)	phenothiazine	(1/54)	May & Baker	II
14 Analeptics	methylphenidate	(1/55)	CIBA	III
15 MAO Inhibitors	iproniazid	(11/57)	Roche	III
16 Dibenzazepine and Derivatives	imipramine	(1/59)	Geigy	II
17 Antiemetics	diphenhydramine	(8/50)	Parke Davis	II
18 Epilepsy Drugs	phenylacetylurea	(6/52)	Abbott	III
19 Antiparkinson Drugs	diphenhydramine	(8/50)	Parke Davis	III
Musculo-Skeletal Disorders				
20 Mephenesin	mephenesin	(11/53)	Clinical	I
21 Muscle Relaxants (Glycols, benzodiazepines)	methocarbamol	(8/58)	A.H. Robins	III

[1] I, Same chemical entity.
II, Same chemical family or closely related family.
III, Similar therapeutic action, different families.

TABLE 2

List of Imitation Cycles
(B)

Drug or Chemical Name	First Drug Issued	First Date of Issue	First Company	Type[1]
Hormones				
22 Modified Progestins	norethynodrel	(11/57)	Searle	II
23 Oral Contraceptives	same	(2/62)	Searle	II
24 Androgens and Modifications	nor-androstenolone phenyl propionate	(9/57)	Organon	II
25 Hydrocortisone	same	(11/55)	Merck Sharp & Dohme	I
26 Prednisolone	same	(6/55)	Upjohn	I
27 Modified ACTH	fluorohydrocortisone acetate	(8/56)	Squibb	II
28 Sulfonylureas	carbutamide	(10/56)	Boots	II
Genito-Urinary System				
29 Non-Thiazide Diuretics	spironolactone	(4/60)	Searle	III
Infections and Infestations				
30 Phenoxymethyl Penicillin (V)	same	(2/56)	Lilly	I
31 Semi-synthetic Penicillins	xanthocillin	(2/59)	Distillers	II
32 Neomycin Sulfate (Dermat.)	same	(7/53)	Squibb	II
33 Streptomycin Family	kanamycin	(11/59)	Bayer Winthrop	II
34 Polypeptide Antibiotics	polymixin B	(4/54)	Wellcome	II
35 Other Antibiotic	tyrothricin	(1/53)	Warner	III
36 Antituberculosis Drugs	PAS	(5/50)	Wander	III
37 Anthelmintics	diethylcarbamazine	(6/53)	British Drug Houses	III
Other Groups				
38 Non-Narcotic Antitussives	carbetapentone citrate	(10/55)	Pfizer	III
39 New Local Anesthetics	amethocaine	(3/56)	Allied	II
40 New Xanthine Derivatives	acepiphylline	(11/55)	Rona	II

[1]
I, Same chemical entity.
II, Same chemical family or closely related family.
III, Similar therapeutic action, different families.

deHaen lists for the period January 1963 to December 1972. Data on patents were obtained through the Merck Index. Data on individual companies were derived from annual reports of individual companies, through telephone calls, and publications such as Standard and Poor (America), and Dun and Bradstreet (United Kingdom). Ownership of companies was derived from Who Owns Whom for the UK and Europe. The most complete coverage of company data relates to the year 1971.

The products of the ethical drugs group of the pharmaceutical industry may be classified in a number of ways dependent on the forms in which individual substances are marketed. In the deHaen index pharmaceutical products are grouped according to chemical form: 1) single chemical entities: new drugs marketed for the first time in America by any manufacturer; 2) duplicate products: single entity drugs that have been previously sold by another manufacturer in America; 3) combination products: containing more than one active ingredient; and 4) new dosage forms. The deHaen type of index is inadequate for use as an index of innovation since such lists frequently contain minor new drug improvements, or competitive introductions, weighted equally, i.e., numerically, with the major new drug discoveries representing significant therapeutic advance. A genuine index of innovation should include only new drugs of major medical importance, hence "unculled" data, such as provided by deHaen, needs to be whittled down according to strict exclusion rules. The classifications employed in this study used forms of both "raw" and "culled" data.

Table 3, which follows, outlines the main therapeutic groups that formed the first classification of the data. Tables 7, 8, and 9 identify the principal American, British and European firms included in the data sample. Appendix Table A6 lists other firms operating in the United Kingdom.

TABLE 3

List of Major Therapeutic Groups[1]

1. Alimentary System
2. Cardiovascular System
3. Central Nervous System
4. Musculo Skeletal Disorders
5. Hormones
6. Genito-urinary System
7. Infections and Infestations
8. Nutrition
9. Respiratory System
10. Ear, Nose and Oropharynx
11. Eye
12. Allergic Disorders
13. Skin
14. Metabolism
15. Surgical
16. Diagnostic Agents

[1]For a more detailed breakdown see appendix Table A1.

2. Characteristics of Imitation Cycles in Pharmaceuticals

a) Competition and Research Plateaus. The nature of rivalry in the pharmaceuticals industry, particularly in ethical drugs, is such that economists are consistently in the dark or in disagreement about the extent of competition or monopoly actually prevalent. The objectives and strategy of research and development activity towards new products and product differentiation are somewhat different from those underlying the price competition in nonresearch-intensive industries. For example, the ethical drug company may enhance its competitive position with the exchange of the use of a discovery for a cross-licencing agreement if it is not directly interested in exploiting its discovery.[7] Because the activity of product introduction is so important, we have

---

[7]Writers such as Steele [1964] suggest that the extent of competition amongst drug companies is much less than generally thought.

---

established a framework by which new product competition can be examined and which easily relates to the analysis of transnational market entry. The result of our work is the concept of the imitation cycle, which is based on the frequently observed pattern of competition within ethical product groups.

The term imitation is used principally to denote the competitive activity within a commercial or scientific area that appears to be directly in response to, or related to, a major advance in knowledge. As the term imitation cycle suggests, the competition between companies in the period following a major discovery often takes the form of a burst of rival activity.

The speed with which firms can respond to the commercial possibilities opened up by the discovery can determine their share of the eventual markets created. Once the leaders have introduced a wide range of new products making

use of the new technology, subsequent firms may increasingly find that technical limitations are obstacles to profitable market entry. Furthermore, once the leaders have taken the easier markets, the pool of potential new entrants may become smaller. These and other factors often lead to a slowing-down of the pace of imitation and to a progressive diminishing of the numbers of new entrant firms. The period over which the slackening of the pace of market entry takes place can be referred to as the plateau period. Generally, an imitation cycle, if measured in terms of new market entrants or with respect to time, will, in its cumulative form, tend to level off, and to form a plateau. This gives the imitation "cycle" a characteristic "S" shape as illustrated in Figure 2. The independent research and development efforts which lead to market entries may also, if aggregated, be seen to plateau.

The imitation cycle in pharmaceuticals constitutes a set of new products which are substitutes in therapy or in usage. Although no actual measurements of this substitution have been undertaken we have tried to establish what drugs were most frequently prescribed within therapeutic areas. This was done with the aid of the Martindale Extra Pharmacopea, the Monthly Index of Medical Specialties (MIMS), and other publications. In the course of this work, it was found that very important chemical groups frequently overlapped each other in their therapeutic applications, or that they developed into chemical or therapeutic branches which could be examined on their own. The classifications eventually arrived at involved a judgment concerning the type of imitative or innovative activity most probably undertaken by firms that entered the markets defined by the groups. Three main types of imitation cycle emerged which are described in a later part of this section.

Pharmaceutical companies go to great lengths to protect their monopoly advantages. The very successful company may be able to limit the numbers of rival entries significantly. Our analysis shows the importance of technical advantages reflected in the number of firms eventually entering therapeutic, chemical, or market groups. To understand the industry more fully the economist may seek to disentangle whether limits to the number of entrants are the result of physical factors, monopoly advantages, strategies or collective welfare decisions. This is not a simple task.[8] Our examination of imitation

---

[8]Some of the problems are mentioned in the paper by Steele [1964].

---

cycles covers those regions of competitive activity where many of the monopoly advantages, for the most part, have broken down.

Our work revealed considerable cross-licencing between companies, sometimes rivals in similar markets. It may be proposed, though by no means established, that such activity amongst larger firms, especially the international ones, constitute the bargaining and exchange of concessions between rival companies for "safe" markets. Such arrangements could operate providing competitors hold key patents to rivals' markets or areas of prospective expansion.

The licencing of British companies was found to be very significant. The impact of the licencing of smaller British companies needs to be considered within the market framework of their competitive activity. The concept of the imitation cycle assisted us in analyzing licencing activity on this basis.

Various explanations of the plateau pattern, that is, the deceleration in the rate of introduction of new chemical entities following an initial burst of activit

have been put forward in the literature.[9] The particular case of the

[9]See Jennings [1971], pp. 247-256; and Cohen, Katz and Beck [1975], pp. 19-26.

antihistamine-based family of drugs is worth special attention in this regard, since it represents one of the most fruitful sources of new drugs of the post-war period. It is also a key to understanding various competitive aspects of the pharmaceuticals industry. The following part looks briefly at the antihistamine group and its bearing on developments in the industry.

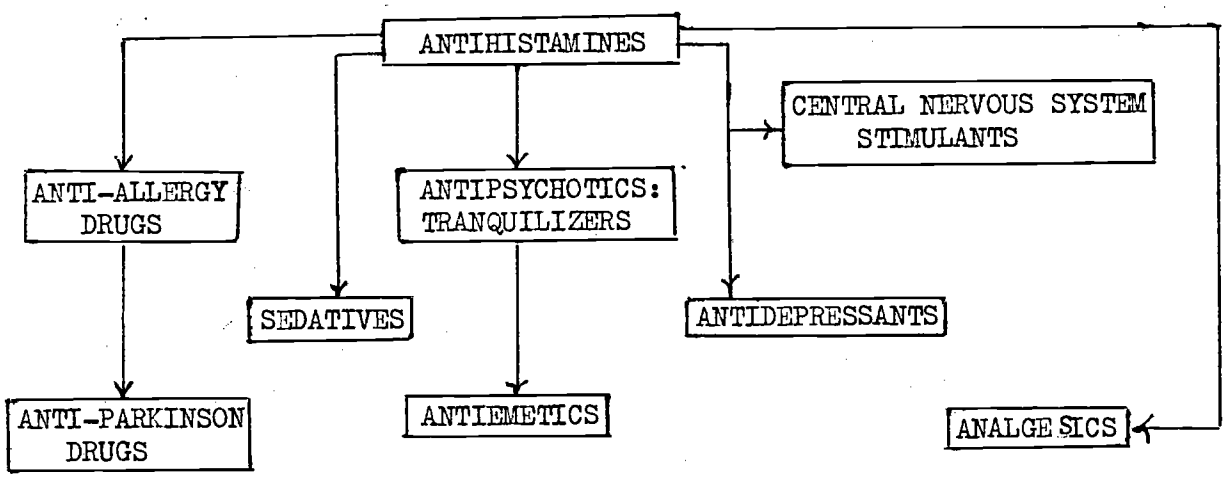
b) The Antihistamines. One of the most prolific chemical groups of the post-war period for new drugs has been the antihistamines. By the early 1960s most of the new chemical entities derived from this group, in excess of five hundred in number, had been tested. Those of therapeutic value, about fifty in total, had been patented. The imitation cycle of antihistamine drugs contains chemical entities of the same basic family. The antihistamines have a number of actions on living organisms branching into a wide range of therapeutic ones as shown in Figure 1. They exhibit the properties of local anesthetic, adrenergic blocking, antispasmodic, sympathomimetic, analgesic, cholinergic blocking, and quinidine (like).[10]

[10]See Wilson, Grisvold and Doerge [1971].

To examine the imitation cycle of this drug group it is necessary to treat all its members as part of a flurry of research activity that in this case has been international. Having done that, it is then possible to consider the

FIGURE 1

Research Into Antihistamines Giving Way to New Chemical Entities in a Wide Number of Therapy Areas



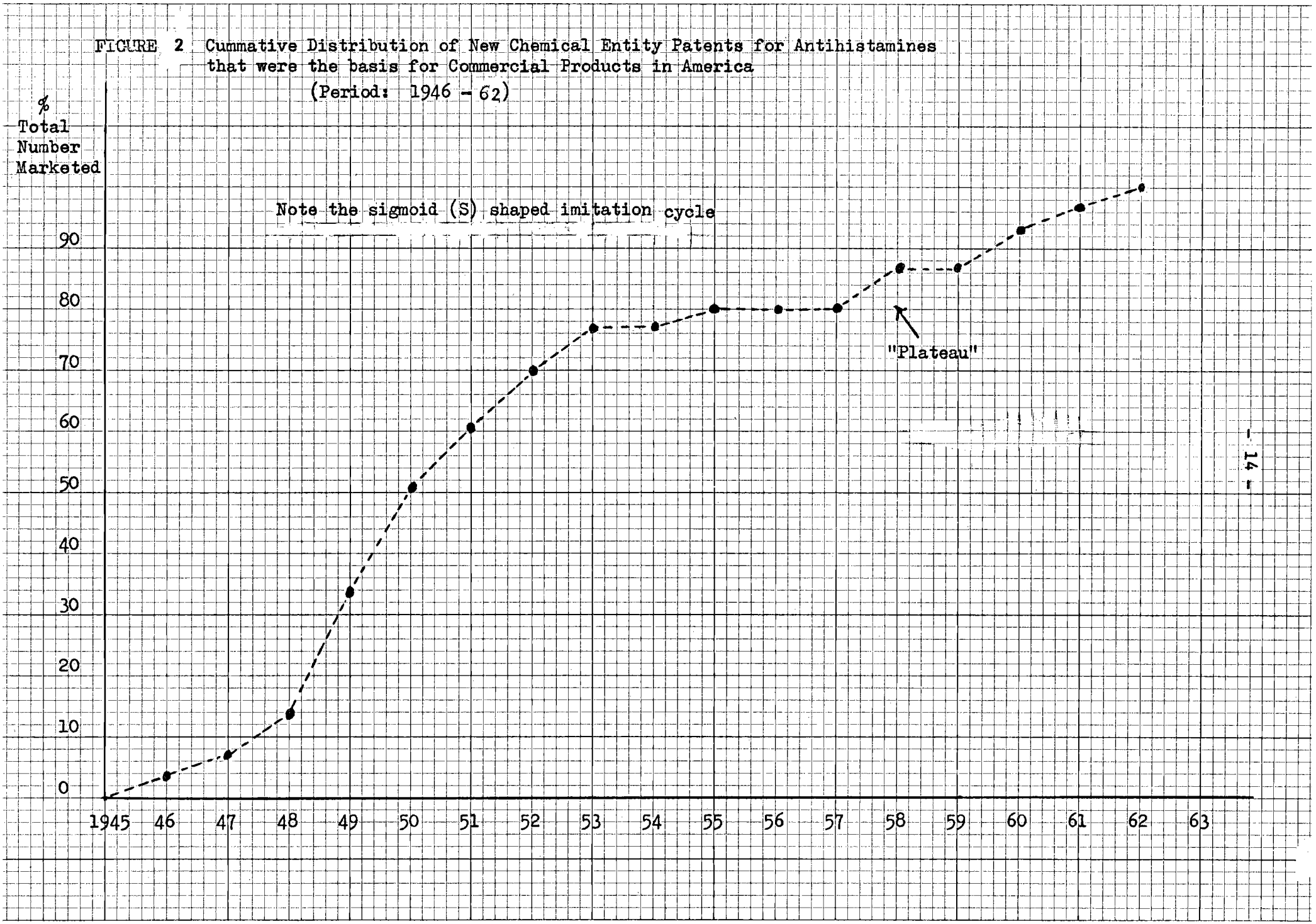
Source: Biel and Martin [1971], p. 87.

sub-groups of chemical entities which go to make up the whole imitation cycle. The sub-groups will often display a particular chemical, as well as therapeutic property, and so a sub-imitation cycle neatly follows. The phenothiazine sub-groups can be considered in this way. The competitive cycle in any one therapeutic group may not be dominated by a given family of chemical entities, and in such cases the term imitation implies competitive activity in the search for chemical entities with certain therapeutic properties, but of a different chemical make-up. Such imitation cycles do not display the same consistency in the pattern of new product timing as cycles within a chemical group, but greater consistency if found if the size of end market is substantial than if it is small. A large market attracts greater numbers of companies to search for new drugs over a wider range of chemical groups, and to concentrate efforts for a solution within a shorter space of time.

The imitation cycle of antihistamine drugs marketed in the States is reflected in the timing of patents issued for the drugs as represented in Figure 2. It is apparent that while patent data on its own may be of limited value, it can be useful when supplemented, and culled, by data on the drugs actually marketed. One of the interesting aspects of the cycle represented in Figure 2 is that the plateau in the discovery of new antihistamines was reached well before the 1962-FDA rule changes. In fact the plateau effects were really being felt as early as 1953. Data on the introduction of new antihistamine products for the post-62 period would, nevertheless, catch the plateau period of antihistamine derivatives, perhaps, as part of the "legislative" effects (i.e., in terms of new drugs introduced).

c) Types of Imitation Cycles. An imitation of a new chemical entity means that the same new substance may be introduced into the host-country by more than one company. Such imitations, identical imitations, are to be distinguished

FIGURE 2 Cummative Distribution of New Chemical Entity Patents for Antihistamines that were the basis for Commercial Products in America
(Period: 1946 - 62)



from imitative substances, that are part of the same chemical family, but whose chemical makeup is slightly different. Imitations can be derivatives of an original substance, which when modified through chemical change, lead to a new substance. They can be analogs of an original discovery, and this means that, though chemically different, the original substance and its analogs have similar structure, or parallel structure. Analogs often show similar chemical activity so that a rival firm, that finds an analog to another company's drug, may have the key to a better or equal substitute for its product.

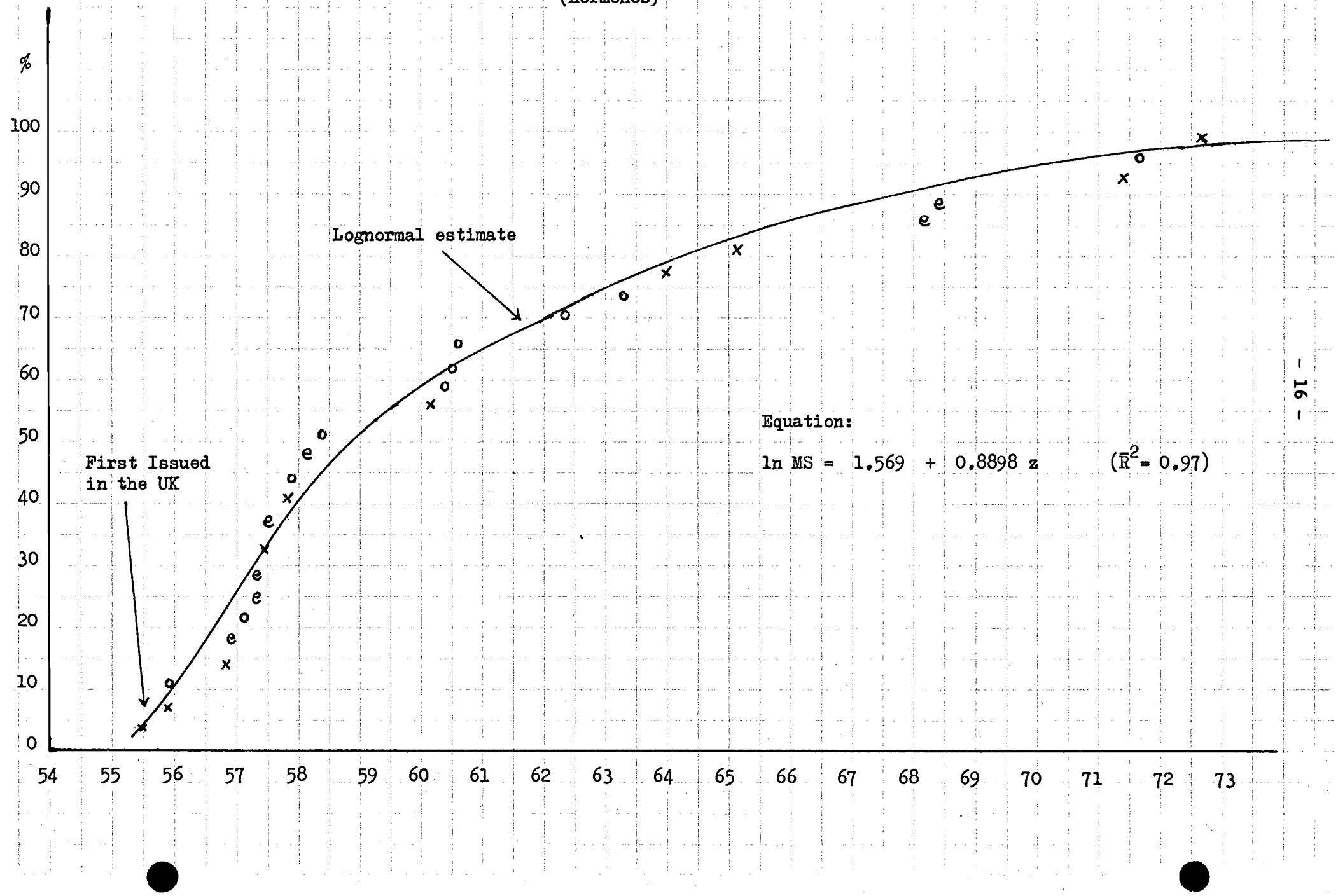
The flurry of competitive activity to find substitutes within a chemical group or across groups tends to display cycle characteristics, i.e., the movement towards a plateau following a rapid period of discoveries. The plateau can frequently be explained as a saturation effect. If a chemical family yields relatively few new drugs, but these are sufficient therapeutically, progress within the therapeutic group may be dominated by the one chemical family, with its best derivatives accounting for the greatest share of the market. A larger market and a less satisfactory therapeutic solution can result in a search for new substitutes in other chemical groups. Then again, a chance discovery in another group may lead to competition in the search for and testing of new derivatives.

Three types of imitation cycle are included in our analyses. The first involves the single chemical entity that is widely imitated. This imitation might be facilitated because there is no patent protection to any particular company, or the discovery is freely licenced by a company that has the patent. Generally when such a cycle is large the scope of the market for which the chemical entity is used is also large. For an example of this type of imitation activity consider Figure 3, which illustrates the imitation cycle for prednisolone,

FIGURE 3

Prednisolone

(Hormones)



a modified hormone derivative of ACTH and hydrocortisone.[11]

---

[11]A brief coverage of the corticorteroid hormone discoveries is given in Henry Steele [1964], pp. 202-212. For a more detailed examination see Applesweig [1962], pp. 9-52.

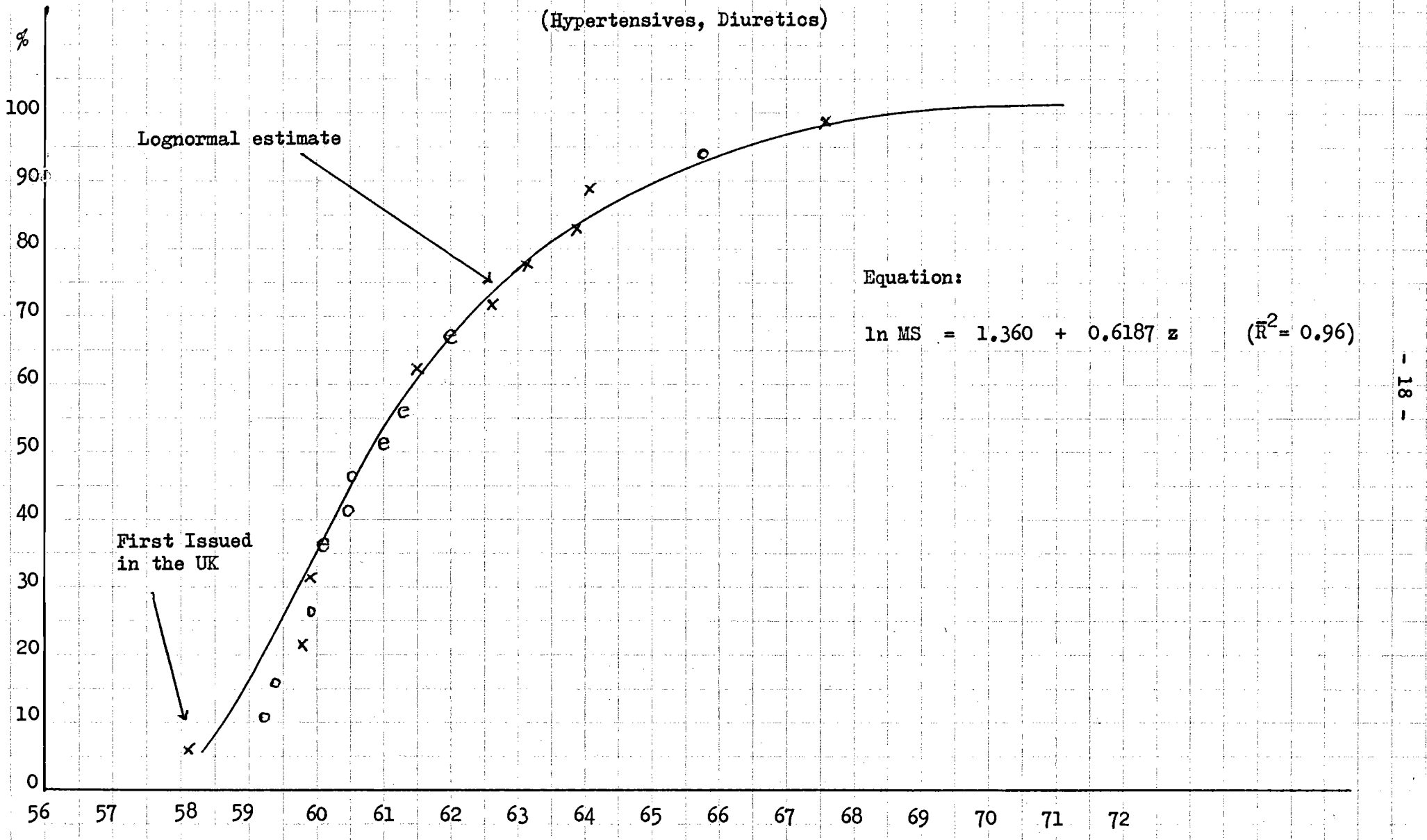
The second type of imitation cycle studied is that of closely related derivatives of a newly emerging chemical group. A good example of such a cycle, illustrated in Figure 4, is that of the thiazides, developed for both hypertensive and diuretic treatment. All the thiazides belong to the same chemical family, and many of the analogs of the thiazide molecule represent little structural change, but the dihydrochlorothiazide derivative has a stronger potency (10 times more than chlorothiazide) and less toxicity. The benzothiadiazine derivatives, as otherwise known, are a substitute for meralluride, a parenteral drug developed in the early 1940s. The thiazide drugs owe their discovery to research carried out on sulfonamides of which they are a subgroup. Like the antihistamine group the sulfonamide group has been a prolific source of new chemical entities, but in both the pre- and post-war periods.

The third type of imitation cycle includes new chemical entities of more than one chemical group, but having similar therapeutic value. The MAO inhibitors are just such a collection of drugs. The original impetus to discovery of this group came from the drug iproniazid, studied for its anti-tuberculosis activity. A related drug isoniazid was found to be more suitable for tuberculosis treatment, since iproniazid tended to have the side effect of exciting patients treated. This stimulant quality of iproniazid was researched at greater depth, and the drug was found to be very useful in psychotherapy applications. The drug is a member of the hydrazine group, and other hydrazines were explored

FIGURE 4

The Thiazides

(Hypertensives, Diuretics)



Equation:

$\ln MS = 1.360 + 0.6187\ z \qquad (\bar{R}^2 = 0.96)$

for the same use. The chemical process by which these hydrazines have their stimulant effect was termed MAO inhibition. In a very short time drugs outside the hydrazines were found that could act in the same way, and in the early 1960s several non-hydrazines were tested. The imitation cycle of the MAO inhibitors introduced into the UK is shown in Figure 5.

All three of the above types of imitation cycle are amenable to experiments using the smooth time profile created with the lognormal model which is developed in the next section. The patent protection offered to new chemical entities can, however, lead to a slightly different pattern of imitative activity. This can occur because of a chemical structure that is not easily imitated, or to which there are few analogs or readily obtainable derivatives. Occasionally, all the derivatives that are found are much less effective than the innovator's patented chemical entity (ies). Once the patent of the drug expires, i.e., after sixteen years in the UK, and if the market for the drug is very large, then a period of intense competitive activity normally results. During this period host-country firms, where the innovator is a foreign company, can share in the drug's market through close imitation. Nothwithstanding this fact, the innovating company may have a reserve strategy, or contingency plan, already in motion. One such strategy involves delaying of the patenting of the original drug's successor, which can be both a costly and risky process. The firm has first to find a superseding drug, and then to delay the patent so as to derive a continuous form of protection for its proprietary expertise.

The tetracycline group of drugs illustrate the intense competitive activity following the period of patent protection. A number of tetracycline drugs have been marketed in the UK by American-owned companies, i.e., Lederle of Cyanamid, and Pfizer. Carlo Erba, an Italian company, has also marketed a drug of the tetracycline family. The period of intense competitive activity following the period of patent protection is shown in Figure 6. It would appear that the more remarkable the original drug the stiffer the competitive situation when the

FIGURE 5

MAO Inhibitors

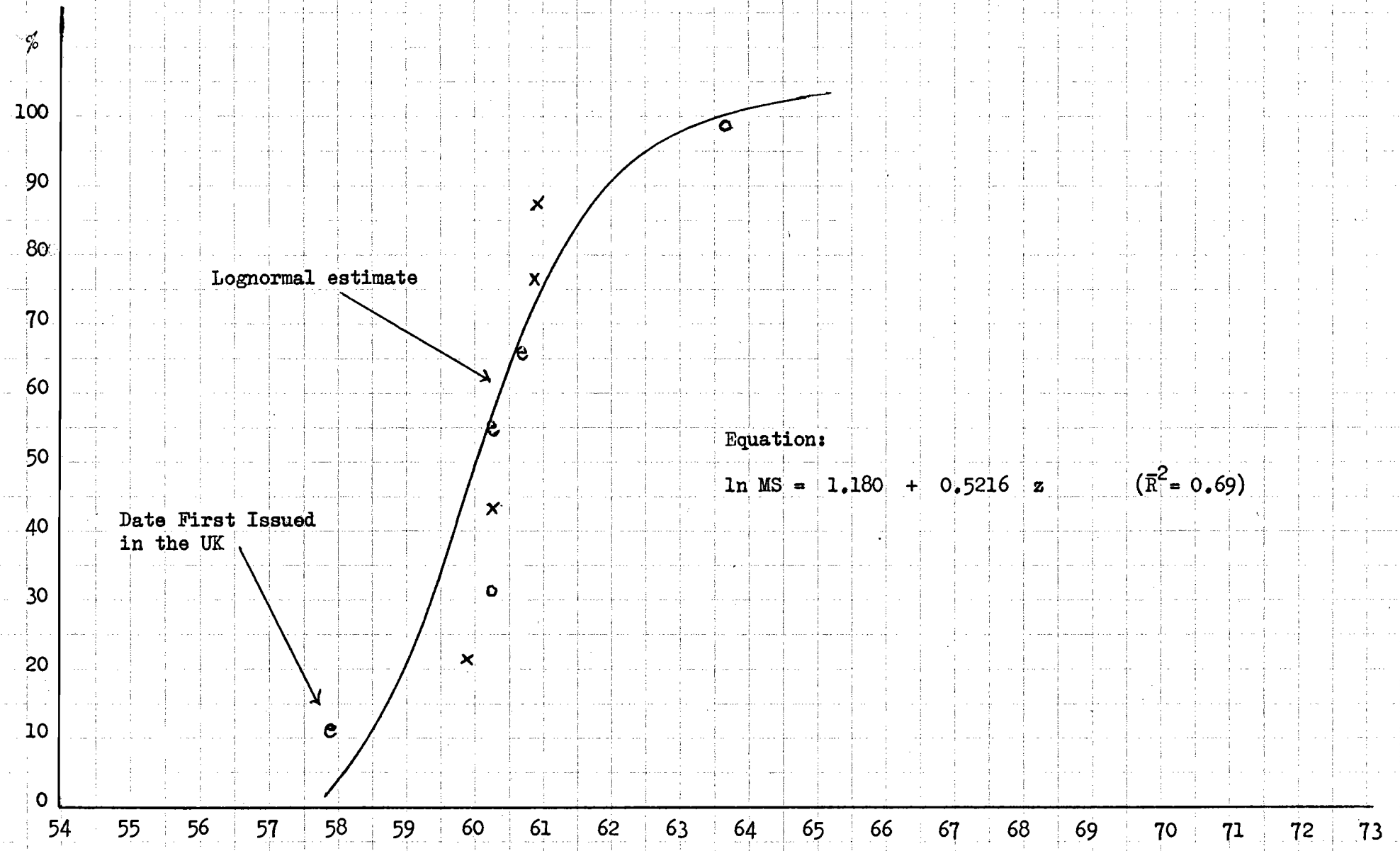
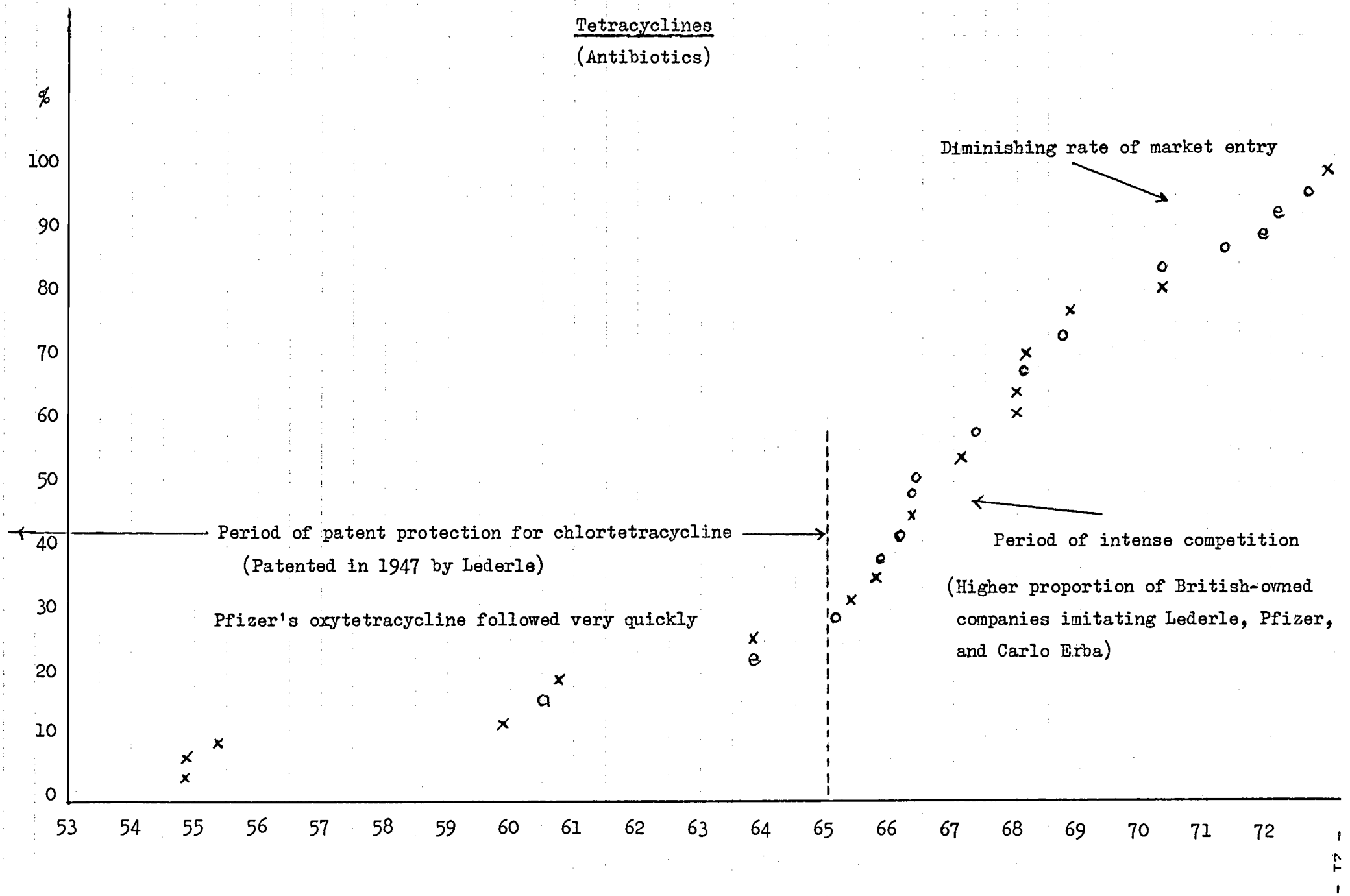


FIGURE 6


Tetracyclines
(Antibiotics)
%
100
90
80
70
60
50
40
30
20
10
0
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
Diminishing rate of market entry
Period of patent protection for chlortetracycline
(Patented in 1947 by Lederle)
Pfizer's oxytetracycline followed very quickly
Period of intense competition
(Higher proportion of British-owned companies imitating Lederle, Pfizer, and Carlo Erba)

patent expires. The imitations, as represented in the graph, do display a pattern similar to the cycles already discussed, but with the monopoly (or oligopoly) period preceding.

d) Technology Transfer and Transnational Market Entry. It becomes apparent from our analysis that the rivalry between leading pharmaceutical companies in the postwar period was rarely confined to national economies. For competitive reasons, many of the leading companies have operations in more than a dozen countries, often marketing on a worldwide basis, and frequently creating new technology or improving existing processes in more than one country. Progressive drug companies, developing new markets or technical areas, often established foreign subsidiaries or made supply and licencing arrangements with foreign companies. Furthermore, very novel pharmaceutical products tended to require a significant marketing and therapeutic effort, which normally called for an increased local presence.

Some of the key factors behind the transfer of drug technology between the United Kingdom and the United States are discussed in section 4. The important aspects of technology transfer considered relate to the direction in which it takes place, the lead or lag between market entry in source and recipient countries, and the firms responsible for technology transfer and creation. A sample of 74 new drug products is used.

3. A Model of the Imitation Cycle

a) Methodology. The experiments carried out on the imitation data are of three basic kinds. The first examines the overall time pattern of market entry taking the imitation lags MS as observations. These are the lags found between the date of the first introduction of a drug into the UK and introductions by imitating companies, and are measured to the month. The lognormal model is used for estimating the characteristics of the time pattern of market-entry

introductions MS. The regressions for the model are based on the following formulation where MS takes its natural log form:

$$\ln MS = \mu \text{ (i.e., mu)} + \sigma \text{ (i.e., sigma) } Z + e \qquad (1)$$

Z = normal equivalent deviates

e = error terms

Each equation estimated thus has two parameters, mu and sigma, which vary from cycle to cycle, and are indicative of the time pattern of each imitation cycle. Variations in mu generally are indicative of forward or backward shifts in the average timing of market entries, while variations in sigma are indicative of bunching or clustering of imitative market-entry activity. A low value for mu thus tells us that firms are generally early in their introductions (the imitation lags on average are short), while a low value for sigma suggests that firms tend to enter together rather than being spread out over the imitation cycle. These parameters of the lognormal model have several other useful properties.[12]

---

[12] A more detailed explanation of the model is given in Lake [1976].

The second kind of experiment is designed for the purpose of assessing individual company positioning within the cycle. Three types of index are used for this purpose, and all pertain to the individual company's activity. The first index, the unweighted index, is a count over all the imitation cycles of the numbers of chemical entities that the particular firm has introduced. The second index, a weighted index, assigns a weight to the participation in individual cycles depending on the positions held by drugs of the company. If the position held is 1st then the weight value (w_1) assigned is 12, 2nd is 11,

and so on to the 12th, which, along with subsequent introductions, is weighted by 1. The index for the jth company thus is compiled as follows:

$$W_j = w_1 m_{1j} + w_2 m_{2j} + w_3 m_{3j} + \ldots + w_n m_{nj} \qquad i = 1, \ldots, n \qquad (2)$$

m_i = number of cycles in which company j was in rank i.

w_i = weight value assigned to rank i ($w_1 = 12$, $w_2 = 11$, $w_3 = 10$ ... $w_{12} = 1$, $w_{13} = 1$ ...).

The final value of the index is W_j. The weighted index gives an estimate of the timing of new chemical entity introductions that is characteristic of the company involved. A company that is consistently first to introduce new drugs in new chemical areas will have a high index value.

A further refinement, index three, makes use of the weight values w_i described above. The sum of these for an imitation cycle k, which is $(\Sigma w_i)_k$, can be used to "normalize" the weights for individual market entries, the w_{ik}. Aggregation of these "normalized" values, i.e., the x_k for the firm, provides us with another measure of performance of the firm for the imitation cycles in which it has participated.[13] Moreover, this "normalized" performance index

---

[13]For example, a firm that is second in imitation cycle three and ninth in imitation cycle twenty-five, receives the index three value: 11/81 + 4/93 = .179. Imitation cycle number three has fourteen participants, and number twenty-five has twenty-six participants; thus $(\Sigma w_i)_3 = 81$ and $(\Sigma w_i)_{25} = 93$.

---

takes into account the eventual number of firms participating in the imitation cycles where market entry is made. Computation of index three is as follows:

$$\text{Index three} = \Sigma x_k = \Sigma \left[w_{ik} / (\Sigma w_i)_k \right] \qquad (3)$$

Furthermore, a measure of average performance can also be derived based on the average values of the "normalized" weights comprising index three. This measure, denoted as $\bar{x}$, is derived as follows:

$$\bar{x} = \Sigma x_k / N$$

where,

$$x_k = w_{ik} / (\Sigma w_i)_k$$

N = the number of market entries made by the firm.

Associated with the average performance of the firm is the standard deviation value s, of the consistency with which the average $\bar{x}$ was maintained. It enables us to examine another important aspect of the individual firm's performance.

The third set of experiments makes use of the dates of market entry within imitation cycles for each company to build up a performance profile based on the imitation lags L_{ij} (for ith company), of the jth imitation cycle. The formulations employed are as follows:

$$L_{ij} = t_{ij} - t_{oj}$$

= imitation lag for the ith company within the jth imitation cycle

where:

t_{oj} = date that the first product of the jth imitation cycle was introduced into the UK (month/year)

t_{ij} = date the product of the ith company was issued (month/year) in the jth imitation cycle.

The average imitation lag for each company i over the imitation cycles is then:

$$\bar{L}_i = \sum_{j=1}^{n} L_{ij}, \qquad (4)$$

n = number of imitation cycles

The values for $\bar{L}_i$ are then used to compare differences between companies and groups of companies on the grounds of nationality of ownership, size, or scope of operation.

b) Estimation and Results. The results of the first two sets of experiments are summarized in this section and those of the third set make up the analysis of section 5. The new drugs covered represent the glamour markets of the pharmaceutical industry. The analysis that follows examines the participation by host-country and foreign-owned firms in these markets in the UK.

The companies of the study have been divided into three groups: American-owned companies, British-owned companies, and companies of other nationality of ownership. Where possible an attempt has been to take the original company rather than the merged enterprise in attributing product introductions, e.g., drugs introduced by Parke Davis are attributed to that company, and a final picture brings together all the drugs under Warner-Lambert with those of William Warner. The sample of imitation cycles covers most of the pharmaceutical markets since an attempt was made to get as complete a coverage as possible given time and resources.[13]

---

[13]Where omissions have occurred, as in the cases of cancer chemotherapy, metal antagonist, and virus drugs, this has been partly due to insufficient data and partly because of the extremely specific nature of the therapy areas. Furthermore, many of the products excluded do not represent profit-making introductions.

The results of the lognormal estimation of imitation cycles given in Table 4 show great variation in values of mu and sigma.[14] It became immediately

---

[14]Normal curves were also estimated, but are not presented in this paper. A modified lognormal model with the base observation, i.e., the first observation, given the values ranging from ln 2, i.e., 0.693, to ln 4, i.e., 1.386, was tried with improvements to the regression coefficients resulting in many cases. These results are also not given in this paper so as to keep the results along the line of the usual lognormal experiments with ln 1, i.e., 0.0, as the base observation. This will permit comparisons to be made with results for imitation cycles estimated in other industries.

---

apparent that the analysis of the pharmaceutical industry would have to differ in important respects from that of other industries because of regulations governing a large part of its competitive behavior. At an early stage the cycles for the post-62 period were examined to see if fundamental differences, such as a marked slowing up of imitative behavior, were characteristic. No definitive conclusion could be reached, but it did appear that new imitation cycles for the post-62 period were remarkably few in number: the oral contraceptives, the post-thiazide diuretics, non-narcotic antitussives (to a limited extent), cancer chemotherapy, the prostaglandins, drugs for rheumatism and arthritis (still few real successes), are some of these. It was also thought that the post-62 period might show itself with an effect on the mature phases of the imitation cycle, making the slowing-up period of new introductions more pronounced, but on this point no definitive answer came. It appeared that no discernible effect of the post-62 period could be found on the imitation cycles already in progress, even for the tranquilizer group. The answer must most

TABLE 4

Results of Lognormal Curve Estimation

Drug or Chemical Name	No.	Mu	Sigma	$\bar{R}^2$
Alimentary System				
Anticholinergics	24	1.912	.7330	0.90
Synthetic Cathartics	9	1.823	.9120	0.77
Cardiovascular System				
Vasodilators (Nitrates)	14	1.825	.9822	0.90
Vasodilators (Excl. Nitrates)	17	1.938	.9341	0.88
Reserpine and Synthetics	21	1.576	.8913	0.91
Adrenergic Sympathetic Amines	14	2.100	.9343	0.77
Thiazides (Diuretics)	19	1.300	.6187	0.96
Non-Thiazide Hypertensives	20	1.983	.8589	0.84
Central Nervous System				
Analgesics (Non Opiate)	11	1.788	.9175	0.88
Analgesics (Synthetic)	13	2.054	.7959	0.80
Sedatives	28	1.951	.9056	0.85
Phenothiazines (Alkyl Piperidyl, and Propyl Piperazine)	19	2.187	.7664	0.85
Phenothiazines (Propyl Dialkylamino)	9	1.441	.9943	0.93
Analeptics	23	1.920	.7214	0.91
MAO Inhibitors	9	1.180	.5216	0.68
Dibenzazepine and Derivatives	10	1.710	.8723	0.88
Antiemetics	13	1.917	1.026	0.86
Epilepsy Drugs	10	1.799	.9648	0.90
Antiparkinson Drugs	13	1.335	.9726	0.91
Musculo-Skeletal Disorders				
Mephenesin	8	.915	.8967	0.93
Muscle Relaxants (Glycols, Benzodiazepines)	21	1.619	.8133	0.92
Hormones				
Modified Progestins	16	1.891	.9256	0.83
Oral Contraceptives	16	1.301	.9283	0.92
Androgens and Modifications	14	1.358	.8988	0.95
Hydrocortisone	26	1.574	.9857	0.94
Prednisolone	27	1.569	.8898	0.97
Modified ACTH	21	1.905	.7897	0.94
Sulfonylureas	8	1.507	1.009	0.74
Genito-Urinary System				
Non-Thiazide Diuretics	9	1.601	.9311	0.92
Infections and Infestations				
Phenoxymethyl Penicillin (V)	14	1.376	.9961	0.93
Semi-synthetic Penicillins	14	1.545	.8260	0.93
Neomycin Sulfate (Dermatological)	23	1.980	.6727	0.88
Streptomycin Family	10	1.409	1.072	0.88
Polypeptide Antibiotics	18	1.655	.9475	0.95
Other Antibiotics	38	1.991	.7663	0.95
Antituberculosis Drugs	25	2.092	.7319	0.91
Anthelmintics	10	1.606	1.268	0.93
Other Groups				
Non-Narcotic Antitussives	19	1.435	.8632	0.97
New Local Anesthetics	16	1.952	.6834	0.79
New Xanthine Derivatives	10	1.317	.9032	0.95

likely lie in the numbers of really new chemical groups being tested, fewer in number, and tried with more thoroughness.

The parameters estimated by the lognormal model were used in a regression analysis with selected variables measuring market participation to ascertain whether an association could be found between the shape of the imitation cycles (as measured by mu and sigma) and the composition and numbers of firms making them up. Would, for example, a larger number of American firms making up an imitation cycle significantly determine its characteristics? The results of this regression study, though inconclusive, suggest that competition between companies may marginally shorten the time profile of imitation cycles through competitive pressure, with a clustering of introductions reflected in a negative sigma coefficient. This has happened when relating numbers of the ten American firms with the largest foreign sales that have entered the market, or numbers of the world's largest twenty pharmaceutical firms, to sigma as follows:[15]

---

[15]The correlation between USFS and WLF is sufficiently large for them not to be included together in the same equation.

$$\sigma = 0.5513 - 0.0087\ \text{USFS} \qquad \bar{R}^2 = 0.06 \qquad (5)$$
$$\quad (16.93)\ \ (-1.11)$$

USFS = number of the ten U.S. firms with largest foreign sales (1971)

or,

$$\sigma = 0.5633 - 0.0066\ \text{WLF} \qquad \bar{R}^2 = 0.04 \qquad (6)$$
$$\quad (18.19)\ \ (-1.596)$$

WLF = number of the world's twenty largest firms (by sales 1971)

When the composition of firms making up the imitation cycles included larger numbers of British or foreign companies, this tended only marginally to lengthen the imitation entry period, thereby influencing mu.

$$\mu = \underset{(31.27)}{2.078} + \underset{(2.013)}{0.0144}\ BF + \underset{(1.526)}{0.0207}\ EF \qquad \bar{R}^2 = 0.09 \qquad (7)$$

BF = number of British companies in the imitation cycles.

EF = number of European or other non-American foreign companies in the imitation cycles.

The effect of having more of the world's largest ten firms in the imitation cycles was similar.

$$\mu = \underset{(27.33)}{2.044} + \underset{(1.908)}{0.0135}\ BF + \underset{(1.792)}{0.0210}\ WL \qquad \bar{R}^2 = 0.11 \qquad (8)$$

WL = number of the world's largest ten firms by sales 1971, making up the imitation cycles.

None of the independent variables showed significant associations with either μ or σ at the 5% level. The results are therefore only suggestive.

The second approach to the analysis of the impact of foreign firms on the UK industry makes use of the indices, already described, for participation frequency, i.e., number of new chemical entities, and imitations, and timing of introductions within imitation cycles. Taking the sales of individual companies in the UK for 1971 as the dependent variable and the indices as independent variables, the regression results given in Table 5 were obtained. The relationships in all cases between sales and the indices individually are significant at 5%; however, in no cases were the constants significant. The strongest association between innovative activity, as measured by the indices, and sales was found for the European and other foreign company groups. The t statistics suggest a more consistent relationship in the case of the indices weighted by the position the firms hold in introducing products within the cycles, than for the unweighted index. Nevertheless, both types of index illustrate the importance of innovative activity to market performance.

TABLE 5

The Introduction and Timing of New Pharmaceutical Products Reflected in Company Sales (Period - 1950 to 1973)

Dependent Variable: Sales in the United Kingdom (£ mn)

Companies Covered	Independent Variables: Constant	Product Nos: Index One	Timing: Index Two	Combined: Index Three	$\bar{R}^2$
British-Owned (23 observations)	-.11 (-.04)	+1.08 (+3.53)			.55
	+1.00 (+.42)		+.19 (+3.80)		.38
	+.84 (+.36)			+16.85 +3.88	.36
American-Owned (21 observations)	-.88 (-.35)	+.89 (+4.30)			.47
	+.73 (+.35)		+.15 (+4.57)		.50
	1.12 (+.54)			+11.85 (+4.40)	.45
European and Other (16 observations)	-2.37 (-1.15)	+1.13 (+4.30)			.76
	-1.35 (-.74)		+.21 (+7.59)		.80
	-2.60 (-1.54)			+19.00 (+8.79)	.83
All Companies (60 observations)	-.95 (-.68)	+1.01 (+8.05)			.52
	+.23 (+.19)		+.18 (+8.44)		.54
	+.02 (+.02)			+15.35 (+8.54)	.54

A comparison of the performance of the leading US, UK and European firms over the 40 imitation cycles, can be made by taking the index averages for the 10 firms scoring highest in each category. The results of this computation for the three indices are presented in Table 6. The group averages of three indices give US subsidiaries the highest scores in each case. Furthermore, as indicated by the standard deviations for each group average, the 10 leading US subsidiaries have tended to have a high consistency of performance.

The market entry activity of US subsidiaries is illustrated in Figure 7 by means of the cumulative frequency distribution based on the positions of entry in UK imitation cycles. Although comprising a smaller group in terms of numbers of firms, US subsidiaries made more market entries and held more of the leading positions than UK firms.

In addition to the three indices of the total performance of individual companies, two measures of average performance were calculated and are presented in Tables 7, 8 and 9. The first is the ratio, index two/index one, and is a measure of the average weight assigned to the market entries of an individual firm. The second, $\bar{x}$, was described in section 3a, and has the advantage that it also takes into account the eventual number of participants of those imitation cycles in which the firm participated, assigning a higher weight where this number was lower.

The measures of average innovative performance were used as independent variables in regressions which are presented in Table 10. Since the variables for average performance tended to be correlated with those of total performance, the regression analysis of these was conducted separately. Furthermore, an association between company size, as measured by UK sales, and average performance became apparent from the regression results. Thus, average performance, as an explanatory variable of company sales, could not be used generally, its usefulness as an explanatory variable itself tending to increase with the size of sales.

Table 6

Indices of Market Entry[1]

Comparisons of Averages for Groups of Leading Firms[2]

Ten Leading:-	Index One	Index Two	Index Three
US Subsidiaries	15 (3.4)	91 (26.2)	1.084 (.318)
UK Firms	12.3 (4.5)	65.4 (28.3)	.770 (.310)
European Subsidiaries	11.9 (7.4)	68.5 (38.5)	.824 (.452)

[1]See section 3a.

[2]Standard deviations are given in brackets below each average figure.

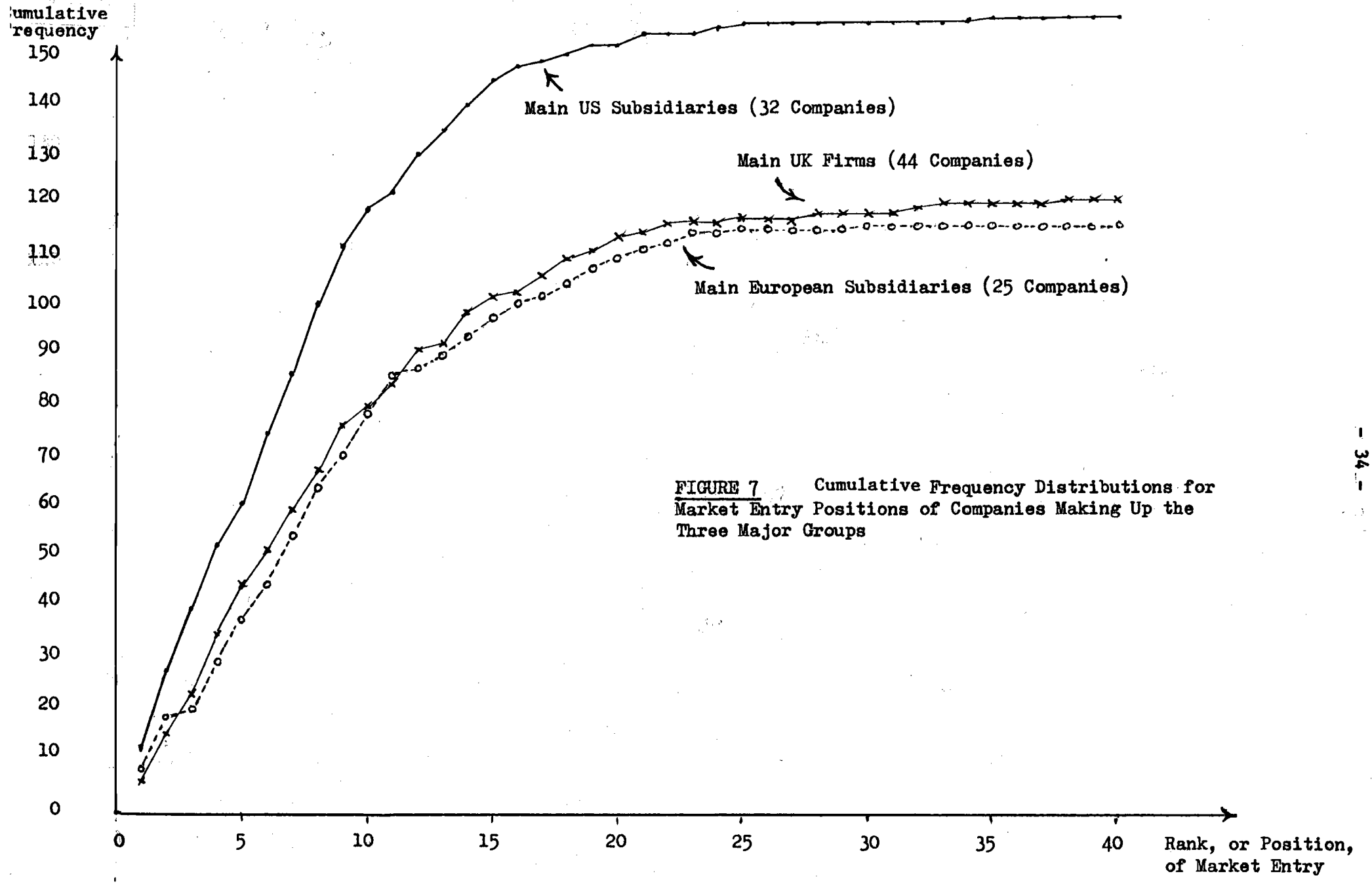


FIGURE 7 Cumulative Frequency Distributions for Market Entry Positions of Companies Making Up the Three Major Groups

TABLE 7

List of Main American Companies and Imitation Data[a]

No.	Company	Index One	Index Two	Index Three	Measures of Average Performance			
					Ratio[b]	$\bar{x}$[c]	s[c]	Average Lag[d] (Years)
1.	Harvey (Pfizer)	1	1	.012	1.0	.012	-	6.11
2.	A. Boehringer (Pfizer)	3	20	.295	6.7	.098	.026	5.75
3.	Pfizer	21	111	1.289	5.3	.061	.052	6.93
4.	Parke Davis (Warner-Lambert)	17	138	1.696	8.1	.100	.035	4.26
5.	Squibb	11	95	1.105	8.6	.100	.045	3.67
6.	Riker (3M Co.)	12	56	.688	4.7	.057	.051	6.96
7.	Wyeth (American Home Products)	14	57	.626	4.1	.045	.040	7.53
8.	Merck, Sharp and Dohme	18	120	1.421	6.7	.079	.043	4.38
9.	Sharp & Dohme (MSD)	1	6	.075	6.0	.075	-	2.50
10.	Searle	12	88	.915	7.3	.076	.915	4.42
11.	Lilly	15	86	1.081	5.7	.072	.051	5.14
12.	Dista (Lilly)	1	2	.025	2.0	.025	-	11.83
13.	Smith, Kline and French	12	59	.711	4.9	.059	.043	4.92
14.	Upjohn	11	45	.520	4.1	.047	.041	7.21
15.	Abbott	7	19	.478	2.7	.068	.098	5.59
16.	Lederle (Cyanamid)	9	24	.279	2.7	.031	.040	9.15
17.	Armour (Greyhound-Armour)	9	32	.378	3.6	.042	.030	5.52
18.	Wallace (Carter-Wallace)	11	17	.196	1.6	.018	.011	8.99
19.	W. Warner (Warner International)	11	69	.845	6.3	.077	.059	5.08
20.	Merrell (Richardson-Merrell)	6	37	.426	6.2	.071	.040	5.74
21.	A. H. Robins	3	23	.271	7.7	.090	.069	4.78
22.	Ortho (Johnson & Johnson)	5	23	.157	4.6	.031	.031	10.65
23.	McNeil (Johnson & Johnson)	1	8	.091	8.0	.091	-	1.42
24.	Bristol-Myers	5	19	.245	3.8	.049	.046	9.20
25.	Sterling-Winthrop	18	88	1.089	4.9	.060	.050	6.94
26.	Ayerst (American Home Products)	1	1	.012	1.0	.012	-	18.42
27.	Stafford Miller	1	7	.075	7.0	.075	-	1.08
28.	Dome (Miles Labs)	2	2	.022	1.0	.011	.000	11.96
29.	Smith Miller Patch (Cooper Labs)	2	2	.022	1.0	.011	.000	9.00
30.	Williams (Warner-Lambert)	1	8	.096	8.0	.096	-	3.83
31.	Syntex[e]	5	6	.072	1.2	.014	.005	11.02
32.	Ashe Chemicals (IT&T)	1	10	.137	10.0	.137	-	2.92
33.	Berk Pharmaceuticals (Revlon)[f]	9	17	.203	1.9	.023	.023	11.64

NOTES TO TABLE 7

a
The indices are described in section 3a.

b
Ratio of Index Two over Index One.

c
See section 3a and note on Index Three.

d
See section 3a.

e
Non-American, but America principal market.

f
Excluded from Figure 7 and some of the analyses.

TABLE 8

List of Main British Companies and Imitation Data[a]

No.	Company	Index One	Index Two	Index Three	Measures of Average Performance			
					Ratio[b]	$\bar{x}$[c]	s[c]	Average Lag[d] (Years)
1.	I.C.I.	13	42	.503	3.2	.039	.036	7.04
2.	Glaxo Laboratories	19	75	.848	3.9	.045	.040	5.78
3.	Allen & Hamburg (Glaxo)	8	36	.455	4.5	.057	.050	7.43
4.	British Drug Houses (Glaxo)	12	93	.931	7.8	.078	.054	3.07
5.	Evans Medical (Glaxo)	2	7	.082	3.5	.041	.040	6.08
6.	Boots Pure Drug	20	101	1.225	5.1	.061	.054	5.76
7.	Crookes Laboratories (Boots)	7	44	.572	6.3	.082	.059	3.51
8.	Wellcome	15	114	1.346	7.6	.090	.050	3.57
9.	Calmic (Wellcome)	5	26	.309	5.2	.062	.017	5.28
10.	Pharmax (London Rubber)	3	4	.045	1.3	.015	.007	11.50
11.	Medo Chemicals (McClure Young)	8	54	.634	6.8	.079	.032	4.92
12.	Duncan, Flockhard (Glaxo)	5	34	.379	6.8	.076	.034	4.82
13.	Beecham	9	46	.569	5.1	.063	.054	6.26
14.	Benchard (Beecham)	3	8	.087	2.7	.029	.021	8.67
15.	Horlicks (Beecham)	1	6	.082	6.0	.082	-	8.50
16.	Distillers	4	37	.451	9.3	.113	.035	1.27
17.	Clinical	1	12	.176	12.0	.176	-	0.00
18.	Moore (Napp)	3	16	.224	5.3	.075	.056	9.11
19.	Bengue	3	21	.234	7.0	.078	.032	4.09
20.	Carlton	4	4	.045	1.0	.011	.000	14.19
21.	Marshall	1	1	.012	1.0	.012	-	9.42
22.	Rona Labs	3	22	.287	7.3	.096	.076	3.56
23.	Napp	3	10	.131	3.3	.044	.040	5.87
24.	Benger (Fisons)	2	13	.159	6.5	.080	.060	3.71
25.	Lewis Laboratories	1	12	.164	12.0	.164	-	0.00
26.	Silten	1	10	.132	10.0	.132	-	1.00
27.	Ward Cassenne	2	10	.109	5.0	.054	.029	4.25
28.	Anglo-French	1	1	.015	1.0	.015	-	7.00
29.	Allied	3	21	.254	7.0	.085	.062	3.53
30.	Norgine	1	9	.095	9.0	.095	-	2.83

(continued)

TABLE 8 (concluded)

No.	Company	Index One	Index Two	Index Three	Measures of Average Performance: Ratio[b]	$\bar{x}$[c]	s[c]	Average Lag[d] (Years)
31.	Fletcher and Fletcher	1	1	.015	1.0	.015	-	12.17
32.	Smith & Nephew	11	51	.614	4.6	.056	.053	7.14
33.	Genatosan (Fisons)	3	6	.070	2.0	.023	.021	4.79
34.	Dales	1	6	.079	6.0	.079	-	5.25
35.	Lloyds Amphor	2	2	.022	1.0	.011	.000	9.13
36.	Reckitt and Colman	1	3	.039	3.0	.039	-	17.92
37.	Carisoma	1	1	.011	1.0	.011	-	5.32
38.	Camden Labs	2	8	.093	4.0	.047	.015	6.79
39.	London Rubber Company	2	5	.067	2.5	.033	.030	6.25
40.	Rendall	2	3	.036	1.5	.018	.009	7.79
41.	Menley and James	2	18	.194	9.0	.097	.027	1.38
42.	Norton	2	3	.037	1.5	.019	.011	10.75
43.	Mycoform	1	1	.010	1.0	.010	-	11.92
44.	Fisons	1	1	.010	1.0	.010	-	13.83

[a]The indices are described in section 3a.

[b]Ratio of Index Two over Index One.

[c]See section 3a, and note on Index Three.

[d]See section 3a.

TABLE 9

List of Main European Companies and Imitation Data[a]

No.	Company	Index One	Index Two	Index Three	Measures of Average Performance: Ratio[b]	$\bar{x}$[c]	s[c]	Average Lag[d] (Years)
	GERMANY							
1.	Bayer Pharmaceuticals (Bayer, AG)	2	10	.134	5.0	.067	.017	9.92
2.	Schering Chemicals (Schering, AG)	9	43	.529	4.8	.059	.050	4.40
3.	Hoechst Pharmaceuticals(Farbwerke Hoechst)	6	43	.560	7.2	.093	.049	4.44
4.	Knoll	1	1	.013	1.0	.013	-	9.58
5.	Geistlich Sons Ltd.	2	15	.191	7.5	.095	.042	7.75
6.	Boehringer Ingelheim	4	33	.420	8.3	.105	.051	5.63
7.	E. Merck Ltd.	1	1	.011	1.0	.011	-	20.50
8.	Wulfinger	1	1	.012	1.0	.012	-	16.83
9.	Richter	1	10	.111	10.0	.111	-	1.58
	SWITZERLAND							
10.	CIBA	23	129	1.434	4.8	.062	.046	5.47
11.	Geigy Pharmaceuticals (CIBA-Geigy)	6	28	.362	4.7	.060	.054	6.01
12.	Sandoz Products Ltd.	5	17	.213	3.4	.043	.032	11.55
13.	Roche	21	104	1.245	5.0	.050	.050	5.98
14.	Wander Pharmaceuticals (Sandoz A, Glaro)	5	36	.420	7.2	.084	.029	4.73
	FRANCE							
15.	May & Baker (Rhône Poulenc)	21	127	1.590	6.1	.076	.052	5.52
16.	Roussel Laboratories (Roussel-UCLAF)	15	76	.899	6.1	.060	.042	5.88
17.	Lepetit Pharmaceuticals (Gruppo Lepetit)	2	2	.020	1.0	.010	.001	18.00
18.	Concept Pharmaceuticals (Pierre Fabre)	1	1	.013	1.0	.013	-	15.58
	SWEDEN							
19.	Astra	7	12	.146	1.7	.021	.016	10.98
20.	Pharmacia	1	1	.011	1.0	.011	-	15.67

(continued)

TABLE 9 (concluded)

No.	Company	Index One	Index Two	Index Three	Measures of Average Performance: Ratio[b]	$\bar{x}$[c]	s[c]	Average Lag[d] (Years)
	ITALY							
21.	Carlo Erba (Montedison)	1	1	.011	1.0	.011	-	12.83
22.	Pharmatilia (Montedison)	3	5	.063	1.7	.021	.016	12.83
	DENMARK							
23.	Leo Laboratories	9	19	.218	2.1	.024	.021	8.89
	THE NETHERLANDS							
24.	Brocades (Gist-Brocades)	1	1	.011	1.0	.011	-	16.67
25.	Organon Laboratories (AKZO)	9	69	.776	7.7	.085	.035	3.09

[a]The indices are described in section 3a.

[b]Ratio of Index Two over Index One.

[c]See section 3a and note on Index Three

[d]See section 3a.

TABLE 10

The Introduction of New Pharmaceutical Products as Reflected in Company Sales (Period - 1950 to 1973)

Dependent Variable: Sales by Company in the United Kingdom (£ mn)

Companies Covered		Independent Variables: Measures of Average Innovative Performance			
		Constant	Ratio[a]	$\bar{x}^a$	$\bar{R}^2$
1.1	Firms with Sales > £ 20 mn (6)	+11.05 (+1.64)		+316.58 (+3.17)	.57
		+11.95 (+1.70)	+3.69 (+2.90)		.52
1.2	Firms with Sales > £ 10 mn (17)	+2.60 (+.28)		287.45 (+1.99)	.10
		+4.07 (+.44)	+3.13 (+1.80)		.07
1.3	All Firms (60)	+4.73 (+1.59)		+56.79 (+1.21)	.02
		+3.90 (+.03)		+.87 (+1.59)	.04
2.1	Selected Firms (36)	+.11 (+.05)		+134.50 (+3.79)	.26
		-.11 (-.06)	+1.64 (+4.19)		.30
2.2	Selected U.S. Firms (16)	-2.03 (-.55)		187.10 (+3.17)	.33
		-2.24 (-.74)	+2.10 (+3.54)		.40
2.3	Selected UK Firms (11)	+1.20 (+.39)		89.56 (+1.44)	.01
		+1.89 (+.67)	+.89 (1.33)		-.02
2.4	Selected European Firms (9)	+3.01 (+.44)		+71.79 (1.24)	-.05
		+.82 (+.17)	+1.33 (+1.67)		.08

[a]The indices are described in section 3a.

Those large firms, which not only tended to make more market entries, but were also more consistent in leading within imitation cycles, tended to have larger sales. Notwithstanding this limitation, average performance was a most useful explanatory variable in the case of the US subsidiaries. The factors influencing their participation within UK imitation cycles are considered in the following section.

4. Market Entry Activity in Pharmaceuticals

a) Transnational Operations of American Companies. A number of factors go to make the foreign investment activity in the pharmaceutical industry a special case even though much of its patterns are similar to other research and marketing-intensive industries. The special qualities of the industry derive primarily from the extent to which it is regulated. The food industry, e.g., sausage making, is regulated internationally by laws of individual countries, or trading areas, to control qualitative aspects of manufacture, and indeed, qualities of the final product, e.g., permitted amounts of food preservative or meat substitute. The pharmaceutical industry, however, is remarkable in the extent of regulation.

International differences regarding the character of the restrictions and requirements for production, testing, and sale of pharmaceutical products are probably an important explanatory variable in the levels and qualities of activity in different countries. Marginal differences or changes in legislation can influence company behavior in a number of ways: cause a company to devote more expenditure and manpower to certain aspects of drug research, development (testing), or manufacture; influence the timing of activities by the company, the extent to which it can simultaneously carry out several aspects of drug introduction; influence the type of companies that will be able to innovate successfully, e.g., by raising standards and costs of research. Three kinds of tests were carried out on data collected on the product-market activity of US subsidiary firms in the UK. The first considers various aspects of technology transfer within and between US companies, and between US companies and other foreign companies. The channels of technology transfer used by companies can be assessed on the basis of the frequency of use, direction, and the lags involved.

The second set of tests relates to the pecking order of companies making new product introductions, or imitating within an imitation cycle. Do the more research-intensive firms tend to introduce products earlier within the cycle? Since size may be an important determinant of the level of activity of an individual company we assessed whether larger firms tended to imitate earlier. By these tests the consistencies of patterns within the imitation cycle are made clearer.

The third set of tests is related to the second, but makes use of the indices of innovative and imitative activity to analyze participation of companies within the imitation cycles. Along these lines we examine the relationship between imitative activity and a range of variables reflecting characteristics of the firms.

Where have American firms tended to innovate earlier, the UK or America? To answer this question the deHaen list of 154 new chemical entities introduced into America over the period January 1963 to December 1972 was used, with the omission of some items. The deHaen list contains chemical entities that, while slightly different in structure from previous entities, are not sufficiently different to produce imitation cycles, e.g., certain salts. Furthermore, a list of all the new chemical entities introduced into the UK will not be the same as that for America, e.g., although Beecham introduced a number of semi-synthetic penicillins into the UK, only a proportion have been sold in America. Of the list of 154 new drugs approximately 50 have not been introduced into the UK either because alternatives have been available, because of toxicity, because introduced in other forms, or because introduced later (than December 1972). Twenty-five others have been introduced into the UK, but at the time of writing the exact dates have not been determined. The remaining 74 new chemical entities form a very good base sample for the test. Two drugs were found to have been introduced simultaneously. A list of the 74 innovations is presented in Table A2 of the appendix.

A new chemical entity introduced into the UK earlier than into America represents a lead for the UK. Of the 74 drugs comprising the test, 52 were found to have been introduced into the UK earlier than into America. Of the remaining 22 drugs, 20 were introduced earlier into America while 2 were introduced simultaneously. This timing of new chemical entity introductions is further illustrated by Figure 8, which divides the timing of introduction according to half-yearly intervals. The leads of market entry in the UK prior to introduction in America tend, on occasion, to be substantial, e.g., twenty-one percent of the drugs have been introduced with a UK lead of greater than 3 1/2 years. The overall average lead (all drugs) to the UK has been 1.34 years (16 months).

An analysis of the drug introductions in the US and the UK, presented in Tables 11 and 12, reveals that a major share, 49%, of the transfers between countries were made within US companies, a further 6% between, and another 18% to US companies. Of the remaining drugs, 27% were transferred outside US companies, 24% were exchanged within or between European companies, and only 3% were exchanged within UK companies.

The figures given in Tables 11, 12, and 13 suggest that transfers within and to US companies were generally more rapid than in the case of European companies. Transfers between companies tended also to be slower, particularly in the few cases between US companies where introduction of a new drug is first made in the UK.

Given the lead that the UK has had for the introduction of new drugs, apparent from Table 13, it might be suggested that many of the transfers of technology occur from the UK to the US. However, while some US firms are known to conduct research and development in the UK, it is more likely that the market entry there was more for marketing reasons than because the original research was carried on in the UK. Nevertheless, it is apparent that US companies have

FIGURE 8

The Timing of New Drug Introduction

Leads and Lags in Issuing the Same Drugs in America and the UK
(Sample: 74 New Drugs Issued Since December, 1962)

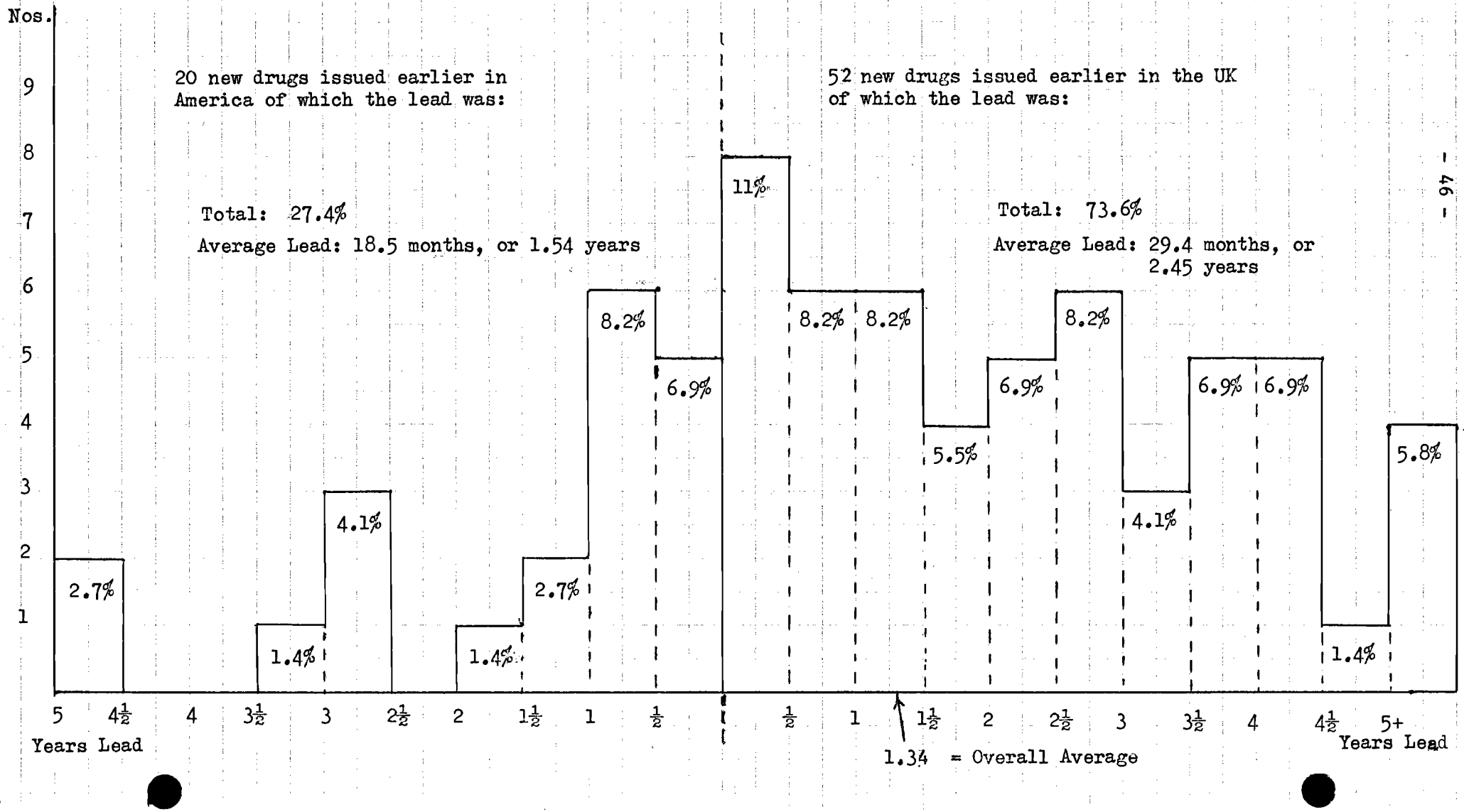


TABLE 11

Average Duration of Leads Between Drug Introduction in the United Kingdom and the United States (1963-72)[a]

Drugs Introduced First Into the United Kingdom

Data in years except numbers of drugs underlined (Sample 74 drugs)

Introduced Into the UK By:-	Subsequent Introduction Into the United States By:-				
	US Companies Parent	US Companies Other	UK Foreign Subsidiaries	Other Foreign Subsidiaries	ALL COMPANIES
US Foreign Subsidiaries	22 1.91 (1.63)	3 3.83 (1.71)	-	1 3.83 -	26 2.21 (1.72)
	25 2.14 (1.68)				
UK Parent Companies	6 2.82 (.81)		2 2.29 (1.31)	1 4.17 -	9 2.85 (1.32)
European or Other Foreign Subsidiaries	7 2.04 (1.35)		-	9* 3.40 (1.96)	1** .58 -	17 2.67 (1.83)
				10 3.37 (2.11)		
ALL COMPANIES	38 2.23 (1.57)		2 2.29 (1.13)	12 3.26 (1.88)		52 2.47 (1.69)

a Numbers underlined are the number of drugs transferred within or between companies. The figures in brackets are the standard deviations for the averages.

* Transferred to subsidiary.

** Transferred to foreign subsidiary of another foreign company.

TABLE 12

Average Duration of Leads Between Drug Introduction in the United States and the United Kingdom (1963-72)[a]

Drugs Introduced First Into the United States

Data in years except numbers of drugs underlined (Sample 74 drugs)

Introduced Into the US by:-	Subsequent Introduction Into the United Kingdom by:-				
	US Companies Subsidiary	US Companies Other	UK Parent Companies	Other Foreign Subsidiaries	ALL COMPANIES
US Parent Companies	<u>14</u> 1.52 (1.43)	<u>2</u> .79 (1.34)	<u>1</u> 1.17 -	<u>2</u> 4.08 (1.07)	<u>19</u> 1.39 (1.57)
	<u>16</u> 1.06 (1.34)				
UK Subsidiaries					
European or Other Foreign Subsidiaries			<u>1</u> 1.58 -	<u>2</u> 1.46 (1.83)	<u>3</u> 1.50 (1.29)
ALL COMPANIES	<u>16</u> 1.06 (1.34)		<u>2</u> 1.38 (.30)	<u>4</u> 2.77 (1.95)	<u>22</u> 1.40 (1.51)

[a] Numbers underlined are the number of drugs transferred within or between companies. The figures in brackets are the standard deviations for the averages.

TABLE 13

The Average Duration of Leads (+) and Lags (-) Between Drug Introduction in the United Kingdom and the United States (1963-72)[a]

Drug Introductions in the United States

Data in years except numbers of drugs underlined

Introduced First by:-	Subsequent Introduction Overseas by:-						
	US Companies		UK Companies	Other Firms		ALL COMPANIES
US Companies	<u>36*</u>	<u>5**</u>	<u>1</u>	<u>3</u>		<u>45</u>
	-.74 (2.14)	-1.98 (2.81)	+1.17 -	+1.47 (4.58)		-.69 (2.43)
	<u>41</u>					
	-.89 (2.23)					
UK Companies	<u>6</u>		<u>2</u>	<u>1</u>		<u>9</u>
	-2.82 (.81)		-2.29 (1.31)	-4.17 -		-2.85 (1.32)
Other Firms	<u>7</u>		<u>1</u>	<u>11*</u>	<u>1**</u>	<u>20</u>
	-2.04 (1.35)		1.58 -	-2.53 (2.69)	-.58 -	-2.05 (2.31)
ALL COMPANIES	<u>54</u>		<u>4</u>	<u>16</u>		<u>74</u>
	-1.25 (2.11)		-.46 (2.70)	-1.75 (3.26)		-1.34 (2.44)

a Numbers underlined are the number of drugs transferred within or between companies. The figures in brackets are the standard deviations for the averages.

* Transferred within an international company, either from subsidiary to parent or parent to subsidiary.

** Transferred to subsidiary of another foreign company, or in the case of US companies to other US companies or their subsidiaries.

utilized market entry in the United Kingdom as a preliminary to entry in the United States.

The channels, direction and lags of technology transfer may have changed over the period 1963-72. An examination of the results of an analysis for two-year periods is given in Table 14. It is readily observable that the numbers of drugs transferred within the sample has tended to fall. Moreover, the leads enjoyed by U.S. and other foreign companies introducing drugs first into the United Kingdom have tended to fall. It would thus appear that the disparities of leads or lags of drug introduction have tended to decline, as well as the frequence although the latter may be a general effect of fewer drugs, as measured by the sample, being transferred. However, it may be a limitation of the sample that more transfers for the most recent years were not found.

What characterizes the American companies that innovate or lead within the imitation cycles in the host country? Those American companies that have subsidiaries in the UK represent only part of the U.S. pharmaceutical industry. By the fact that they have foreign operations they are already a select group.

This second test of American companies operating in the UK pharmaceutical industry involved an analysis of those imitation cycles where the proportion of American companies was sufficiently high for the methodology adopted, i.e., six or more U.S. companies. This criterion resulted in a sample of thirteen imitation cycles.

The positions of individual American companies within the imitation cycles were determined according to the products introduced by the subsidiary. The ranks so derived were suitable for rank correlation analysis with other variables. In selecting the variable to be tested, a number of variables such as the foreign sales of American companies and their total r and d spending were found to be

TABLE 14

The Average Duration of Leads (+) and Lags (-) Between Drug Introduction in the United Kingdom and the United States (1963-72)[1]

Data in years except numbers of drugs underlined (Sample 74 drugs)

Period	Drugs Introduced First into the United States:-			Drugs Introduced First into the United Kingdom Classified According to:-						ALL	
				Date Introduced into the United Kingdom:-			Date Introduced into the United States:-				
	US Subsidiaries	Other	ALL(1)	US Firms	Other	ALL(2)	US Firms	Other	ALL(3)	(1 + 2)	(1 + 3)
Pre 1963, 1963, 1964	5	1	6	14	16	30	9	2	11	36	17
	+1.63 (.96)	+2.75 -	+1.82 (.97)	-2.51 (1.72)	-3.02 (1.55)	-2.75 (1.63)	-1.66 (.94)	-2.00 (.71)	-1.72 (.88)	-1.99 (2.31)	-.47 (1.96)
1965, 1966	6	1	7	4	6	10	10	5	15	17	22
	+2.50 (2.17)	+1.58 -	+2.37 (2.01)	-2.52 (1.92)	-2.21 (2.05)	-2.33 (1.89)	-1.81 (1.12)	-2.23 (1.67)	-1.95 (1.28)	-.40 (3.04)	-.58 (2.55)
1967, 1968	3	-	3	6	3	9	9	2	11	12	14
	+.17 (.14)	-	+.17 (.14)	-1.85 (1.80)	-2.97 (1.21)	-2.22 (1.65)	-2.32 (1.99)	-4.08 (.35)	-2.69 (1.85)	-1.63 (1.77)	-2.08 (2.03)
1969, 1970	4	1	5	1	1	2	4	3	7	7	12
	+.67 (.54)	+.17 (.52)	+.57 (.52)	-.92 -	-.58 -	-.75 (.24)	-2.96 (1.65)	-5.19 (2.04)	-3.92 (2.04)	+.19 (.78)	-2.05 (2.78)
1971, 1972	1	-	1	1	-	1	5	3	8	2	9
	+0 -	-	+0 -	-.17 -	-	-.17 -	-2.90 (2.23)	-2.92 (2.03)	-2.91 (2.01)	-.17 (.12)	-2.58 (2.11)

[1]Numbers underlined are the number of drugs transferred within or between companies. Standard deviations are in brackets.

correlated with Index Two (part of the third type of tests carried out), and are thus related to an American subsidiary's innovative activity in the UK. Research intensiveness, as measured by the ratio of r and d expenditure to total company sales, was found to be very poorly related to Index Two, and was therefore not used. However, an alternative variable, the quality of research effort for the period 1963-72, was used, and was defined as the number of r and d personnel (1969) in the U.S. per new drug introduced in the U.S. during 1963-72. Furthermore, total company r and d spending in 1971 was eventually chosen as a variable. The reason for this choice in preference to the foreign sales variable comes from the analysis of the timing of innovation between America and the U.K. above. Foreign sales would reflect innovative activity, and so are probably best represented as a dependent, rather than independent variable, in relation to innovative activity. A company's r and d spending, though related indirectly to sales, i.e., through profit savings, provides a better independent variable for innovative activity.

The ordinary rank correlations derived from rankings of r and d spending in 1971 and the quality of r and d with respect to company positions in the imitation cycles are given in Table 15. They show a tendency for those firms leading in r and d spending and in the quality of r and d to be early within the imitation cycles. Two contrasting reasons for this pattern might be offered. The first is that r and d spending and a high quality of r and d reflects the companies' desire not only to introduce a new product, but to introduce it earlier. Increases in r and d spending can be reflected in the numbers of new products introduced, but it can also be reflected in the timing of the introductions. A company's savings, and future r and d spending, are probably related to the timing of its introductions. This leads us to the alternative reason for the pattern to be observed, as in Table 15. The r and d figures for spending relate to 1971, and may therefore reflect the performance

TABLE 15

Rank Correlations for American Companies in the UK

Variables Related: (1) Size of Research and Development Expenditure (1971)

(2) R & D Personnel (1969) in the USA per New Drug Introduced (1963-72) in the U.S.[a]

Positions of Individual Companies in Introducing Pharmaceutical Products for Imitation Cycles With Six or More American Companies

		(1)	(2)	
1.	Anticholinergics	+.50	+.71	12 Companies
2.	Vasodilators (Nitrates)	+.82	+.46	7
3.	Reserpine and Analogs	-.17	-.05	9
4.	Thiazides	+.76	+.07	8
5.	Phenothiazines (Propyl Piperazine and Alkyl Piperidyl)	+.26	-.31	6
6.	Antiemetics	+.60	+.31	6
7.	Muscle relaxants (Glycols and Benzodiazepines)	+.21	-.07	7
8.	Hydrocortisone	+.42	+.60	10
9.	Prednisolone	+.53	+.60	9
10.	Modified ACTH	+.49	+.77	6
11.	Neomycin Sulfate	+.62	+.60	8
12.	Other antibiotics	+.03	-.77	6
13.	Antihistamines	+.78	+.15	10
	Average	+.45	+.24	8
	(Standard deviation)	(+.30)	(+.45)	(1.91)

[a]See Cohen, Katz and Beck [1975], who developed this variable for their study of U.S. pharmaceutical companies.

of the company in introducing products earlier. The earlier a firm introduces an innovation the higher its profits and saving, and hence the higher its future r and d spending.

The circularity between r and d spending, the timing and numbers of the innovations, and the extent of the foreign sales of American companies operating in the UK is again seen in the following tests, using indices of innovative behavior to reflect the timing and numbers of innovations. In the discussion so far the qualitative aspects of the products introduced have not been related to the timing of product introductions. Two assumptions have been made. The first is that the products of late entrants may be qualitatively better than that of the innovator, but where the qualitative difference is substantial we have a beginning to a new imitation cycle. Put together the two imitation cycles form a double cycle or "wave." This effect can be seen in Figure A4, where the imitation cycle of oral contraceptives has been drawn. The beginning of a second cycle in the autumn of 1972 is clearly apparent. The new products introduced then were the single hormone contraceptives. Earlier pills consisted of two hormones.

The second assumption relates to the definition one assumes for assessing the quality of a product. An innovation has the quality of being available early, rather than late. In a commercial sense this quality of the good can enable profits and savings to be made by a company even though later products may be superior in other qualitative features. This time-related quality of pharmaceutical products is an important element in company research strategy, not only in terms of where a product is introduced first, but how soon.

What structural patterns can be detected between innovative performance and a company's production and sales in the host country? We have already been reminded that the relationship between sales and research activity is circular. A high level of r and d, relative to other firms and absolutely, when judiciously spent, tends to reflect itself in innovative performance, more new products, and earlier market entry. This can mean larger sales, and more foreign sales (perhaps as a necessary rather than sufficient condition). Larger sales can mean greater corporate savings, which can lead to higher r and d expenditure, and so on. This pattern may be termed as "benign."

The indices of innovative performance have been designed so as to permit an analysis of the "benign pattern" by means of regression tests. Additional data used for this purpose were based on information on individual companies giving total expenditures on r and d, foreign (outside USA) sales, UK sales, total company sales, employees in the UK. All data, as presented in Table 16, apart from the indices and employment figures, were for the year 1971. From these basic variables composite variables were derived: 1) r and d/total company sales, a measure of research intensiveness, 2) UK/foreign (outside USA) sales, an estimate of the relative importance to the company of UK sales compared to other foreign markets, 3) UK/total company sales, giving the relative importance to each company of UK sales. Apart from the two indices of innovative performance by each company in the UK market, the variables and derived composite variables were employed as independent estimators. In a structural sense the first index, that describes the numerical value of new product introductions (as well as the second index measuring the timing of company product introductions), forms an interdependent relationship to many of the variables mentioned above. Thus r and d spending can be thought of both as a result of innovative performance and as an important determinant of future innovative performance.

TABLE 16

Data on Selected American Companies Operating in the United Kingdom

No.	Company	Total R & D[a] (1971)	UK Sales[b] (1971)	Foreign Sales[a] (1971)	Total Sales[a] (1971)	UK Employment[c] (1972)	Index One[d]	Index Two[d]
		$ mn.	£ mn.	$ mn.	$ mn.			
15.	Abbott	28.8	3.99	145.9	458.1	550	7	19
7.	American Home Products-Wyeth	53.0	12.9	388.7	568.0	1,034	15	58
24.	Bristol-Myers	40.0	6.02	1098.9	263.5	550	5	19
16.	Cyanamid-Lederle	21.8	10.63	150.0	257.1	1,020	9	36
11.	Lilly	67.5	12.90	224.9	723.4	2,100	16	88
8.	Merck, Sharp & Dohme	70.5	19.45	331.4	847.9	1,200	19	126
28.	Miles Labs	12.2	4.45	72.8	288.3	550	2	2
22.	Johnson & Johnson - Ortho	46.8	1.83	355.0	1140.5	275	6	31
3.	Pfizer	37.2	14.60	462.6	992.9	2,800	25	132
20.	Richardson Merrell	18.0	5.54	172.1	408.5	600	6	37
10.	Searle	27.1	18.83	87.4	226.9	2,600	12	88
13.	Smith, Kline & French	35.8	7.37	85.2	367.5	770	12	59
5.	Squibb	33.1	6.14	221.6	674.8	700	11	95
25.	Sterling-Winthrop	23.0	30.71	263.5	625.4	2,903	18	88
14.	Upjohn	45.4	3.88	148.4	438.4	390	11	45
19.	W. Warner	55.6	10.38	498.3	1346.0	1,250	12	74
31.	Syntex**	11.6	0.79	46.5	117.4	200	5	6

* Non-American. [a] Poor's company and industry reports. [b] Extract Services; Extel Services. [c] Kompass, Companies.

[d] See section 3a.

A virtue of presenting all the non-performance variables as independent variables lies in the fact that it permits a quick assessment of the strengths of relationships between the two groups of variables. The regression results for a sample of 17 American companies operating in the UK are presented in Tables 17 and 18. The first point to be made is that r and d expenditure, UK employee numbers, and company foreign sales, all show a consistent relationship with both indices of innovative performance. There are very good reasons along the lines of the "benign pattern," above, as to why they should. The relationship between UK employees numbers (both scientific and manufacturing staff) and innovative performance is an interesting one, and deserves further study in another paper. The composite variables, especially the one to reflect each research intensiveness, i.e., r and d/total sales, did not display strong consistencies, but the variable measuring the relative importance of UK sales is suggestive. It implies, but only, that companies selling a higher proportion of their total sales to the UK tend to be more innovative, or perhaps as a condition of these sales need to be more innovative, i.e., both in numbers of products and the timing of their introductions within the imitation cycles.

In addition to the regression analysis already described, further regressions were made using the variable measuring the quality of research effort in the United States during 1963-72 as an independent variable. The analysis when conducted on a sample of 11 U.S. companies resulted in the following equations:

$$\text{Index One} = \underset{(+2.58)}{+6.07} \quad \underset{(+2.77)}{+.0807\ \text{QRE}} \qquad \bar{R}^2 = .41 \qquad (9)$$

QRE = quality of research effort, i.e., r and d personnel (1969) in the U.S. per new drug introduced during 1963-72 in the U.S.

and,

$$\text{Index Two} = \underset{(+.58)}{+6.36} \quad \underset{(+5.61)}{+.7500\ \text{QRE}} \qquad \bar{R}^2 = .73 \qquad (10)$$

TABLE 17

New Product Introductions by American Companies
(Period Covered - 1950 to 1973)

Dependent Variable: New Product Introductions Either Under Patent or Licencing Agreement

$ mn (17 Companies)

Form of Dependent Variable	Constant	Total R&D (1971)	UK Sales (1971)	Foreign Sales (1971)	Total Sales (1971)	R&D/Total Sales (1971)	UK/Foreign Sales (1971)	UK/Total Sales (1971)	UK Employment	$\bar{R}^2$
Index One		+.15 (+5.34)							+.0049 (+6.12)	0.73
"		+.153 (+4.36)	+.22 (4.64)							0.62
"				+.005 (+5.08)					+.022 (+4.12)	0.64
"					+5.36 (+3.36)				+.005 (+4.61)	0.56
"	+4.66 (+1.48)		0.23 (+3.91)			+14.00 (+.37)				0.46
"		+.23 (+6.05)					+19.47 (+2.20)			0.30
"		+1.20 (+5.36)						+321.3 (+2.41)		0.42

TABLE 18

New Product Introductions by American Companies
(Period Covered - 1950 to 1973)

Dependent Variable: New Product Introductions Either Under Patent or Licencing Agreement

$ mn (17 Companies)

Form of Dependent Variable	Constant	Total R&D (1971)	UK Sales (1971)	Foreign Sales (1971)	Total Sales (1971)	R&D/Total Sales (1971)	UK/Foreign Sales (1971)	UK/Total Sales (1971)	UK Employment	$\bar{R}^2$
Index Two		+.783 (+3.86)							+.028 (+4.82)	0.68
"		+.797 (+3.36)	+1.26 (+3.93)							0.60
"				+.029 (+4.26)					+.108 (+2.94)	0.60
"					+.034 (+2.64)				+.032 (+4.95)	0.57
"	+21.21 (+.98)		+1.48 (+3.58)			+31.10 (+.12)				0.40
"		+1.20 (+5.19)					+122.0 (+2.25)			0.40
"		+.23 (+6.31)						54.34 (+2.54)		0.35

The inclusion of additional observations in the case of Index Two reduces the $\bar{R}^2$ values in the case of Index Two very sharply so that with 14 observations $\bar{R}^2$ = .31 while $\beta 1$ = 27.08 and $\beta 2$ = .536. A number of firms, particularly Pfizer, William Warner, and Sterling-Winthrop excluded from equations (9) and (10) above, appear to have been highly innovative despite a significantly lower quality of research effort as measured by the variable QRE.[16] The results

---

[16]The average QRE value for 14 companies including the three mentioned was 61.4 employees per new drug with a standard deviation of 38.9 employees. However, the average for these three companies was 25.7 employees.

---

otherwise support the conclusion that a high quality of research effort in the United States is associated with better market entry performance in the United Kingdom.

In summary we can say that the evidence tends to support the concept of the "benign pattern." American firms tend to introduce products into the UK earlier than into the USA. Companies with a higher relative expenditure on r and d and a higher quality of research effort in the United States tend to be the leaders in introducing products within the UK imitation cycles.

b) The Competitive Response of British Companies. In what ways does the entry of multinational companies into the host-country industry influence the strategies or native companies? One possible view is that the large international company is primarily responsible for all the really major innovations in the industry. This can be explained on the basis of their size, their access to investment or research capital, the proprietary skills they possess in marketing, in organizing for successful research and development, and in carrying through the whole tangent of activities that go to make for commercial

success. Along these lines of thinking the host-country firms are generally characterized as being responsive to the initiatives taken by the innovators, the large international firms, who are very large because they know how to innovate. An alternative view is that the large international companies, while they hold a major share of the commercial markets in the host country, do not necessarily lead it with their innovations, but in contrast make great use of local initiatives taken to stimulate their own research and marketing efforts. Along this argument the host-country firms could be the innovators from which the large companies get their inspirations. Taken one step further, an argument might claim that when the larger firm innovates it is because it is led rather than leader, but owing to its superior resource capabilities, power to acquire, as well as develop, an idea, it has the greater ability to follow through with commercial products at an earlier date.

It is apparent from the figures of total r and d activity in the United Kingdom that the British pharmaceutical industry spends considerably less than the U.S. In 1972 it amounted to only £28 million compared to a U.S. figure of $726 million or approximately ten times that amount.[17] Several

---

[17]See Wood [1973]. Direct comparisons of research expenditure are apt to be misleading. In real terms UK spending is higher than implied. See MacDonald [1973], pp. 477-494.

American companies, Lilly, Merck, Sharp and Dohme, Warner-Lambert, allocated almost as much individually on r and d as the UK industry as a whole. In 1973 Roche claims to have spent $280 million on research and development, and recently opened a £2 1/2 million UK research facility.

The value of having foreign subsidiaries in Britain as a stimulant to host-country industry must take into account the extent to which this makes the British industry increasingly dependent on foreign technology.[18] Foreign

[18]Dr. F. A. Robinson, president of the biomedical sciences division of the British Association for the Advancement of Science, is one of several authorities who view the current developments of the UK industry with alarm. See Wood [1973].

companies have benefited from the liberal attitude of British firms towards the publishing of scientific results, and by transnational activity have increased their access to new ideas.[19] There are signs that British companies

[19]The Wellcome Foundation has long been transnational, while ICI, Beecham, Glaxo, and Fisons are emerging with international pharmaceutical operations. See Pharmaceutical Industry Report, "Wellcome Sharpens Image, Doubles Profit," The Pharmaceutical Journal, January 17, 1970, pp. 62-3.

are taking greater interest in an international approach to future research and growth.[20] Part of the strategy underlying British response to foreign

[20]American companies have found it especially useful to conduct clinical testing from a UK laboratory, as well as using it as an outpost for scanning European developments. See Shedden [1973], p. 48.

market-entry would appear to be by reciprocal investment in source-country markets, particularly in the case of America. Many view the international deployment of activities as a basic aspect of surviving, given the lead of foreign competitors. Host-country companies, especially those that are not capable of mounting a large research program, can eventually make use of a proportion of the products originally introduced into the UK by foreign firms for which patents have expired, but which have not been totally superseded. Our work suggests that in the later stages of the product cycles (which make up the imitation cycles), manufacturing cost and marketing tend to become increasingly important aspects of competition while the uniqueness of individual chemical entities is diminished through the increasing availability of combinations and permutations of existing drugs representing no significant medical advance.

The analysis that follows suggests the means to innovation available to the host-country firm. Let us suppose, for the moment, that because the costs of developing really new chemical entities, i.e., those that would form the basis of an imitation cycle, and that would go on to take a large share of the relatively large markets, are very high, these are largely the prerogative of the large international company. It is now fruitful to speculate as to what products the local industry can survive on, or if fortunate, grow on. By and large, we are probably forced to accept that host-country firms, at least the bulk of companies, will be resigned to follow the lead of the innovators, which, we assume, tend to be the larger firms in any significant product area.

There are at least four types of imitative activity that can be undertaken by late-comers. The first is the easiest, and involves simply finding those products for which patent protection has run out, i.e., over 16 years old in the UK, such products as some of the barbitones, the early penicillins, many of the

plant drugs of the pre-war period, a number of sulfa drugs, and a few of the post-war synthetics, and there are other possibilities. The imitator "simply" ascertains a more economical means for manufacturing or distributing these products. In recent years, firms that have adopted this approach to market entry have sometimes made use of the slow speed with which officialdom can force the infringer of a patent to stop production. An imitator, of the less scrupulous variety, can, if it wants, begin production and sales of a product still under the legal protection of the patent. It needs only to calculate the speed with which the courts can operate to stop its production, and to see if this is longer than the duration of patent protection.

The second method of imitation is more resourceful, and requires that the firm have sufficient know-how to be able to produce an already successful, or tested, product, and in exceptional cases, an untried product, under a licencing agreement. Such firms may be the subsidiaries of large international companies but be relatively new to the industry. This can pose a problem for the smaller firm that wants to produce under licence, since the licensor may insist on previous production experience, or research and development capability, that smaller firms tend not to have.

British-owned companies have made considerable use of the licencing facility in their introduction of new chemical entities into the UK market. An estimate of this method of participation is given in Table 19. It is likely that the method has just as much application in the case of direct imitations as in introducing new entities for the first time. The estimates shown in Table 19 suggest that licences are, more or less, evenly distributed in number between American and other foreign companies.

TABLE 19

Numbers of New Chemical Entities (of Study) Introduced Into the United Kingdom by British-Owned Companies

Conditions of Introduction: Licencing or Internal R&D

Therapeutic Groups	Internal R&D			Under Licencing Agreement		TOTAL
	Patent	No Patent	Expired Patent	with American Firm	with Other Firms	
1. Alimentary System	3	6	1	2	3	15
2. Cardiovascular System	6	4	1	5	4	20
3. Central Nervous System	8	6	0	10	8	32
4. Musculo-Skeletal Disorders	0	1	0	0	1	2
5. Hormones	5	5	0	2	2	14
6. Genito-Urinary System	0	0	0	0	0	0
7. Infections and Infestations	13	6	0	7	3	29
8. Respiratory System and Allergic Disorders	5	3	0	3	6	17
9. Other (Carcinochemotherapy, Surgical)	5	2	0	0	1	8
(Study) Total	45	33	2	29	28	137

The third form of imitative activity requires a fairly high level of research and development capability. This is to scan the existing range of manufactured products, preferably those that are in large markets and are selling well (under the patent period). It involves the firm deriving the same chemical entity, but by a new chemical route, and a patentable one. Since many of the larger firms try to guard against this type of imitation by finding and patenting all the easy routes, the small firm that engages in this type of imitation needs to know what it is doing, for the risks are great. Some of the products introduced by British-owned companies involve this kind of imitative or innovative research and development. Beecham, for example, was able to come up with the synthetic penicillin, Penbritin, i.e., ampicillin, and this involved finding the synthetic route to penicillin.

The fourth form of imitative activity can require almost as much technical skill as a major innovation, but generally represents a mid-way house between the research of completely unchartered areas, and areas that are fairly well known. It consists primarily in carrying out parallel research to that already performed elsewhere and already resulting in a major innovation. The research is based on the hope of finding a derivative or analog to the entity that has been found (and probably tested before it is revealed). The "imitator" may attempt to find a substitute for the discovery by means of a chemical entity with the same site of action but of a dissimilar structure. This is not always possible, depending on the uniqueness of the innovation.

Firms embarking on the fourth form of imitative research strategy will usually have strong research teams competing with them. They may find nothing of use, and a great deal to go through. Even when a suitable chemical entity has been isolated, the firm will need to keep its momentum. When competing against a larger firm in the same area, it may find the task of protecting its discovery and creating a market for its product a major challenge.

Many of the innovations introduced by British companies have been by research of the fourth type of "imitative" activity described above. In Table 19 the numbers of new chemical entities introduced first by a British-owned company are outlined. The success of host-country firms is noticeable in the infections and infestations groups, i.e., antibiotics, antimalarials, anthelmintics, anti-tuberculosis drugs.

Licencing has been an important means whereby British-owned companies introduce a new chemical entity first into the UK market; however, the more important route has been that of internal r and d. The greater use of licencing has come with product introductions by British companies for chemical entities already issued. A number of the new drugs introduced first by British companies have not been under patent. These are rediscoveries of new uses for chemical entities that are known, or chemical entities for which patent protection adds nothing to the market life of the chemical entity, since, for example, it competes against other readily available substitutes, possibly superior, or it is of relatively minor medical importance and small commercial value. We now turn to the product-market activity of American companies in the UK pharmaceutical industry.

5. Positions of Companies Within Imitation Cycles

a) Characteristics of Leading Firms. The following analysis was based on the record of 35 leading companies in UK ethicals markets as given in Table 20.[21]

---

[21] A leading company by our definition has, at least, an Index-One value of 5, and an Index-Two value of 32.

There was considerable variation in the nationality of ownership for this group. Of the 35 firms, 14 (40%) were American, 12 (34%) were British, and 9 (26%) European. The five leading companies were Parke Davis of Warner-Lambert, CIBA, May and Baker

TABLE 20

The 35 Leading Companies in the Imitation Cycles

Company	Index One[a]	Index Two[a]	Average Lag (Years)	Average Performance $\bar{x}$[b]	U K Employees[a] (1972)	U K Sales, £mn.[c] (1971)	Nationality of Ownership
1. Parke Davis (Warner-Lambert)	17	138	4.26	.100	1,250	NA	American
2. CIBA	23	129	5.47	.062	6,000 (G)	35.0 (G)	Swiss
3. May and Baker	21	127	5.52	.076	6,700	34.6	French
4. Merck, Sharp and Dohme	18	120	4.38	.079	1,200	19.5	American
5. The Wellcome Foundation	15	114	3.57	.090	6,750	40.0*	British
6. Pfizer	21	111	6.93	.061	2,500	14.6	American
7. Roche	21	104	5.98	.050	NA	18.1	Swiss
8. Boots Pure Drug	20	101	5.76	.061	59,000 (G)	4.0*	British
9. Squibb	11	95	3.67	.100	700	6.1	American
10. British Drug Houses	12	93	3.07	.078	1,000	4.4	British
11. Sterling-Winthrop	18	88	6.94	.060	NA	30.7	American
12. Searle	12	88	4.42	.076	2,600	18.8	American
13. Eli Lilly	15	86	5.14	.072	2,100	12.9	American
14. Roussel-UCLAF	15	76	5.88	.060	850	9.4	French
15. Glaxo	19	75	5.78	.045	17,000 (G)	25.0*	British
16. W. Warner	11	69	5.08	.077	NA	10.4	American
17. Organon	9	69	3.09	.085	500	3.6	Dutch
18. Smith, Kline & French	12	59	4.92	.059	770	7.4	American
19. Wyeth	14	57	7.53	.045	NA	8.5	American
20. Riker	12	56	6.96	.057	750 (G)	5.3	American
21. Medo Chemicals	8	54	4.92	.079	NA	NA	British
22. Smith & Nephew	11	51	7.14	.056	NA	13.0	British
23. Beecham Labs	9	46	6.26	.063	14,380 (G)	26.0*	British
24. Upjohn	11	45	7.21	.047	390	3.9	American
25. Crookes Labs	7	44	3.51	.082	250	0.9	British
26. Schering A.G.	9	43	4.40	.059	NA	2.9	West German
27. Hoechst A.G.	6	43	4.44	.093	700	6.0	West German
28. ICI Pharmaceuticals	13	42	7.04	.039	3,400	9.5*	British
29. Merrell	6	37	5.74	.071	600	5.5	American
30. Distillers	4	37	1.27	.113	NA	NA	British
31. Wander	5	36	4.73	.084	800 (G)	10.4	Swiss
32. Allen & Hanbury	8	36	7.43	.057	1,870	11.2	British
33. Duncan Flockhart	5	34	4.82	.076	NA	NA	British
34. B. Ingelheim	4	33	5.63	.105	NA	2.2	West German
35. Armour Chemicals	9	32	5.52	.042	NA	1.9	American

[a]Companies and company indices such as that of Dun & Bradstreet. [b]See section 3a. [c]Companies, Extract services.

*Estimate NA = not available. (G) Data relates to group or associate companies.

of Rhone Poulenc, Merck, Sharp and Dohme, and The Wellcome Foundation. Each had a value of 15 or more for Index One, measuring the frequency of imitation activity, and 110 for Index Two, measuring the weighted total for each company's market entries within imitation cycles.[22]

---

[22]As calculated according to the formulation in section 3a.

Entry Concentration. Of the 431 chemical entities introduced by the leaders, 187 (43%) were from American subsidiaries, 131 (30%) from British companies, and the remaining 113 (26%) from European firms. CIBA alone introduced 23, almost one-fourth of the total number from European companies. Together the three companies CIBA, May and Baker of Rhone Poulenc, and Roche have accounted for almost 60% of the introductions from the leaders of European firms. The contributions by American and British firms were more widely distributed with the largest values for individual members of each group being not much greater than 10% of the American and 15% of the British leaders. The concentration of market entries measured by Index One suggests that European firms were the most concentrated and American firms the least concentrated of the groups.

Entry Positioning. The aggregate value of Index Two for the 35 leaders was 2,468 and when divided according to nationality of ownership came to 1,081 (44%) American, 854 (35%) British, and 533 (21%) European. The concentration of the European group was again apparent with CIBA, May and Baker of Rhone Poulenc, and Roche comprising two-thirds of the European value. The three leading American and British firms took 34% and 36% of their totals respectively.

Imitation Lags. Earlier we considered leads and lags associated with the introduction of the same chemical entity into the United States and the United Kingdom. In this section we consider for individual firms the lags that occur following a major innovation in the UK and which leads to subsequent imitation within what we have defined as imitation cycles. Discussion of how these lags are calculated has been given in section 3a.

The average imitation lag, which is measured according to the valuation of $\bar{L}_i$,[23] of the 35 leaders given in Table 20 was 5.37 years. Of the same group

---

[23]See the note in section 3a, equation 4.

---

of firms the 14 American subsidiaries averaged 5.62 years, higher than either of the British or European groups, with averages of 5.05 years and 5.02 years respectively. The shortest average lags for individual firms were recorded for Distillers, 1.27 years; British Drug Houses, 3.07 years; Organon, 3.09 years; Crookes Labs, 3.51 years; The Wellcome Foundation, 3.57 years; and Squibb, 3.67 years. As expected, the companies with lower values of Index Two had longer imitation lags on the average. The mean for the first ten leaders was 4.86 years; second ten, 5.57 years; and last 14 companies, 5.62 years, i.e., excluding Distillers.[24]

---

[24]Including Distillers the figure was 5.33 years.

Taking just the first five leaders of each nationality group, the British companies did well with a mean of 4.62 years. The average lags for the first five of American and European groups were 5.24 years and 5.19 years respectively.

Average Performance. Where the average performance of the leaders was measured by the values for $\bar{x}$, the measure of average performance weighted by company positions within the imitation cycles (and accounting for the total number of market entries),we found an overall average value of .0703. In the case of the ten leading U.S. subsidiaries the average value was .0729; (higher than the UK average value of .0705 (including Distillers) or .0650 (excluding Distillers), but lower than the average value for European subsidiaries which was .0734. Although it can be said generally that the larger leading firms would tend to have better average performance values, it is also apparent that small companies have innovated or led in imitation cycles. However, company size is associated with consistency of the firm over the longer period whereby previous successes are the basis for a growth in company sales.

b) American and Host-Country Comparisons. The analysis of this section compares two groups of ten leading firms, one group American and the other British,[25] and is partly based on results given in Table 6. It was found that

---

[25]They are the ten leading firms in Tables 7 and 8 and as measured by Index Two (see section 3a).

---

the average value of Index One for the American group was 15 and for the British 12.3. The American firms thus tended to be more active in introducing new products into the UK ethicals markets.[26] Similarly, in the case of Index Two,

---

[26]It was also apparent that more of the American introductions were based on internal research rather than licencing compared to the leading UK companies (however, no data are given here).

American firms outperformed their British rivals with an average of 91.0 per firm; that of the host-country group was 65.4 per firm or 39.1% lower. Leading American firms thus not only entered the markets with more new products, but also tended to have better positions (numerically) for entries, than British companies. The average lag for the ten leading American companies, overall, was approximately 5.33 years, compared to 4.83 years (including Distillers) or 5.45 years (excluding Distillers) in the case of the leading UK companies.

c) Positions of Other Foreign Companies. The following analysis is based primarily on the results for ten leading European firms operating in the United Kingdom.[27] The average value for Index One of these companies was 11.9,

---

[27] Aspro-Nicholas, which deserves special mention, recently decided to discontinue r and d activity in the UK. Its values for Index One and Two were 6 and 25 respectively, and its subsidiary, British Schering, 3 and 18.

---

marginally lower than that of the ten leading host-country firms. However, the mean value for Index Two of this European group was 68.5 or 4.7% higher than the ten leading UK firms. The average lag was 5.12 years, representing the shortest for the three nationality groups.

The performance of this group of ten European firms representing four countries was slightly better than that of ten leading UK firms (in terms of numbers of introductions, positioning (numerically), and average imitation lag. However, the concentration of activity by a few firms is more pronounced within the European group.

6. Summary and Conclusions

The influence of American and other foreign companies on the UK pharmaceutical industry as a whole and on the performance of individual UK companies, has been considerable. With its estimation and analysis of imitation cycles, our study shows that the transfer of technology at the market level has stimulated UK companies both to conduct research of a high quality and to perform competitively within a very wide range of new drug technologies. Moreover, at the production level, British companies have made great use of licenses from American and other foreign companies in order to participate earlier within imitation cycles, although the results of domestic research and development generally have been adequate to meet the challenge of transnational market entry. Despite the fact that leading American companies have on average performed better than their UK counterparts, a number of British firms have maintained very high levels of performance and have remained competitive.

The study succeeded in developing and estimating three types of imitation cycle characteristic of ethical drug markets. It was marginally successful in establishing an association between the composition by nationality or size group of firms making up the imitation cycles and the time profiles of market entry. In the case of the largest U.S. firms with foreign sales and the largest 20 international companies, there was a slight association, but not significant, between numbers of these and the clustering of drug introductions. Larger numbers of British and European companies had the effect, but not significant, of lengthening the time profile of market entries.

A strong association was found to exist between innovative activity in the UK and company sales. In the case of Index Two accounting for the frequency and timing of new drug introductions, significant associations were also found between it and size of U.S. r and d programmes measured in millions of U.S. dollars and size of operation in the UK measured by UK employment. Furthermore, a variable

measuring the quality of r and d effort in the U.S. was strongly associated with innovativeness in the UK.

American companies thus have been very active in the UK pharmaceuticals industry, and for the post-1962 period, at least, they introduced many new products into the UK market prior to market entry in America. Moreover, from an analysis of 74 new chemical entities, it was discovered that the number of drugs transferred appeared to have fallen as well as the length of the UK leads for transnational market entry by U.S. and other companies (introducing first in the United Kingdom). Various estimates of lags associated with inter-firm and intra-firm technology transfer were made and it was concluded that intra-firm transfers, as expected, generally were shorter.

Our study established that British companies have tended to rely fairly heavily on foreign technology, both as a stimulus to domestic r and d activity and as a source of know-how for marketable products. Moreover in terms of the composition of the 35 leading firms in UK ethical markets, British companies were not exceptional (34% being British). American and European companies on the other hand were highly competitive. However, the activity of continental European firms was concentrated in a few very substantial companies. It could be concluded, nevertheless, that British firms were capable of carrying out the full idea-to-market cycle necessary for independent market entry, and were also capable of a quick response to innovation through the development of a competitive product (or imitation).

The pressure on host-country firms to undertake research and development was considerable. Local firms which were not innovative quickly lost their position within the ethicals market. Competition between drug companies appears to be intense though only a "moderate" proportion of market entry activity was truly innovative. Rivalry between U.S. companies and other foreign companies as well as host-country firms accelerates the rate of technology transfer within imitation

cycles. Although the overall number of new imitation cycles being created appears to have diminished a few major companies are innovative despite the general trend for a slower pace of new drug introduction.

Bibliography

Applezweig, N., Steroid Drugs (McGraw-Hill, London), 1962, pp. 9-52.

Association of the British Pharmaceutical Industry (ABPI), Supplementary Memorandum of Evidence to the Committee to Examine the Patent System and Patent Law, December 1968.

Bailey, Martin N., "Research and Development Costs and Returns: The U.S. Pharmaceutical Industry," Journal of Political Economy (January/February 1972), pp. 70-85.

Bathe, Peter, "Major Expansion of ICI Pharmaceutical Production Capacity," Manufacturing Chemist and Aerosol News, January 1972, pp. 44-45.

Belloc, Paola, "Assolutamente insufficienti l'innovazione e la ricenca nell'Industria Farmaceutica Italiana," Quadrante Scientifico, Quaderni ISRIL, Anno II, n 1, Gen.-Mar. 1971, pp. 43-53.

Biel, John and Yvonne Martin, "Organic Synthesis as a Source of New Drugs," in B. Bloom and G. Ullyot, Eds. (1971).

Bloom, Barry M., "The Rate of Contemporary Drug Discovery," in B. Bloom and G. Ullyot, Eds. (1971), pp. 176-184.

Bloom, B. and G. Ullyot, Drug Discovery, Science, and Development in a Changing Society (American Chemical Society, Washington, D.C.), 1971.

Burger, A., Medicinal Chemistry (Wiley-Interscience, New York), Parts 1 and 2, 1970.

Burstall, Mike, "Multinational Enterprises in the Pharmaceutical Industry," OECD/EAG Working Paper, 1975/76 (unpublished).

Carpenter, J.G.D., "Innovation in Chemical Structure in a Group of 267 Recently Marketed Drugs" [referred to in the EDC Chemicals study (below) as a private communication].

Cohen, Benjamin, Jorge Katz and William Beck, "Innovation and Foreign Investment Behavior in the U.S. Pharmaceutical Industry," NBER Working Paper 101, August 1975.

Cooper, M.H., Prices and Profits in the Pharmaceutical Industry (Pergamon Press, Oxford), 1966.

Comanor, W.S., "Research and Technical Change in the Pharmaceutical Industry," Review of Economics and Statistics, May 1965, pp. 182-90.

Cox, William E., "Product Life Cycles as Marketing Models," Journal of Business, Vol. 40 (Oct. 1967), No. 4, pp. 375-384.

Davey, D. G., "The Concern Over Drug Safety and Its Implications for the Industry's Innovation and Growth," NEDO Conference (1973), pp. 31-42.

deHaen, Paul, New Products Parade, Annual Review of New Drugs.

Douglas, R. D., "Commercial Implications of Patents for the Pharmaceutical Industry," NEDO Conference (1973), pp. 20-30.

Farrn, Peter, and Derek Riley, "The West European Pharmaceutical Industry," (Eurofinance-Economic Research Department Report), 1971.

Fishburn, A. G., "Pharmaceutical Research Laboratories' Role," The Pharmaceutical Journal, Jan. 3, 1970, pp. 19-21.

Gay, Paul, "Automation Aids the Repeatability of Batch Process," Manufacturing Chemist and Areosol News, Nov. 1973, pp. 44-45.

Grabowski, Henry G., "The Determinants of Industrial Research and Development: A Study of the Chemical, Drug, and Petroleum Industries," Journal of Political Economy, Vol. 76 (1968), pp. 292-366.

IMS Pharmaceutical Market Letter, "Nicholas Closes its Major Research Unit," Vol. 2, No. 23, June 9, 1975.

Jennings, John, "Government Regulations and Drug Development, FDA," in B. Bloom and G. Ullyot, Eds. (1971), pp. 247-256.

Kipling, Stewart W. and Robert H. Jones, "Marketing Strategies," in Teeling-Smith (1969), pp. 51-70.

Lake, Arthur, "Transnational Activity and Market Entry in the Semiconductor Industry," NBER Working Paper 126, March 1976.

Lall, Sanjaya, "International Pharmaceutical Industry and Less-Developed Countries," Oxford Bulletin of Economics and Statistics, Aug. 1974.

Lees, K. A., "Advances in Pharmaceutical Technology," The Pharmaceutical Journal, Feb. 21, 1970, pp. 180-183.

MacDonald, A. S., "Exchange Rates for National Expenditures on Research and Development," Economic Journal, June 1973.

McDonald, D. P., "Pharmaceutical Plant—A Question of Small Scale Equipment," Manufacturing Chemist and Aerosol News, Aug. 1973, pp. 23-27.

Mansfield, E., J. Rapoport, and J. Schnee, "Innovation and Discovery in the Ethical Pharmaceutical Industry," in Research and Innovation in the Modern Corporation (W. W. Norton, U.S.A.), 1971, pp. 187-185.

Markham, Jesse W., "Market Structure, Business Conduction and Innovation," American Economic Review, Vol. 55 (May 1965), pp. 323-32.

Moxey, Patrick, "More Automation in Packaging Machines and Processes," Manufacturing Chemist and Areosol News, Sept. 1972, pp. 21-22.

NEDO (National Economic Development Office), Chemicals Economic Development Committee, Innovative Activity in the Pharmaceutical Industry (H.M.S.O., London), 1973.

_____, Speeches Given at the NEDO Conference Held at the Royal College of Physicians, London, on 3rd May 1973, 1973.

OECD, Gaps in Technology--Pharmaceuticals, 1969.

Reekie, Duncan W., "Barriers to Entry and Competition," in Teeling-Smith (1969), pp. 1-20.

_____, Economics of Innovation with Special Reference to the Pharmaceutical Industry, Ph.D. Thesis, University of Strathclyde, 1969.

Ross, Walter, "The Prostaglandins are Coming," Readers Digest, July 1975, pp. 51-54.

Scheindlin, Stanley, "New Developments in Plant Drugs," American Journal of Pharmacology, September-October 1964, pp. 216-226.

Sheddon, W.I.H., "The Global Deployment of Research and Development Resources," NEDO Conference (1973), pp. 43-49.

Smith, G. Teeling, "Cost Effectiveness in Pharmaceuticals Research and Development," NEDO Conference (1973), pp. 1-13.

Smith, G. Teeling, Ed., Economics and Innovation in the Pharmaceutical Industry, Office of Health Economics, 1969.

Star, Steven H., "Pfizer International," in Vernon (1973), pp. 333-364.

Steele, Henry, "Patent Restrictions and Price Competition in the Ethical Drugs Industry," Journal of Industrial Economics (July 1964), pp. 198-223.

Stockbrokers report, "Industry's Status 'May Deteriorate'," Chemist and Druggist, March 20, 1971, p. 317.

Vernon, John M. and Peter Gusen, "Technical Change and Firm Size: The Pharmaceutical Industry," Review of Economics and Statistics, August 1974, pp. 294-302.

Vernon, R., "International Investment and International Trade in the Product Cycle," Quarterly Journal of Economics, Vol. 80 (May 1966), pp. 190-207.

Wilson, C. O., G. Grisvold and R. F. Doerge, Textbook of Organic, Medicinal, and Pharmaceutical Chemistry (J. B. Lippincott Company, Philadelphia), 1971.

Wood, Robin, "Is Pharmaceutical Research in the U.K. Without a Future?", Manufacturing Chemist and Aerosol News, November 1973, p. 51; "The Industrial Slum," same, April 1973, p. 43.

Wortzel, L. H., Technology Transfer in the Pharmaceutical Industry, U.N.T.A.R., 1972.

TABLE A1

List of Therapeutic Groups[1]

Alimentary System

1. Antacids
2. Gastro-intestinal sedatives
3. Laxatives, purgatives and lubricants
4. Drugs acting locally on the rectum
5. Antidiarrhoeals
6. Pancreatic preparations

Cardiovascular System

7. Cardiac disorders
8. Anginal drugs and coronary vasodilators
9. Peripheral vasodilators
10. Anti-hypertensives
11. Vasoconstrictors and migraine treatments
12. Anticoagulants
13. Miscellaneous cardio-vascular drugs

Central Nervous System

14. Analgesics and antipyretics
15. Hypnotics
16. Sedatives and tranquilizers
17. Antidepressants
18. Anti-emetics and anti-nauseants
19. Anticonvulsants
20. Rigidity and tremor controllers
21. C.N.S. stimulants

Musculo-Skeletal Disorders

22. Non-steroid anti-inflammatory drugs
23. Muscle relaxants
24. Rubefacients
25. Neuromuscular drugs

Hormones

26. Gonadal hormones and related synthetic compounds
27. Oral contraceptives
28. Corticosteroids and related drugs
29. Trophic hormones and related drugs
30. Insulin preparations; hyper- and hypo-glycaemics
31. Thyroid and antithyroid drugs
32. Other hormones

Genito-Urinary System

33. Diuretics and antidiuretics
34. Urinary anti-infectives and anti-spasmodics
35. Local and systemic drugs for vaginal and urethral infections
36. Drugs acting on the uterus
37. Spermicidal contraceptives

Infections and Infestations

38. Antibiotics
39. Sulphonamides and other anti-bacterials
40. Antituberculous drugs
41. Antileprotics
42. Antifungals
43. Anti-amoebics
44. Antimalarials
45. Anthelmintics and other anti-infestive drugs
46. Antivirals
47. Vaccines

(continued)

TABLE A1 (concluded)

Nutrition

48. Tonics: appetite stimulants
49. Iron; erythrotropic drugs
50. Mineral and nutritional additives
51. Vitamins
52. Anti-obesity drugs
53. Anabolic drugs
54. Food products

Respiratory System

55. Respiratory stimulants
56. Bronchospasm relaxants
57. Expectorants, cough suppressants, mucolytics, decongestant

Ear, Nose and Oropharynx

58. Local reactants on the nasopharynx
59. Oropharyngeal preparations
60. Aural preparations

Eye

61. Anti-infective preparations
62. Anti-inflammatory and anti-allergic preparations (steroid and non-steroid)
63. Glaucoma
64. Mydriatics and cycloplegics
65. Diagnostic and miscellaneous ophthalmic preparations

Allergic Disorders

66. Anti-allergic drugs
67. Desensitizing preparations

Skin

68. Soothing and protective preparations
69. Keratolytics and cleansers
70. Topical non-steroid antipruritic and anti-inflammatory preparations
71. Topical antifungal and anti-infestive preparations
72. Topical anti-infective preparations
73. Psoriasis (non-steroid preparations)
74. Acne (including steroid preparations)
75. Topical steroid preparations
76. Miscellaneous skin preparations

Metabolism

77. Carcino-chemotherapeutic drugs
78. Immunosuppressants
79. Gout
80. Poisoning and metabolic dysfunction
81. Drug dependence (tolerance, physiological and psychological dependence)

Surgical

82. Anaesthetics and agents for pre-medication
83. Surgical antibacterial
84. Mucolytic, proteolytic and other enzymes
85. Plasma expanders
86. Haemostatics
87. Surgical dressings

Diagnostic Agents

88. Same

1
Source: Monthly Index of Medical Specialties (MIMS).

TABLE A2

The Sample of New Chemical Entities of Study Introduced into America and the United Kingdom

	Trade Name	Chemical Name	Therapeutic Group	Firm in America	U.S. Date of Introduction[a]	Firm in United Kingdom[b]	U.K. Date of Introduction[b]	Lag (Months)[c]
1.	Eutonyl	pargyline	hypotensives	Abbott	2/63	Abbott	11/63	9
2.	Jectofer	iron sorbitex	hematinics	Astra (Sweden)	1/65	Astra-Hewlett	10/61	(39)
3.	Citanest	prilocaine HCl	anesthetics	Astra (Sweden)	1/66	Astra	3/65	(9)
4.	Atromid	clofibrate	cholestrol reduction	Ayerst (USA)	4/67	I.C.I.	3/63	(49)
5.	Polycillin	ampicillin	penicillin	Bristol	12/63	Beecham	7/61	(29)
6.	Tegopen	cloxacillin	penicillin	Bristol	4/65	Beecham	10/62	(30)
7.	Zyloprim	allopurinol	antiarthritics	B. Wellcome	9/66	Wellcome	6/66	(3)
8.	Trest	methixine HCl	antispasmodics	Dorsey, Sandoz (Switz.)	5/64	Wander	11/62	(18)
9.	Symmetral	amantadine	antispasmodics	Du Pont (USA)	12/66	Geigy	4/70	40
10.	Trisoralen	methixene HCl	pigment-enhancer	Elder (USA)	3/65	Wander	11/62	(25)
11.	Lasix	fursemide	diuretics	Hoechst	9/66	Hoechst	12/63	(33)
12.	Amicar Intravenus	amincaproic acid	coagulant	Lederle	6/64	AB Kabi (Sweden)	12/63	(6)
13.	Myambutol	ethambutol	antituberculosis	Lederle	12/67	Lederle	10/67	(2)
14.	Anhydron	cyclothiazide	diuretics	Lilly	11/63	CIBA	3/61	(33)
15.	Oncovin	vincristine sulfate	cancer chemotherapy	Lilly	7/63	Lilly	2/66	31
16.	Dymelor	acetohexamide	hypoglycaemic	Lilly	3/64	Lilly	9/62	(18)
17.	Aventyl HCl	nortriptyline	psychostimulant	Lilly	1/65	Lilly	9/63	(16)
18.	Haldol	haloperidol	ataraxics	McNeil	4/67	Searle	9/61	(67)
19.	Mucomyst	acetylcysteine	mucolytiagent	Mead Johnson (USA)	10/63	British Drug Houses	1/65	14
20.	Aldomet	methyldopa	hypotensive	Merck Sharp & Dohme	1/63	Merck Sharp & Dohme	4/62	(9)
21.	Indocin	indomethacin	antiinflamatory	Merck Sharp & Dohme	6/65	Merck Sharp & Dohme	12/64	(6)
22.	Edecrin	ethacrynic acid	diuretics	Merck Sharp & Dohme	2/67	Merck Sharp & Dohme	10/65	(16)
23.	Mintezol	thiabendazole	anthelmintics	Merck Sharp & Dohme	7/67	Merck Sharp & Dohme	8/67	1
24.	Maxibolin	ethylestrenol	anabolics	Organon	7/64	Organon	1/62	(30)
25.	Ponstel	mefenamic acid	analgesic	Parke Davis	8/67	Parke Davis	11/63	(45)
26.	Vas-measles-K	vaccine	biologicals	Pfizer	6/63	Pfizer	3/66	33
27.	Rondomycin	methacycline HCl	antibiotic	Pfizer	9/66	Pfizer	10/63	(35)
28.	Vibramycin	doxycycline	antibiotic	Pfizer	9/67	Pfizer	1/68	4

(continued)

TABLE A2 (continued)

	Trade Name	Chemical Name	Therapeutic Group	Firm in America	U.S. Date of Introduction[a]	Firm in United Kingdom[b]	U.K. Date of Introduction[b]	Lag (Months)[c]
29.	Hiprex	methenamine	antibacterials	Riker	11/67	Warner	9/65	(26)
30.	Dopram	doxapram	analeptics	Robins	9/65	Robins	9/71	60
31.	Navane	thiothixene	antaraxics	Pfizer	9/67	Pfizer	10/67	1
32.	Quaalude	methaqualone	sedative	Rorer	11/65	Roussel	9/65	(2)
33.	Afrin	oxymetazoline	nasal decongestant	Schering (West Germany)	8/64	Allen & Hanbury	11/62	(21)
34.	Celestone	betamethasone	hormone	Roussel	3/65	Glaxo	2/61	(50)
35.	Tinactin	tolnaftate	dermatological fungicide	Japan	3/65	Glaxo	10/66	19
36.	Garamycin	gentamicin sulfate	antibiotics	Schering (West Germany)	6/66	Schering (Australia)	7/66	1
37.	Candeptin	candicidin	topical fungicide	Schmid	11/64	J. Schmid (W. Germany)	8/67	33
38.	Flagyl	metronidazole	antibacterials	Searle	7/63	May & Baker	7/60	(36)
39.	Ovulen	hormone	birth control	Searle	5/66	Searle	12/63	(29)
40.	Dyrenium	triamterene	diuretics	SKF	9/64	SKF	11/62	(21)
41.	Osmitrol	mannitol	diuretics	Travenol, Baxter (USA)	6/64	Smith Miller Patch	5/65	11
42.	Serc	betahistine HCl	vasodilators	Unimed (USA)	12/66	Duphar (Holland)	10/70	58
43.	Lincocin	lincomycin HCl	antibiotic	Upjohn	1/65	Upjohn	11/63	(14)
44.	Tolinase	tolazamide	hypoglycemics	Upjohn	7/66	Upjohn	4/65	(15)
45.	Solocen	tybamate	ataraxics	Wallace	5/65	Wallace	5/66	12
46.	Presate	chlorphentermine HCl	antiobesity	Warner	4/65	Upjohn	7/61	(45)
47.	Negram	nalidixic acid	antibiotic	Winthrop	3/64	Winthrop	9/63	(6)
48.	Talwin	pentazocine	analgesic	Winthrop	7/67	Bayer Winthrop	4/67	(3)
49.	Sertax	oxazepan	antiaraxics	Wyeth	6/65	Wyeth	3/66	9
50.	Velsapen	hetacillin	penicillin-derivative	Bristol	1/71	Bristol	1/67	(48)
51.	Imuran	azathioprine	immunosuppresant	Wellcome	4/68	Wellcome	12/63	(52)
52.	Desferal Maysilate	deferoxamine mysilate	antidotes-chelating agent	CIBA	8/68	Wallace	10/64	(46)
53.	Locorten	flumethasone bivalate	corticoids-local	CIBA	1/70	CIBA	4/65	(57)
54.	Rimactane	rifampin	antitubercular	CIBA, Dow	5/71	Lepetit (France)	10/70	(7)
55.	Tridesilon	desonide	corticoids-local	Dome (Miles)	4/72	Dome (Miles)	2/72	(2)
56.	Aristospan	triamcinolone trexacetonide	corticoids-local	Lederle	9/69	Squibb, Lederle	5/64	(64)
57.	Loridine	cephaloridine	antibiotics	Lilly	3/68	Glaxo	11/64	(40)
58.	Capastat Sulfate	capreomycin	antituberculars	Lilly	9/71	Lilly	5/66	(64)

(continued)

TABLE A2 (concluded)

	Trade Name	Chemical Name	Therapeutic Group	Firm in America	U.S. Date of Introduction[a]	Firm in United Kingdom[b]	U.K. Date of Introduction[b]	Lag (Months)[c]
59.	Darvon-N	propoxyphene hapsylate	analgesic	Lilly	10/71	Dista (Lilly)	9/67	(49)
60.	Keflex	cephalexin monohydrate	antibiotics	Lilly	3/71	Lilly	2/70	(11)
61.	Inapsine	droperidol	antaraxics	McNeil	7/70	Janssen (Denmark)	9/68	(22)
62.	Meruvax	rubella vaccine	biologicals	Merck Sharp & Dohme	6/69	SKF	2/70	8
63.	Cortrosyn	cosyntropin (syn. ACTH)	hormones	Organon (Holland)	8/71	CIBA (Switzerland)	9/66	(47)
64.	Pavulon	pancuronium bromide	muscle relaxants	Organon (Holland)	11/72	Organon (Holland)	9/68	(51)
65.	Mithracin	mithramycin	cancer chemotherapy	Pfizer	5/70	Pfizer	5/70	0
66.	Matulane	procarbazine	cancer chemotherapy	Roche	10/69	Roche	5/66	(41)
67.	Levodopa	levodopa	muscle relaxants	Roche	6/70	Roche	8/70	2
68.	Geopen	carbenicillin	penicillin	Roerig (Pfizer)	8/70	Beecham	10/67	(34)
69.	Diapid	lypressin	antidiuretics	Sandoz (Switzerland)	9/70	Sandoz (Switzerland)	5/63	(89)
70.	Urispas	flavoxate HCl	muscle relaxant	SKF	5/71	Syntex (Panama)	5/71	0
71.	Hydrea	hydroxyurea	leukemia	Squibb	1/68	Squibb	4/67	(9)
72.	Cytostar	cytarabine HCl	cancer	Upjohn	11/69	Upjohn	7/70	8
73.	Cleocin HCl	clindamycin HCl	antibiotics	Upjohn	8/70	Upjohn	12/71	16
74.	Talwin	pentazocine HCl	analgesic	Winthrop	2/69	Winthrop	4/67	(22)

[a] De Haen.

[b] See Data section.

[c] Figures in parentheses indicate UK lead, otherwise US lead.

TABLE A3

Numbers of New Chemical Entities (of Study) Introduced Into the United Kingdom

First Issue	Number	Percentage (1950 - 1972)
1/1953 - 12/1957	145	27.8
1/1958 - 12/1962	183	35.1
1/1963 - 12/1967	117	22.6
1/1968 - 12/1972	51	10.0

TABLE A4

Numbers of New Chemical Entities (of Study) Introduced Into the United Kingdom

Therapeutic Groups (MIMS Classification)	Period 1950-62	Period 1963-72	1950-70
1. Alimentary System	25	10	35
2. Cardiovascular System	51	27	78
3. Central Nervous System	69	43	112
4. Musculo-Skeletal Disorders	8	3	11
5. Hormones	48	17	65
6. Genito-Urinary System	5	10	15
7. Infections and Infestation	75	33	108
8. Respiratory System, and Allergic Disorders	51	11	62
9. Other (Carcino-chemotherapy, Surgical)	21	14	35
(Study) Total	353	168	521

TABLE A5

Numbers of New Chemical Entities (of Study) Introduced Into the UK by Nationality of Company

Coverage: From January 1950 to December 1972

Nationality of Company	Number	Percentage
American	206	39.5
British	137	26.3
Swiss	70	13.4
French	37	7.1
German	25	4.8
Dutch	11	2.1
Italian	6	1.2
Swedish	5	1.0
Danish	3	0.6
Other	18	3.4
Total (Sample)	521	100.0

TABLE A6

Other Companies

1. Genatosan
2. Aspro Nicholas (Australia)
3. British Schering
4. Techniche
5. Zyma (UK)
6. AB Kabi
7. Selpharm
8. Tillotts Laboratories
9. Veritas
10. Rybar Laboratories
11. DDSA
12. Trommsdorf
13. Ashe Laboratories (USA)
14. West Pharmaceuticals
15. Mathews & Wilson (Woodword)
16. Ward Bleckinsop
17. Carnrick, G.W. & Co.
18. Radiol Chemicals Ltd.
19. Cambrian Chemicals
20. Genethic
21. Brookes, Washington
22. Syntex Pharmaceuticals (Panama)
23. Lloyd Hamol
24. Cuxon Gerrard
25. Cortiform
26. Smith, Miller, & Patch (USA)
27. Labs. Dr. Bouchard
28. Inter-Alia Pharmaceutical Services
29. Independent Research Laboratories
30. Therapharm
31. J. Schmid
32. Or Lupman Ubman
33. Kents
34. Cidag
35. Hommel Pharmaceuticals
36. Glenwood
37. Connegies of Welwyn
38. Reckitt & Colman Pharmaceutical Division
39. Maws Pharmacy Supplies
40. Pharmaceutical Manufacturing
41. MCP Pharmaceuticals
42. Brook and Baker

FIGURE A1

Reserpine and Synthetic Analogs

(Hypertensives)

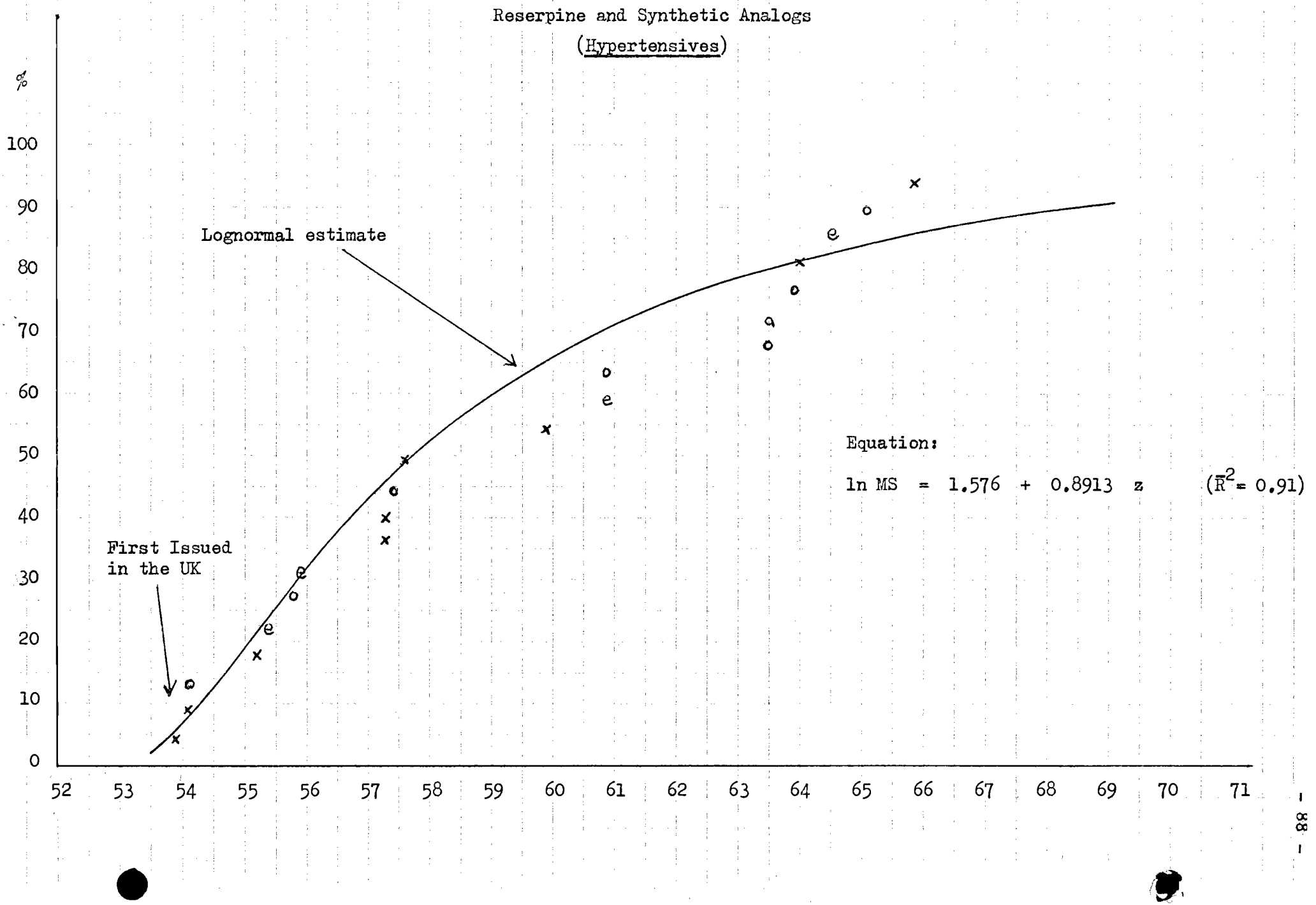


FIGURE A2

Antiemetics

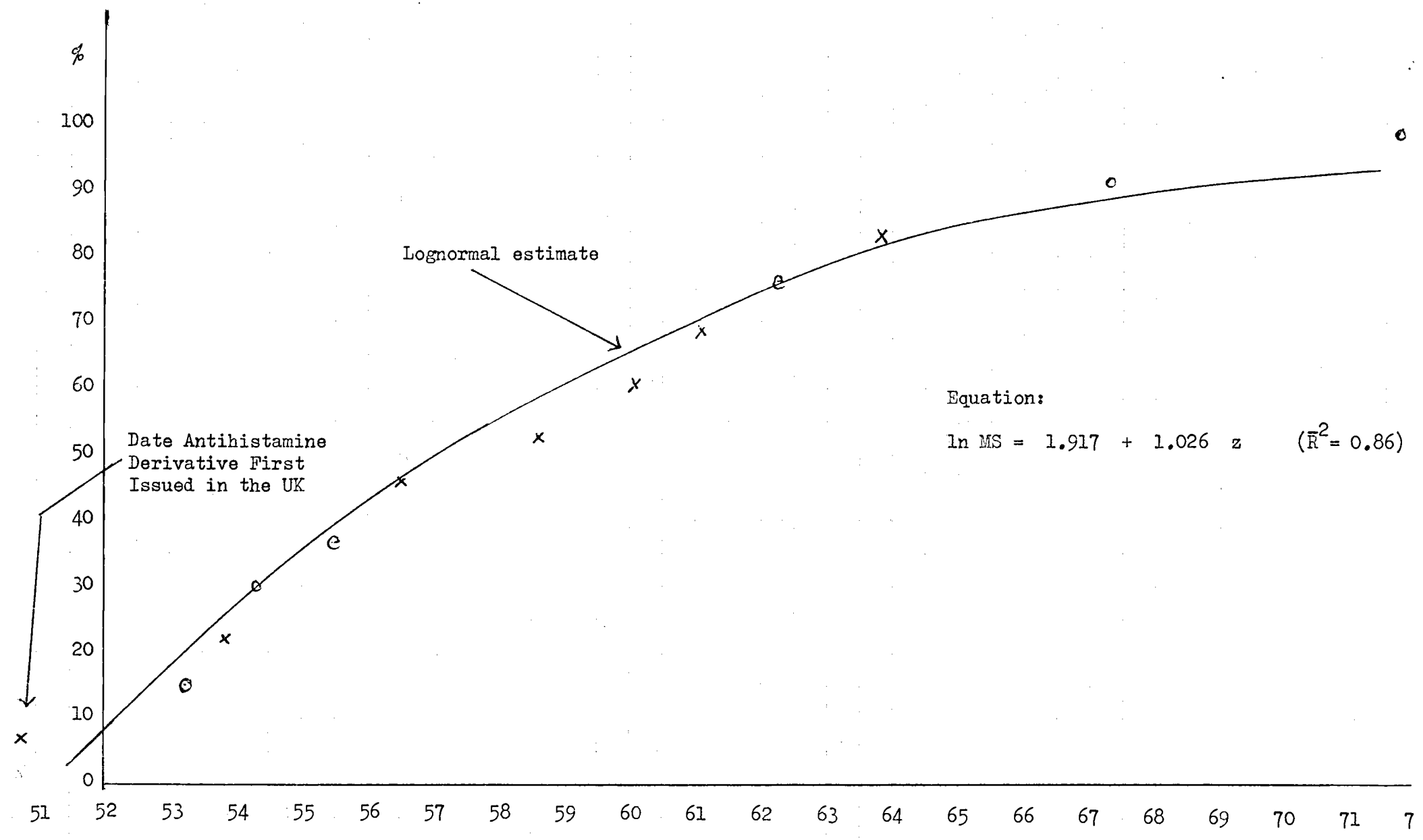


FIGURE A3

Penicillin V

(Antibiotics)

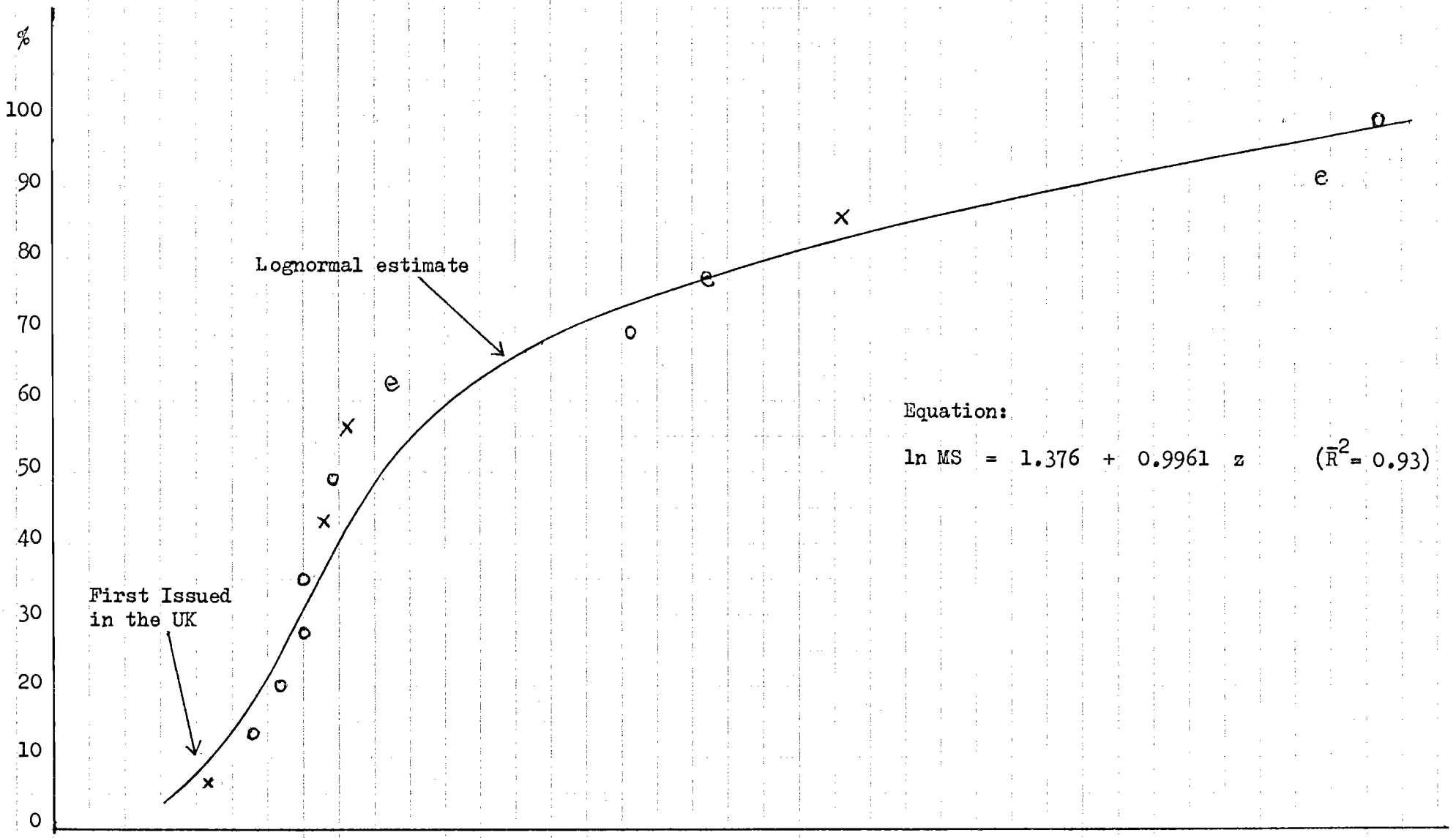


FIGURE A4

Oral Contraceptives

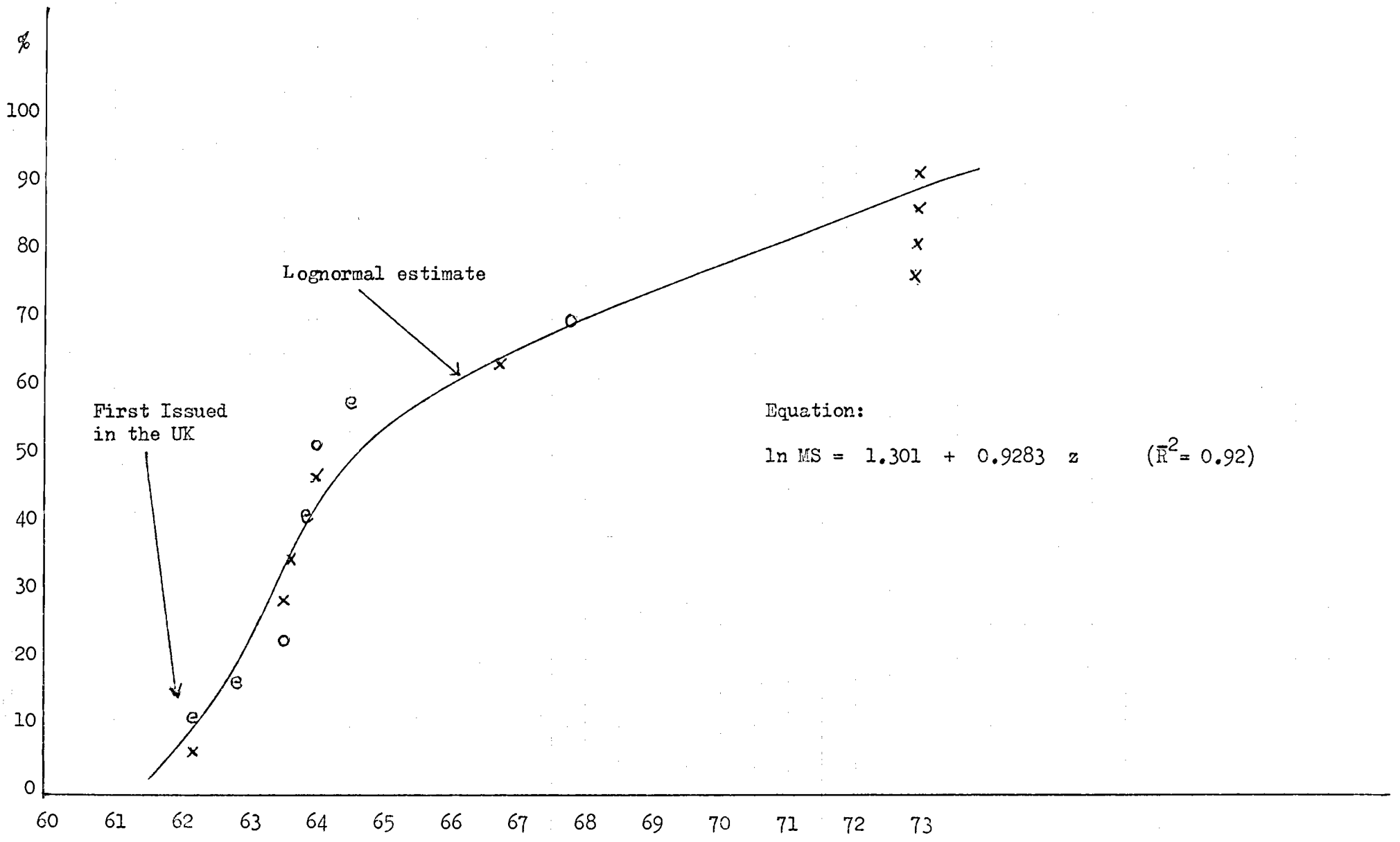


FIGURE A5

Antiparkinson Drugs