OHE

The Future for Pharmaceuticals: the Potential; the Pattern and the Problems

The eighth in a series of
Office of Health Economics monographs
dealing with aspects of the
prescription medicine market

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Office of Health Economics

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Foreword

Britain has very little to be proud of on the industrial front in the 1980s. Many of its traditional industries – the so-called 'smokestack industries' – are in decline. It has so far begun only slowly to share in the development of the new 'sunrise industries' – for example, electronics, nuclear energy, and those based on the latest biotechnologies. Amongst these latter, pharmaceuticals represent an outstanding and exceptional example of British achievement. It is a modern successful innovative industry in which Britain holds a leading position.

This booklet does not pretend to be a new empirical economic analysis of the industry's success. Instead, it is a statement of the continuing contribution which the pharmaceutical industry can make to the medical and economic wellbeing of Britain over the next twenty years.

As a positive statement of the achievements which are possible, this booklet is also a warning of the amount which is at risk if the industry were to be unfavourably treated. Under successive governments over the past thirty years the pharmaceutical industry recognises that it has received fair treatment in Britain. It is proud of the record which it has been able to achieve in the consequent generally favourable social and economic climate.

The Office of Health Economics is confident that future British governments will continue to recognise the economic importance of the pharmaceutical industry and that the optimistic prospects described in this booklet will come to fruition.

George Teeling Smith

Introduction

Pharmaceuticals have made a major contribution to the achievements of the National Health Service over the past 35 years. In the early days, the use of the antituberculosis compounds conquered the disease and released large numbers of hospital beds for the elderly and chronic sick. The childhood infections, such as diphtheria, scarlet fever and measles, are no longer major causes of death and it is estimated that over 250,000 people alive in Britain today would have died in childhood from these causes had the modern vaccines and antibacterial medicines not been developed.[1] More recently, the triumphs of major surgery, such as hip replacements, renal transplants and repairs after traumatic accidents are made possible by modern anaesthetics, muscle relaxants and immunosuppressive compounds. In psychiatry, the treatment of mental illness has been revolutionised by the development of the tranquillisers and antidepressants. Even in those diseases for which prevention or cure is not yet possible, much suffering is alleviated by medicines which reduce pain and disability.

Thus the pharmaceutical industry is an integral part of the health care system in Britain. It has an intimate and sometimes sensitive relationship with the National Health Service.[2] But in addition it has made a vital contribution to the national economy. In 1982, the pharmaceutical industry in Britain achieved exports of almost £1,000 million, and made a positive contribution of £600 million to the nation's balance of trade. In the latter respect, Figure 1 shows that it was excelled only by five industrial categories – petroleum and related products, power generating machinery, specialised machinery, other transport equipment and general industrial machinery. As Figure 2 shows, in the Department of Trade's league table of industries' contribution to Britain's trade surplus, pharmaceuticals has consistently lain between 4th and 6th place since 1975, having moved up from 8th place in 1970.

This economic success of Britain's pharmaceutical industry depends on its record of innovation. Worldwide, it is increasingly recognised that it is the private enterprise, competitive, multinational pharmaceutical companies which are largely responsible for the discovery and development of new medicines. In a now classic study, the American

1 Teeling Smith G (1982). The Contribution of Industrial Pharmacy to Health Care. *Die Pharmazeutische Industrie* 44;1;61.

2 Report of the Committee of Enquiry into the Relationship of the Pharmaceutical Industry and the National Health Service 1965–67 ('The Sainsbury Report'). HMSO Cmnd. 3410.

1 All UK visible exporters with positive trade surplus – 1982

Division (Industry)	*Exports (fob) £m*	*Imports (cif) £m*	*Trade balance £m*	*Rank*
33 (petroleum, and related products)	10,642	6,274	4,368	1
71 (power generating machinery)	2,809	1,483	1,326	2
72 (specialised machinery)	2,604	1,485	1,119	3
79 (other transport equipment)	2,033	989	1,043	4
74 (general industrial machinery)	2,412	1,634	778	5
54 (medicinal and pharmaceutical preparations)	978	375	603	6
11 (beverages)	1,059	518	541	7
69 (manufactures of metal)	1,395	950	445	8
51 (organic chemicals)	1,592	1,172	420	9
59 (chemical materials)	905	499	406	10
55 (essential oils & perfume)	524	242	282	11
53 (dyeing and tanning)	464	198	266	12
04 (cereals and cereals preparations)	774	550	224	13
87 (scientific instruments)	1,255	1,053	202	14
52 (inorganic chemicals)	695	539	155	15
73 (metal working machinery)	522	380	142	16
32 (coal, coke and briquettes)	330	224	106	17
62 (rubber manufactures)	418	326	92	18
66 (non metalic manufactures)	1,611	1,520	91	19
12 (tobacco)	391	319	72	20
61 (leather manufactures)	202	155	48	21
00 (live animals – for food)	179	133	46	22
57 (explosives and pyrotechnic products)	37	11	26	23
81 (sanitary, plumbing, and heating, etc)	107	104	3	24

Source Customs and Excise (Overseas Trade Statistics, December 1982).

Note Division 54 excludes pharmaceutical chemicals.

2 UK top 20 visible exporters with trade surplus

Division (Industry)	Ranking by size of positive trade surplus							
	1970	1975	1976	1977	1978	1979	1980	1982
33 (petroleum, and related products)	–	–	–	–	–	–	–	1
71 (power generating machinery)	–	1	1	1	2	2	2	2
72 (specialised machinery)	–	3	3	3	1	1	1	3
79 (other transport equipment)	2	–	–	–	–	5	7	4
74 (general industrial machinery)	1	–	–	–	3	3	3	5
54 (medicinal and pharmaceutical preparations)	8	5	6	6	5	6	4	6
11 (beverages)	5	6	7	7	6	7	5	7
69 (manufactures of metal)	4	4	4	4	4	4	6	8
51 (organic chemicals)	–	–	11	8	–	13	8	9
59 (chemical materials)	12	7	9	9	9	9	9	10
55 (essential oils and perfume)	15	12	13	12	10	10	10	11
53 (dyeing and tanning)	13	8	10	11	11	12	11	12
04 (cereals and cereals preparations)	–	–	–	–	–	–	–	13
87 (scientific instruments)	10	–	–	–	14	14	13	14
52 (inorganic chemicals)	–	–	–	–	15	11	14	15
73 (metal working machinery)	–	–	–	–	–	–	–	16
32 (coal, coke and briquettes)	16	–	–	–	–	–	–	17
62 (rubber manufactures)	11	10	12	13	16	15	15	18
66 (non-metalic manufactures)	21	11	5	5	7	8	16	19
12 (tobacco)	–	–	–	–	–	–	19	20

Source Customs and Excise Overseas Trade Statistics.

Notes
Division 54 excludes pharmaceutical chemicals.
UK trade figures for 1981 are not available because of the civil servants dispute in that year.
Prior to 1977, some Divisions were affected by the reallocations of constituent items to other groups, and hence they are not strictly comparable with later years.

economist, David Schwartzman, showed that between 1950 and 1969, these companies were responsible for 88 per cent of all the new pharmaceutical chemical entities to reach the market.[3] More significantly, Figure 3 shows that this percentage rose from 86 per cent in the 1950s to 91 per cent in the 1960s. Since then the percentage has almost certainly increased still further. In 1981, every one of the top twenty pharmaceuticals on sale in Britain had been developed within their respective pharmaceutical companies. Strikingly, ten out of these twenty medicines had been developed in British industrial research laboratories.

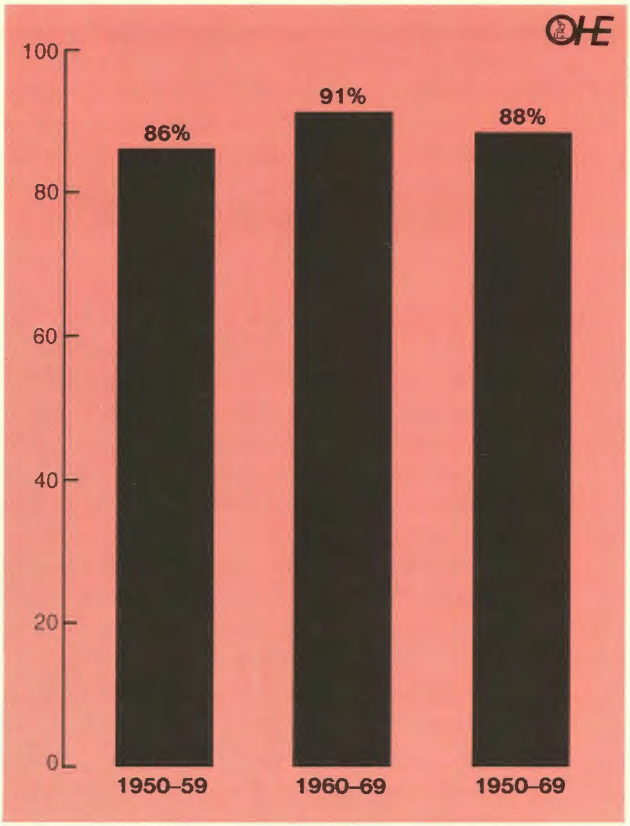
This predominance of the industrial contribution to pharmaceutical innovation is not surprising. A recent estimate suggested that it now costs on average more than £50 million to develop a single successful new pharmaceutical chemical compound.[4] For an organisation to expect even limited success in pharmaceutical innovation, therefore, it must invest recurring sums of this order of magnitude within relatively short periods of time – say a minimum of £20 million a year. With investment of this magnitude at risk, neither government research establishments nor academic institutions are inclined or feel able to invest the funds necessary to discover new medicines.

Nevertheless, the industry's record of innovation depends essentially on basic pharmacological and pathological knowledge developed in academic institutions and government research establishments. In countries such as Britain with a successful record in the development of new medicines, there is close collaboration between academia and industry, often with scientists from either side working together or even exchanging roles. In Britain, the academic investment in this fundamental research is very substantial. The government funded Medical Research Council spent about £100 million in 1981/82 on basic biomedical research,[5] in addition to the amounts funded by the University Grants Committee and by the medical charities.

Additionally, as this paper will discuss in detail in its final section, there needs to be a social and economic climate in which the pharmaceutical industry's research can flourish. Again Britain has in the past been fortunate in this respect. However, as the

3 Schwartzman D (1976). Innovation in the Pharmaceutical Industry. The Johns Hopkins University Press. Baltimore and London.
4 Chemicals Economic Development Committee (1981). Research and Development Costs, Patents and Regulatory Controls; a consultative document. National Economic Development Office, London.
5 Medical Research Council (1982). Annual Report 1981–82.

3 Percentage of new chemical entities discovered and introduced by the pharmaceutical industry 1950–59, 1960–69 and 1950–69



Source Schwartzmann D. (1976)

evidence in this paper will demonstrate it is only in those countries where the government creates a favourable environment for pharmaceutical innovation that substantial numbers of new medicines are developed. A hostile environment is inimical to successful pharmaceutical research. Therefore, because the pharmaceutical industry in Britain is continuing to face criticism for some of the very features which have been responsible for its success, it is important to create a better understanding of its potential progress in the future, of the probable international pattern of its development and of the problems which companies will face. There is no automatic right for Britain to continue to enjoy the success in pharmaceutical innovation which has contributed so substantially to the national health and the national economy over the past 30 years. Those concerned with the health of the nation must understand and accept the social and economic conditions which are necessary if the pharmaceutical industry is to continue to flourish in Britain. Success in export markets depends on a strong and stable home market. This paper sets out to describe the potential, the pattern and the problems, and then to review the prospects for the pharmaceutical industry in Britain.

The Potential

In order to understand the potential for future progress in pharmaceutical innovation, it is necessary first to understand the background.

The 'first therapeutic revolution', as it can be called, occurred between the 1940s and the 1960s. Thus the multinational research-based pharmaceutical industry as it exists today dates back only about 35 years. Before that, pharmaceutical production had been based mainly on the extraction of active ingredients from naturally occurring compounds whose use had been traditional for centuries, such as atropine from belladonna, digoxin from digitalis, morphine from opium, and strychnine from nux vomica. However, the antecedents of the industry go back to the 19th century. In the 1860s, the development of the germ theory by Pasteur and his basic understanding of immunology laid the basis for the industry. By identifying a specific causative organism for infection, he set the scene for the discovery of ways of controlling it. The approach which was finally successful was precisely envisaged by Ehrlich in the 1890s. He dreamed of a 'Magic Bullet' which would single out and attack the invading germs without damaging their human host.

Further development of the theoretical basis for the later therapeutic revolution was characterised by the work of Barger and Dale in the Wellcome Physiological Research Laboratories in the early years of this century. They described the chemical basis for the control of the autonomic nervous system, which is responsible for normally automatic bodily functions such as the digestion and breathing. The realisation that faults in the operation of this nervous system could be caused chemically opened the way for the development of biochemicals to correct these defects.

These developments in the basic understanding of tissue or *intercellular* biochemistry led in due course to the wave of pharmaceutical innovation illustrated in Figure 4. Ehrlich's dream of a 'Magic Bullet' was realised in the 1930s with the discovery first of the antibacterial 'Prontosil' by Domagk in the German Bayer laboratories, and then of 'M and B 693' in the May and Baker laboratories in Britain. It was of this latter medicine that Churchill said after a bout of pneumonia:

> This admirable M and B, from which I did not suffer inconvenience, was used at the earliest moment and after a week's fever, the intruders were repelled.[6]

These early antibacterial discoveries were followed in the 1940s with the development, for example, of penicillin, the broad-spectrum antibiotics, the anti-hypertensives, the psychotropics and later the synthetic anti-inflammatory preparations and the β-blockers for heart disease.

From this time on, the pharmaceutical industry became primarily concerned with the discovery and development of new medicines; their eventual production became almost a subsidiary activity. The whole subsequent upsurge of pharmaceutical discoveries and the social and economic contribution which resulted, has been well-documented.[7]

Nevertheless, a pessimistic view is that this Golden Age of Innovation is over, and that the adverse factors illustrated in Figure 5 will cause the innovative pharmaceutical industry to go into a decline.

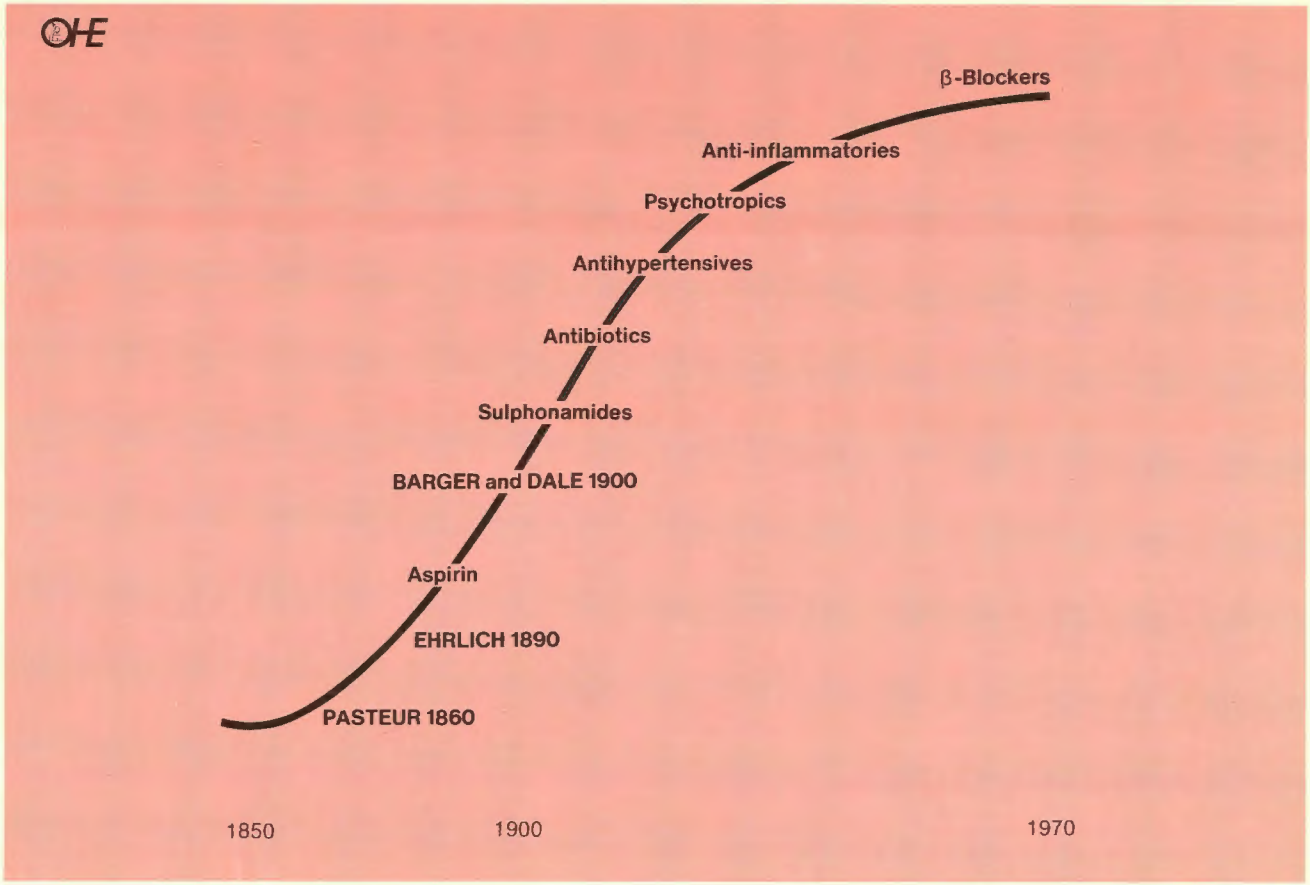
However, the optimistic view of the potential for the industry is very different from this. Just as Pasteur's basic understanding led on eventually to the first therapeutic revolution, it seems likely that fundamental scientific discoveries in the 1950s will pave the way for a new upsurge of pharmaceutical innovation in the 1980s and beyond. Elsewhere, OHE has argued that this new wave of innovation will justify the epithet of 'The Second Pharmacological Revolution',[8] and this concept is starting to gain general acceptance. The key scientific discovery on which this optimistic scenario is based is the elucidation of the structure of the DNA molecule by Watson and Crick in 1953. This, together with much other work on molecular biology at Cambridge and elsewhere, has opened the way for fundamental developments in *intracellular* biochemistry. Just as the discoveries of the 19th century led to a spate of pharmaceuticals acting at the level of intercellular chemistry, so the discoveries of the 20th century will lead to pharmaceuticals acting at the intracellular level – inside the human cells.

There are three obvious examples of types of disease which are likely to benefit from these new developments. They are the virus infections, the cancers and the so-called 'autoimmune diseases', each of whose causes and methods of control may be to some extent interrelated. This new wave of innovation is illustrated in Figure 6.

Already the first specific antiviral agents are on the market. 'Acyclovir' has been shown to be effective against virus infections of the eye, genital herpes and shingles. Recently, Vane of Wellcome, a Nobel prizewinner in Medicine in 1982, suggested that soon 'a protein sniffed up the nose would prevent and may cure a common cold'.[9]

Cancers, like virus infections, are processes which take place inside the human cells. Hence an understanding of intracellular biochemistry is likely to lead in the foreseeable future to methods of preventing or controlling the growth of cancer cells. These new anticancer agents are likely to be very

4 The first therapeutic revolution



much less toxic than the compounds which are used with some success at present. By the 21st century, cancer may have become a scourge from the past, in the same way as diseases like tuberculosis and scarlet fever have been brought under control in the 20th century.

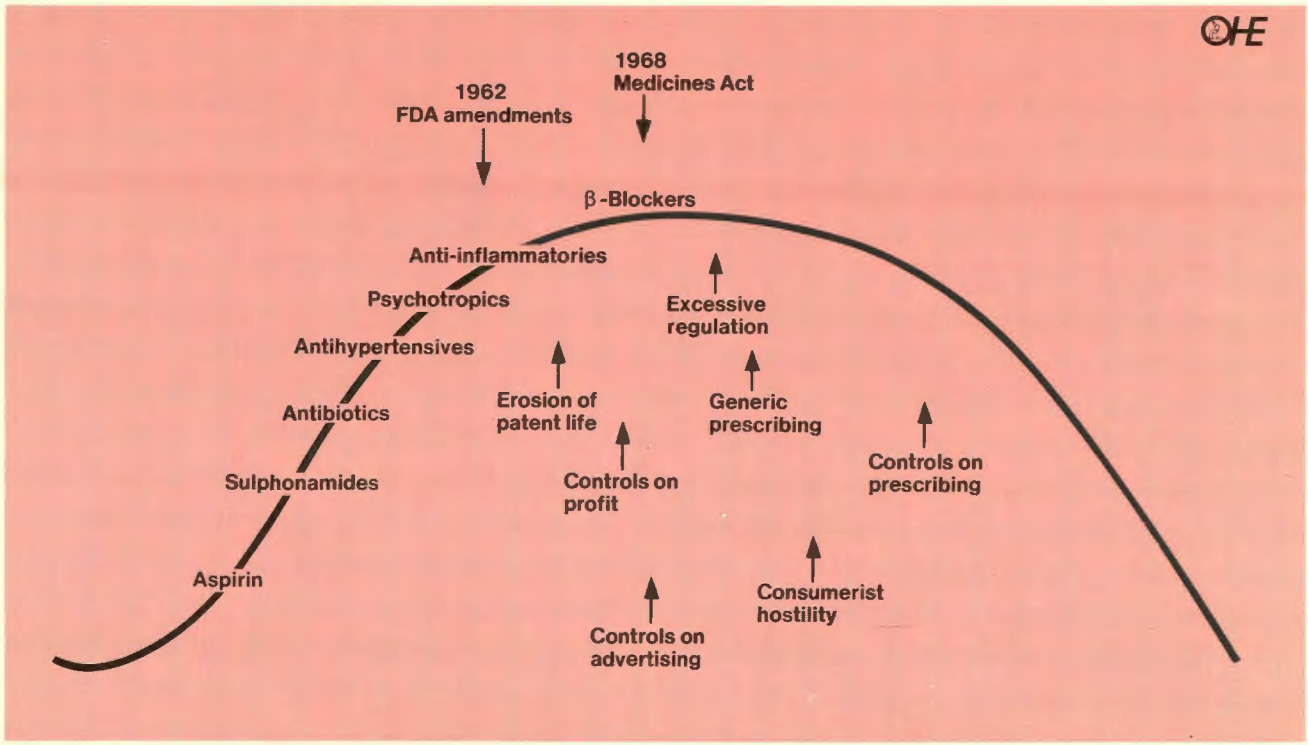
In the third example, the scope for the avoidance of the auto-immune diseases has still to be fully identified. These are conditions where the body's own defence mechanism gets out of control and instead of attacking invading foreign organisms turns instead against the healthy tissues of the body itself. The full complexity of this process is not yet completely understood, but it is likely that many diseases such as multiple sclerosis, Parkinson's disease and rheumatoid arthritis may be caused in this way.

The process is reasonably well understood in the case of early-onset or insulin-dependent diabetes. Here the body's immune mechanism attacks and destroys the Islets of Langerhans in the pancreas, which are responsible for the production of insulin. Although it is not yet known exactly how the malfunction of the defences is triggered off, it is known that people with certain genetic factors are more prone to early-onset diabetes than others. Thus it is possible to identify children at risk, and it should be possible to protect them against damage as soon as the infection or infections which can trigger the harmful immune response are identifed. In the opinion of Professor Batchelor from Hammersmith Hospital, prevention is a sufficiently realistic possibility for a scientific working party to be set up to take matters forward.[10] Other diseases caused by the autoimmune response may also yield to advances in understanding and hence be avoidable in the foreseeable future.

Advances in genetic engineering are also likely to bring progress against single-gene inherited defects,

6 Quoted in: Calder R (1961). The Life Savers. Pan Books, London.
7 See, for example, reference in Footnote 1.
8 Wells N E J (Ed) (1983). The Second Pharmacological Revolution. Office of Health Economics, London.
9 Vane J R (1983). Prostaglandins and Antivirals. In: Wells N E J (Ed). The Second Pharmacological Revolution. Office of Health Economics, London.
10 Batchelor J R (1983). Autoimmune Disease. In: Wells N E J (Ed). The Second Pharmacological Revolution. Office of Health Economics, London.

5 Pharmaceutical progress under threat



such as phenylketonuria. At present the best that can be done is to maintain children born with this defect on a special diet to prevent their becoming mentally retarded. In the future, it should be possible to detect the defective genetic material in the foetus, and either to abort the birth or, eventually, to replace the faulty gene with a perfect one.[11]

Apart from the pharmaceutical progress which is likely to come from intracellular biochemistry, there is also still an important potential from developments in tissue biochemistry. The whole field of prostaglandins is an example here. It is quite possible that within the next few years developments in this area may lead to a reduction of heart disease. In mental illness, also, an understanding of the endorphins and enkephalins may lead to important advances and new compounds will continue to be identified in the tissues of the brain. This and similar research offers the possibility of the prevention of conditions such as schizophrenia, senile dementia and drug and alcohol dependence.

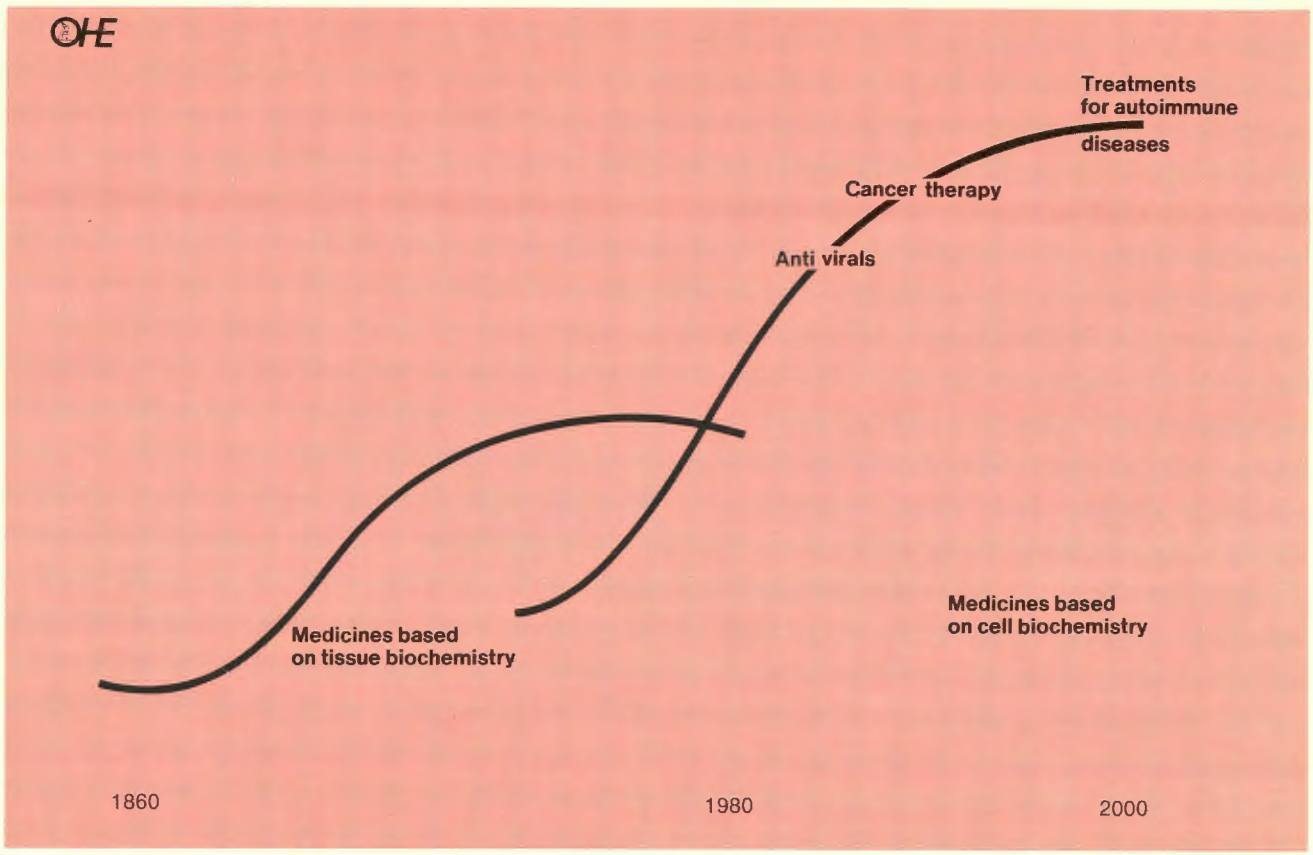
Finally, there are two other fields of research which should be recorded as an important part of the potential for future progress. The first is with 'targeted drug-delivery systems', which will make the action of future medicine much more precise. Instead of circulating freely in all the body tissues, the active ingredient of the medicine will be released only at the site where its activity is required. There will also be concurrent improvements in the rate of release of the medicament, based on a better understanding of the exact concentrations over time which produce the best therapeutic action and the least harmful effects.

The other probable advance will be specifically in reducing adverse reactions to medicines. Again here an understanding of the intracellular immune mechanism will be one way of making progress. For example, with the anti-hypertensive compound, hydralazine, it has been shown that only people with particular genetic immune factors react adversely by developing the symptoms of systemic lupus erythematosus. It is possible to screen patients for the relevant genetic factors, and to avoid prescribing hydralazine for those identified as being 'at risk'. This would completely avoid this particular adverse reaction, and a similar principle is likely to be applicable to other medicines.

Thus, there are very real advances in the pipeline, which will bring both relief from suffering and economic benefits. The next section of this paper considers how these benefits are likely to be distributed geographically.

11 Genetic engineering also has a direct relevance to advances in methods of pharmaceutical production, but these are outside the scope of this paper.

6 The second pharmacological revolution

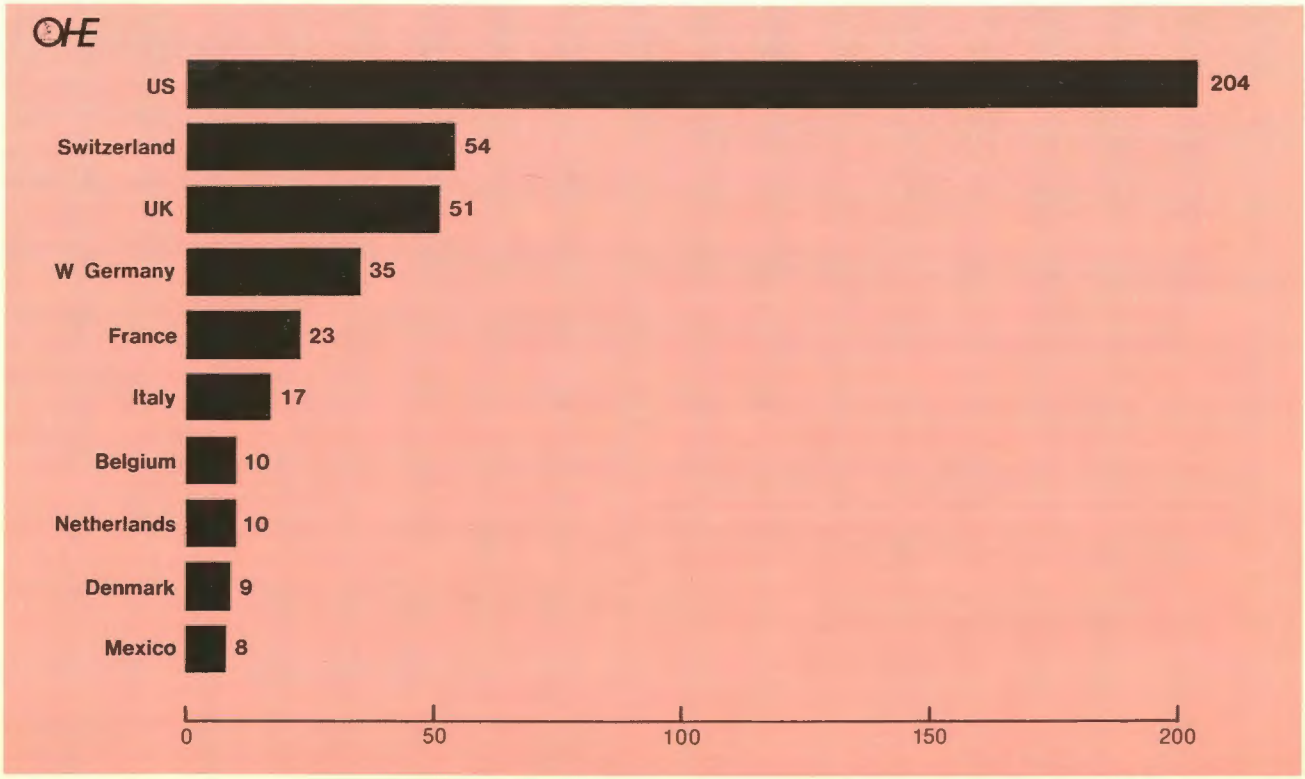


During the past 30 years of 'the first therapeutic revolution' only five countries have dominated the scene, both as sources of innovation and in terms of their contribution to world trade in pharmaceuticals. These countries are Great Britain, France, West Germany, Switzerland and the United States. A study for the National Economic Development Office in 1973 showed that these were the five countries which had developed the largest number of new pharmaceutical chemical entities between 1958 and 1970.[12] The results of the study are shown in Figure 7. The dominant position of these five countries in terms of international trade is even more marked, as Figure 8 shows. No other country, apart from these five, has a substantial positive balance of trade in pharmaceuticals. As will be discussed later, among the largest industrial nations Japan is a notable exception from the list of innovators and exporters. So too are the countries of Eastern Europe: apparently because of the nationalised control of the pharmaceutical industry in those countries, no major pharmaceutical innovations have emerged from them over the past 35 years.

It is particularly significant that four out of the five successful countries – Great Britain, West Germany, Switzerland and the United States – have a particularly favourable government and academic climate to support their pharmaceutical industry. There is freedom for pharmaceutical prices in the three latter countries, and in Britain the Pharmaceutical Price Regulation Scheme specifically allows research spending as a cost and takes account of the need to stimulate a 'strong, efficient and profitable pharmaceutical industry', as well as ensuring reasonable prices for the National Health Service. These countries also have a healthy respect for patents and brand names. Similarly, there is a strong base of pharmacological science in the same four successful countries. By contrast, other countries such as Australia, Belgium, Canada, Italy and Spain have restrictive economic controls on their pharmaceutical industries, which take no account of the importance of supporting the costs of innovation. Many of them also lack a strong infrastructure of basic biological science.

Against this background, the prospects for the future are particularly interesting. It seems very possible that Japan will come into a leading position as an innovator and exporter. Figure 9 shows that already Japanese pharmaceutical research spending has

7 Number of new pharmaceutical chemical entities 1958–70, by country of origin



Source NEDO (1973)

8 Pharmaceutical balance of trade for leading exporting countries

Values in US $M

Country	1980 Exports	Imports	Balance
West Germany	2,272	1,291	981
USA	2,020	803	1,217
UK	1,734	517	1,217
Switzerland	1,615	411	1,204
France	1,497	701	796
Italy	688	652	36
Belgium	669	655	14
Netherlands	619	569	50
Denmark	308	205	103
Sweden	305	326	–21
Japan	295	1,074	–779
Austria	201	350	–149
Yugoslavia	193	84	109
Spain	191	245	–54
Ireland	166	156	10
EEC (the 10)	7,975	4,906	3,069

Source OECD trade databank

9 Pharmaceutical research and development expenditure

Country	Year	R and D Expenditure	£m
United States	1980	$1,524mn[1]	655
West Germany	1980	DM1,800mn[2]	425
Japan	1979	Y167.8bn	360
Switzerland	1979	SFr1,100mn[3]	312
United Kingdom	1980	£280mn[4]	280
France	1979	FF1,951	216
Italy	1980	L150bn	75
Sweden	1981	SKr522mn[5]	51
Netherlands	1978	Fl170mn	41
Denmark	1981	DKr236mn	16

Exchange rates to pounds taken as the moving annual average for the year in question.

Notes

1 Excludes expenditure outside USA.
2 Includes some expenditure outside Germany.
3 Three leading companies only. Includes expenditure outside Switzerland.
4 Includes capital expenditure.
5 Two leading companies only (Astra SKr373mn, Pharmacia SKr149mn).

Sources

USA : US Pharmaceutical Manufacturers' Association 1979–80 Annual Survey Report.
West Germany : BPI. Pharma Jahresbericht 1981–82.
Japan : JPMA Annual Report 1981.
Switzerland : Pharma Information, per *Chemische Rundschau*, 22/4/1981, p17.
UK : ABPI Annual Report 1980–81.
France : FFIM. Chiffres Clés 1982.
Italy : Europa Chemie, 1981, No 12, p195.
Sweden : Company Reports.
Netherlands : *Scrip* – 30 June 1979.
Denmark : MEFA *Facts* 1982.

10 100 leading international pharmaceutical products in 1980

Country of origin	Number of products	% of world market	% of 100 product sales
Leading 100 products	100	24.1	100.0
USA	35	9.5	39.4
United Kingdom	14	4.2	17.4
Germany	14	3.3	13.7
Switzerland	12	2.5	10.4
Japan	8	1.7	7.0
France	3	0.6	2.5
Italy	2	0.4	1.7
Belgium	2	0.3	1.2
Canada	2	0.3	1.2
Denmark	1	0.3	1.2
USSR	1	0.3	1.2
Sweden	1	0.1	0.4
Unclassifiable	5	0.7	

Source Derived from IMS 'MIDAS' audit.

overtaken that of Switzerland and the United States, and that France has been relegated to sixth place.[13] In general, as the previous paragraph hinted, France is in some ways an exception amongst the 'top five'. The French position appears relatively less strong when compared with that of the other four successful innovators. Its pharmacology has in the past been weaker: British pharmacologists, for example, have referred disparagingly to the French method of evaluating new medicines as the 'French Impressionist' principle. They were slow to adopt the concept of the randomised controlled clinical trial and relied instead on the clinical impressions of 'experts'. In France, also, pharmaceutical prices are now held down by restrictive price controls. Finally, the decision of the Mitterand government to take the major French pharmaceutical companies into state ownership raises interesting questions. Only time can tell whether state ownership in France manages to avoid the stagnation of pharmaceutical innovation which appears to have been a feature of the state owned industries in Eastern Europe.

Figure 10, which shows the source of the leading international pharmaceutical products in 1980, again suggests that Japan is starting to replace France in the top five nations.[14] In general, therefore, it looks

12 Chemicals Economic Development Committee (1973). Innovative Activity in the Pharmaceutical Industry. National Economic Development Office, London.

13 Pharmaceuticals Sector Working Party, Economic Development Committee for the Chemical Industry (1982). Confidential Assessment; EDC/Chem/Ph (82)19.

14 Derived from Intercontinental Medicinal Statistics 'MIDAS' Audit (1982).

as if Great Britain, Germany, Japan, Switzerland and the United States may be the five leading countries both for pharmaceutical innovation and international trade in pharmaceuticals by the end of the present decade. However, it must be pointed out once again that Britain has no automatic right to remain among these leaders. If the problems to be outlined in the next section were to beset the British industry more seriously in the 1980s, Britain also could drop out of the top bracket.

The underlying problem facing the pharmaceutical industry is the rising cost of research. In 1963, Palmer of Glaxo recorded that pharmaceutical industry research spending in Britain 'must now be approaching £10 million per annum'. However, he concluded that 'for an annual expenditure of between £150,000 and £200,000 a company may reasonably be expected to build up valuable research and development capacitty in a restricted field'. For a 'substantial stake in a broad field of pharmaceutical research and development' Palmer estimated that over one million pounds per annum was required.[15] These figures of twenty years ago look trivial compared with the present estimate that it costs on average over £50 million per successful compound developed. In total, the British industry in 1982 was spending over £350 million per year on pharmaceutical research and development. In real terms, this is about a six-fold increase over 1963 and three times the research budget of the Medical Research Council. Nevertheless, by international standards British company spending is fairly modest. It is estimated that by 1979 Hoffmann-La Roche of Switzerland alone was already spending about £150 million a year on research and development.[16] Worldwide, the pharmaceutical industry is estimated to have spent about £4,000 million on research and development in 1981. Thus Britain spends about 8 per cent of the worldwide pharmaceutical research budget, although its home market accounts for only 4 per cent ot total world sales.

The problem in financing the industry's research can be set out under seven headings. All of these are interrelated, but it is clearer to describe and discuss them separately. These headings are excessive regulation, restrictions on prices and profits, erosion of patent protection, the undermining of brand names, restrictions on promotion, pressures on prescribing and consumer criticisms.

Excessive Regulation

The history of regulation in the pharmaceutical industry goes back more than a century and a half. In the United States 1813 there was a Vaccines Act to regulate the production and sale of smallpox vaccine. Again in the United States, the first major regulations to control the testing and marketing of new medicines were introduced by the Food and Drug Administration in 1938 in response to a disaster with the elixir of sulphanilamide. This occurred because the manufacturers used a toxic solvent to produce the elixir which killed 107 people before the mistake was realised.[17]

However, it was the thalidomide tragedy in 1961 which precipitated the stricter pharmaceutical

15 Palmer H W (1963). The Pharmaceutical Industry: What it is and what it does; *Proceedings of the Royal Society of Medicine;* 56;7;547–554.

16 Burstall M L, Dunning J H and Lake A (1981). Multinational Enterprises, Governments and Technology: Pharmaceutical Industry. OECD, Paris.

17 Crout J R (1978). The Nature of Regulatory Choices. Centre for the Study of Drug Development, Rochester.

regulations in force today, which are embodied in the 1962 Amendments to the Food and Drug Regulations in the United States and in the 1968 Medicines Act in Britain. This British Act gave statutory backing to voluntary drug safety arrangements which had been introduced in 1964 under the Dunlop Committee.

The pharmaceutical industry is not opposed to such regulations. Since the thalidomide tragedy, it has recognised a need for government to provide additional safeguards to reduce the risk of adverse reactions from medicines. Indeed the industry welcomes a system of licensing of medicines prior to marketing in order to keep out any irresponsible manufacturers who might otherwise be tempted to cut corners and to bring the whole industry into disrepute. Nevertheless, it is also recognised that the inevitable element of bureaucracy involved in a government scheme of regulatory controls brings with it costs. These include the manpower needed in both government and industry to deal with the regulatory affairs in each country. More importantly, the 'costs' include delays in marketing new medicines. A recent study by Maynard and Hartley from the University of York estimated that, apart from other factors, the British 1968 Medicines Act, and its subsequent regulations, had by themselves resulted in annual costs of between £30 and £85 million (at 1978 prices), absorbed the time of over 1,000 staff, and added two years on to the time required to develop a new medicine for marketing.[18] This is in addition to the increased costs and longer delays caused by the greater sophistication of pharmaceutical development as a whole. Figure 11 gives Hartley and Maynard's breakdown of the median total time taken for the different stages between synthesis and marketing for a new pharmaceutical compound.

Hartley and Maynard concluded that 'in the circumstances of mounting criticisms and genuine doubts about the value of the 1968 Medicines Act we would argue that now is the time for a serious re-appraisal of the UK's regulatory arrangements.' In fact, since the Hartley and Maynard study was conducted there has been an important move to reduce the effects of regulation by the introduction of a Clinical Trial Certificate Exemption Scheme. This has cut out much of the purely bureaucratic delay which previously occurred in Britain before a new medicine could first be tested in man, but it has not substantially altered the overall picture.

Similarly, in the United States, there have also been moves to relax the previously extremely burdensome regulatory measures required before new medicines could be introduced. Nevertheless, the average delay between first discovery of a new pharmaceutical chemical entity and its marketing is there also still about 10 years. There is a feeling, at least in the pharmaceutical industry, that society as a whole would benefit if this delay could be reduced and if new medicines could be made available sooner without reducing their margin of safety. Apart from safety measures before a new medicine

18 Hartley K and Maynard A (1982). The Regulation of the UK Pharmaceutical Industry: A Cost-Benefit Analysis. Managerial and Decision Economics; 3;3;122.

11 Median time for various stages in the development of a new pharmaceutical chemical entity

Time Scales: 1963–79; data from 17 companies

Stage	*Time*	*Range of estimates*
Medians (unless otherwise specified)		
1 Chemical synthesis to patent	2m	1m– 50m
2 Chemical synthesis to pharmacological definition	1m	0m– 12m
3 Pharmacological definition to first administration to human volunteers	4yrs 1m	0m– 69m
4 First volunteers to clinical trial certificate application	1yr 7m	8m– 37m
5 Application to approval of clinical trial certificate (average)	5.4m	1m– 12m
6 Clinical trial certificate approval to first administration to patients	2m	0m– 6m
7 First patients to product licence application	3yrs 2m	4m– 65m
8 Product licence to approval (average)	8.2m	3m– 16m
9 Product licence approval to first marketing in UK (average)	6.6m	1m– 39m
10 Product licence approval to first marketing outside UK	8m	2m– 29m
11 Chemical synthesis to UK marketing (average)	9yrs 11m	79m–160m
12 Patent to UK marketing (average)	8yrs 9m	44m–156m

The sample is based on drugs whose chemical synthesis started before 1968 but were not marketed until 1970 or after.

Source Hartley and Maynard; 1982. The costs and benefits of regulating new product development in the UK pharmaceutical industry; OHE.

is introduced, there is particular concern at the start of 1983 about the effectiveness of what is described as 'post-marketing surveillance' after a new medicine has actually been marketed. This arises largely from the experience with the antirheumatic benoxaprofen which was withdrawn from sale in 1982 after 61 deaths had been reported in association with its use. The toxic effects which are alleged to have been responsible for these deaths in the elderly had not been recognised before the medicine was put on the market. The Committee on Safety of Medicines, which recommended the suspension of the preparation's licence for sale after reports of the deaths had been received, was accused of acting too slowly. However, it must be remembered that in the affected group of elderly patients very many more deaths were also occurring from natural causes. Nevertheless, as a result, there is a strong current pressure to increase the intensity of the monitoring of the use of new medicines in order to try to pick up at an earlier stage any serious adverse reactions. However, here again, costs are involved.[19]

The fact remains that despite the recent relaxation in some aspects of pharmaceutical regulation in Britain and the United States, the inexorable process of tightening the controls on the testing and introduction of new medicines seems likely to continue in the future.

The trouble is that all too often these extra 'safety measures' are more an act of faith than a practical step towards reducing risks. As Agatha put it in 'The Family Reunion' by Eliot; it is done

> 'Not for the good that it will do
> But that nothing may be left undone
> On the margin of the impossible.[20]

However, even if the increased testing and monitoring of new medicines to 'prevent' adverse effects of medicines may often by of doubtful value, there is no doubt about the extra resources which it will consume. The costs which this will add to the marketing of a new medicine throw into sharp relief the problem of increasing downward pressure on pharmaceutical prices.

Restriction on prices and profits

In many ways the problems facing the pharmaceutical industry over the question of prices and profits follow the pattern described above for the industry as a whole. It has already been pointed out that it is probably no coincidence that three of the most successful pharmaceutical innovators – West Germany, Switzerland and the United States – have price freedom for pharmaceuticals and a fourth country – Britain – has a more reasonable price regulation scheme than those in other countries. By contrast, countries such as Australia, Belgium, Italy and Spain which have rigid price controls have been relatively unsuccessful both as pharmaceutical innovators and as pharmaceutical exporters. In other words, there seems to be a distinction between the 'haves' and 'have-nots' in terms of the international research-based industry. In general, those countries which have a strong research-based pharmaceutical industry allow reasonable prices; those who have not; impose strict price controls. Nevertheless, although Britain has relatively high pharmaceutical prices, the level of expenditure on pharmaceuticals in Britain is low compared with that of the rest of Europe and the United States. Figure 12 shows that relationship between pharmaceutical spending and gross domestic product. Britain, a relatively poor country in GDP terms, is also a low pharmaceutical spender.

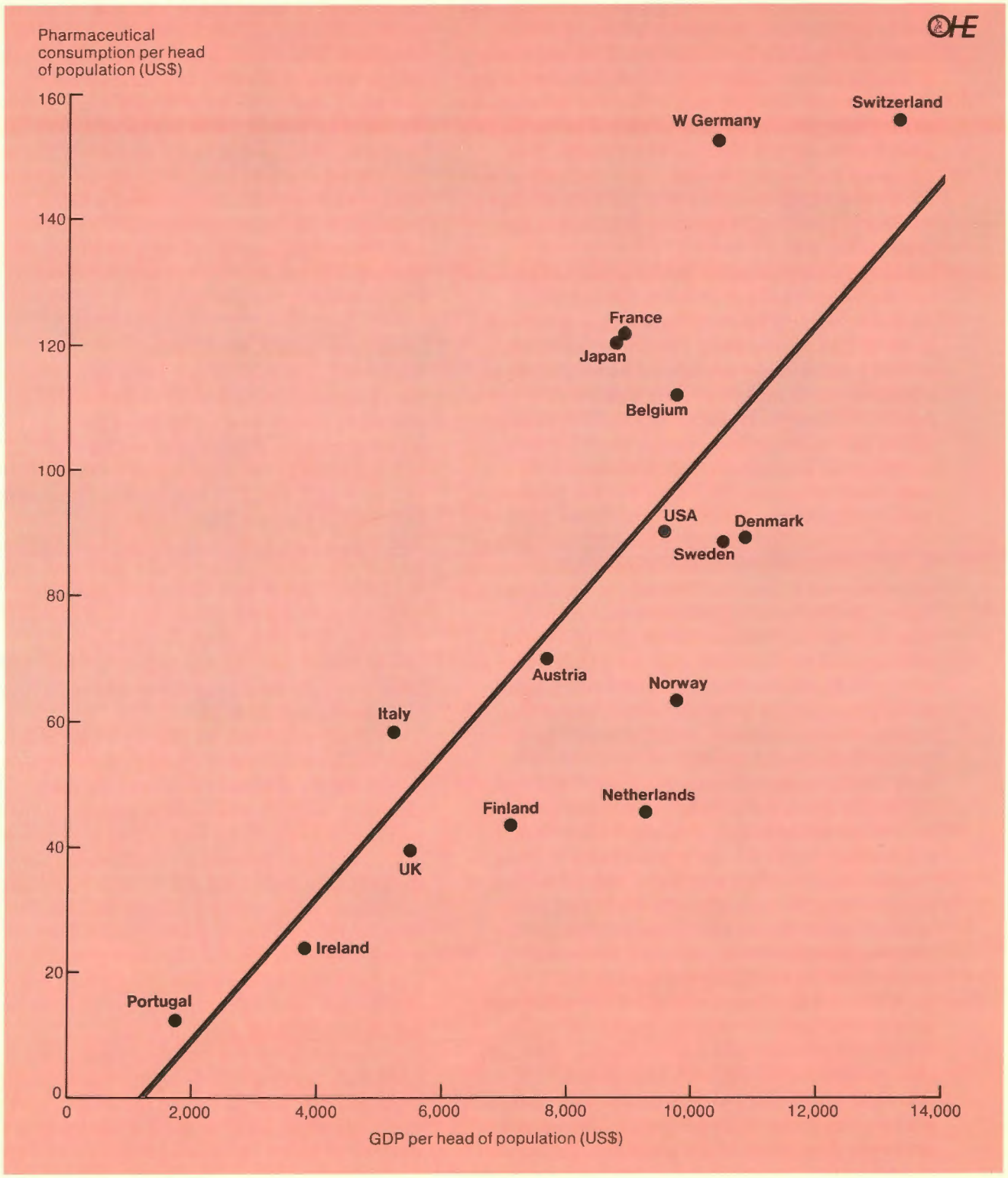
Looking at the general relationship between higher pharmaceutical prices and the national success in pharmaceutical innovation, it is hard to say which is cause and which effect. On the one hand, one is forced to the conclusion that the 'have-not' countries may be applying the classical 'free-rider' economic approach to their pharmaceutical costs. They want the innovations from those countries which have successful pharmaceutical research, but are not prepared to contribute their full share of the cost of developing new medicines in those countries. On the other hand, the experience over pharmaceutical pricing in Japan suggests that at least in their case they may deliberately be allowing high local prices to stimulate Japanese innovation as a basis for the development of future international trade in pharmaceuticals. At present, Japan is a substantial net importer of pharmaceuticals, with a negative balance of trade of £780 million dollars in 1980.[21] However, in 1981, Japanese prices at manufacturers'

19 A theoretical calculation suggests that it could cost as much as £55 million per life saved, if measures were taken to monitor extensively the use of every new medicine introduced. This estimate is based on the cost of following up 100,000 patients for three years on each of 20 new pharmaceutical chemicals introduced each year. This cost could be as much as £420 million a year according to estimates given by Bowler and Godfrey of the Wellcome Foundation. Over a 20 year period the cost would be £8,400 million, and based on the experience of serious adverse reactions over the past 20 years this might save about 150 lives. In the specific case of benoxaprofen, for example, 'optimum monitoring' could theoretically have cut the number of deaths from the reported 61 to the 10 which would have been recorded after 100,000 patients had been monitored. Three such major episodes of adverse effects have occurred since 1962 – thalidomide, practolol and benoxaprofen. These calculations were made by the author when talking to a Conference of Scottish Pharmacists in Aviemore on 21 November 1982. The paper was reported in the *Pharmaceutical Journal*; 229;6202;624.

20 This was quoted in a broader context by Professor A L Cochrane in 'Effectiveness and Efficiency; Random Reflections on Health Services' (1972). Nuffield Provincial Hospitals Trust.

21 OECD Data Bank.

12 Relationship between pharmaceutical per capita consumption and Gross Domestic Product (GDP) per capita in selected countries 1978



Source OHE estimates

levels were on average more than double those in Europe and the United States.[22] The implication is that the Japanese are allowing high pharmaceutical prices in their home market in order to provide substantial funding for research and development. It is reasonable to assume that they hope to break into world markets with pharmaceuticals in the same way as they have previously done with motor cycles, cars and electronics. It is certainly also possible that countries such as Britain, Germany, Switzerland and the United States owe their pharmaceutical success to the acceptance of reasonable pharmaceutical prices in the past.

Looking specifically at the British situation, Reekie in the study quoted above showed that British pharmaceutical prices were on average level with those of Europe as a whole. However, within that overall pattern, there are variations for individual countries; those with strict price control have lower prices and those with price freedom have rather higher prices. More importantly, there are very considerable international price variations for individual medicines. This has led to the problem of 'parallel importing'. This is the practice of dealers buying products in a low-priced market and selling them in competition with the original manufacturer in higher-priced markets. This sort of trade applies to many classes of goods, and is not unique to pharmaceuticals. However, with pharmaceuticals, it poses special problems because the goods which are subject to parallel importing do not have a local national licence for their sale in their country of import. This has resulted in the prosecution of a parallel importer in Britain.[23]

In economic terms, the important point with parallel importing is that the benefit – that is, the profit – goes to the opportunistic importer rather than the original innovator. Hence, it contributes nothing to research and development funds. Nor in the case of pharmaceuticals does it benefit the British public through lower prices. The taxpayer, through the National Health Service, still pays the normal manufacturer's local price for the medicine. The importer and the pharmacist share the difference between the lower foreign price and the 'official' British price for the particular medicine. Ironically, also, parallel importing, with its economic disadvantage for the pharmaceutical manufacturers, is a two-way trade. Where individual British prices are lower than those on the continent, the parallel importers buy cheaply in Britain and sell at a profit in countries such as Germany.

Thus suggestions that the existence of parallel importing indicates a breakdown of the effectiveness of pharmaceutical price control in Britain are ill-conceived. The fact that the Pharmaceutical Price Regulation Scheme explicitly recognises the importance of maintaining 'a strong, efficient and profitable pharmaceutical industry in the United Kingdom' is in no small part responsible for the effectiveness of Britain as a pharmaceutical innovator and exporter. If Britain were to switch to a 'cheap drug' policy, the whole success of the industry would be endangered. In the meantime, the growing tendency for other countries to impose unreasonable restrictions on prices also presents a threat to Britain, because of the existence of parallel importing and more especially because of the political hostility towards the industry's prices which has been engendered by the practice.

Erosion of patent protection

Under the 1977 Patents Act, the length of patent life for all innovations in Britain was extended from sixteen to twenty years. The cover for pharmaceuticals in particular was further strengthened by the abolition of Section 41 of the previous 1948 Act. This had allowed compulsory licensing of pharmaceutical patents on request, and had been a hangover from the days of the First World War when Britain found itself embarrassingly dependent on German-owned patents in the pharmaceutical field. Although the abolition of the provision of Section 41 was an important psychological point for the industry, it had in practice been very little used over the 60 odd years that it had been on the statute book.

The twenty year term for patents brought Britain into line with the rest of Europe. In the United States, patent life is still limited to seventeen years. However, with pharmaceutical patents the major problem arises because so much of the intended period of patent protection is lost during the development and testing of the new pharmaceutical compound prior to its marketing. The Hartley and Maynard study already quoted found that on average it took 9 years 11 months between chemical synthesis and marketing in the United Kingdom. On average, almost nine years of patent life were lost during development. As a result, in Britain, the Pharmaceutical Sector Working Party of the Chemicals Economic Development Committee has proposed that patents should run from a later date in order to restore some of the intended patent life.[24] In the United States legislation to effect such a change

22 Reekie W D (1981). Price Comparisons of Identical Products in Japan, the United States and Europe. Office of Health Economics, London.

23 Pharmaceutical Journal (1982). 'Parallel Importing lead to £6,360 fines.' *Pharmaceutical Journal*; 229;6183;36.

24 See reference in Footnote 4.

was narrowly defeated in the Senate in 1982.[25] However, the US pharmaceutical manufacturers are continuing to pursue their efforts to get legislation for the 'restoration of patent term'. In Japan, also, there are moves afoot to allow pharmaceutical patents to run from a later date, to take account of the long period of development.

The pharmaceutical industry is not alone in thinking that the intended term of pharmaceutical patents should in some way be restored. A recent editorial in the *British Medical Journal* suggested that there would be less commercial pressure to get rapid widespread use of a new medicine if the length of patent protection could be extended.[26] The real danger is that patent protection could in the future be further eroded if the more complex pharmaceuticals which emerge for 'the second pharmacological revolution' require even longer for evaluation and testing than those being developed at present.

Undermining of brand names

The case in favour of the use of brand names in prescribing and dispensing has been fully set out in an earlier OHE publication.[27] It depends in part on the assurance that a branded medicine will always come from the same source, and hence will have a consistent formulation and consistent bioavailability. Perhaps more importantly, however, the use of brand names is part of the economic infrastructure underpinning the cost of pharmaceutical innovation. The fact that effective patent protection is often limited to ten years or less means that the innovating company is still dependent on the financial contribution from its new products when their patent expires. At that stage, the only protection left for the 'industrial property' inherent in the innovation is its brand name. If doctors were prevented from prescribing by brand name, or if pharmacists were permitted to substitute a non-innovating competitor's product for the branded medicine which had been prescribed, the original innovator would lose his total sales when the patent expired. This may not matter too much if a company has a broad range of products, and can partly compensate for lost sales by a price increase which it is able to make on other preparations. However, very often a company cannot increase prices because of competition. In other cases, the company may be heavily dependent on a single product. For example, when the original patents ran out on Pfizer's 'Terramycin' in the 1960s, the company would have been unable to survive, if generic substitution had been permitted.

Generic substitution is, of course, already permitted in some US states. However, in the absence of a National Health Service or any comprehensive system of national health insurance, the structure of the market there is very different from that in Europe. There is no price control and much of the use of medicines in the United States is on private prescription. About 90 per cent of the cost of medicines in the United States are paid for directly by the patient.[28] The contribution of either the government health schemes or private health insurance is minimal.

Thus generic substitution is merely a serious irritation in the US situation. Most medicines are in practice still dispensed as the branded preparation. Very often the individual patient chooses the more costly branded medicine because of the confidence he has in an identified manufacturer. By contrast, under the National Health Service or other European health insurance schemes, generic substitution would mean that the pharmacist had invariably to supply the cheaper unbranded medicine. This is why generic substitution could be an economic disaster for the pharmaceutical industry in the European context.

As an aside, it is ironic that the British pharmaceutical industry, in relation to brand names, is now facing a threat from the political left. Twenty years ago its measures to protect the 'industrial property' of innovation were instead attacked by the political right-wing arch-priest of market economics, Enoch Powell. As a philosophical point, which does not seem to be understood either by extreme free-market economists or left-wing politicians, it is important to realise than an industry such as pharmaceuticals which is wholly dependent on innovation for survival must to some extent be sheltered from the unbridled forces of competition. Both sides have failed to realise that brand names are an essential part of the competitive structure of an innovative industry, and do not grant undesirable monopolies to the innovator. Attempts to introduce unfettered competition (for example, by the use of compulsory licences to undermine its patent protection by Enoch Powell in 1962 or with proposals for generic substitution in the 1980s) would result in the economically predictable consequence of inhibiting the industry's innovative progress. Since the work of the economist Schumpeter in the 1940s it has been recognised that the innovator must be

25 Scrip (1982). 'Vote against US Patent Bill'. *Scrip*; 729;8.
26 British Medical Journal (1982). 'Benoxaprofen'. *British Medical Journal*; 285;6340;459.
27 Office of Health Economics (1976). Brand Names in Prescribing. Office of Health Economics, London.
28 Gibson R M (1980). National Health Expenditures, 1979. *Health Care Financing Review*; Summer.

protected by patents and brand names.[29] If a company is to fund its investment in research and the promotion of new discoveries it must be sheltered in this way from the untrammelled forces of classical price-only competition. In an innovative industry, competition depends more on the advantages offered by the properties of its new products than it does on a mere price advantage.

Restrictions on promotion

This general philosophical point needs further expansion when it comes to a discussion of the information which the industry provides to doctors and pharmacists. This is because what the industry needs to build up its economic strength is a strong and fair system of ground rules to protect the innovating industry as a whole; but nevertheless what it also needs is as much freedom as possible to compete within this overall economic framework.

An analogy with football is perhaps appropriate. To make a good game, the rules must be strictly observed: only eleven players are allowed on each side; there is a clearly defined field within which the play must be confined; the goal posts must remain fixed; and unfair practices such as deliberately wounding the opposition are prohibited. But if in addition to these rules each player is fitted with a shackle the game is ruined.

Similarly, with pharmaceutical innovation, the industry needs patents and brand names to protect its innovative policy, and it accepts the licensing of new medicines to protect the interests of both the public and the legitimate innovators. But if over and above that there are excessive restrictions imposed on the information which it can provide to prescribers the whole process of innovation is slowed down.

Nevertheless, in most countries, there are in fact already both voluntary and statutory restraints on the industry's sales promotion activities. In Britain since 1958, the pharmaceutical industry has had its own Code of Practice to ensure that advertising is accurate and responsible. This is policed by a Committee under the Chairmanship of an independent barrister. In addition, the 1968 Medicines Act imposed further restrictions. For example, every advertisement must be approved by both a doctor and a pharmacist before it is published. Each medicine must have a 'Data Sheet' which sets out the limits of the claims which can be made for the medicine, and its adverse effects and contra-indications. In addition, the volume of 'permitted' sales promotion in Britain is limited to 10 per cent of sales: any spending above this limit is added back to profits in price negotiations under the Price Regulation Scheme.

These voluntary and statutory controls on the industry's sales promotion have generally been effective in preventing misleading claims and in ensuring a reasonably balanced and honest presentation of a medicine's advantages. There are, however, very real difficulties in trying to cut back on promotion expenditure. Thus there is apparent extravagance in spending by certain companies. The industry's strict Code of Practice which specifically prohibits excessive entertainment of doctors is particularly hard to administer. Doctors are flattered by generous and unusual entertainments provided to attract their attention. In addition, competition between companies has resulted in each trying to out-do the other in their effort to attract doctors' attention. The recipients of lavish hospitality do not complain. The uninitiated do. Hence, the industry, despite its strict Code of Practice to avoid extravagant promotion, and the limits imposed on its total spending, finds it difficult to avoid being pilloried as still being wasteful and extravagant in its promotional activities.

The problem in imposing further restrictions on both the content and volume of information provided to doctors is that it tends to crystallise existing patterns of usage in the market. It can be argued that conservatism in therapy is desirable from the patients' point of view. New medicines do have inherent risks. However, on the other hand, even the best medicines do not sell themselves, and delays in introducing genuine advances in treatment can do very much more harm. For example, it has been estimated by the Office of Health Economics that if the introduction of all the new medicines of the 1940s, 1950s and 1960s had been delayed by a year almost 10,000 additional children would have died because they would have been denied the benefits of the therapeutic innovations of those years. If the introduction of treatments for today's fatal diseases, such as cancer and heart disease, were to be delayed similar unnecessary mortality in adults would occur. There is already evidence that doctors have become slower to adopt the use of new medicines since the thalidomide tragedy in the 1960s.[30] Further measures to cut down communication between the pharmaceutical manufacturers and the prescribers could, therefore, be harmful. On the other hand, genuine steps to improve the efficiency of this communication, perhaps at lower costs, should always be considered. The difficulty is to achieve this

29 Schumpeter J A (1942). Capitalism, Socialism and Democracy. Harper and Row.

30 See reference in Footnote 12.

without inhibiting the desirable element of competition which has been responsible for therapeutic progress over the past forty years. Looking to the future, advances in information technology should certainly contribute to better communication between pharmaceutical innovators and prescribers, and improve the efficiency of the whole process.

Pressures on prescribing

Apart from the restrictions imposed on the pharmaceutical industry, the doctors are also subject to pressures to prescribe 'economically'. Clearly this is desirable insofar as it avoids wasteful and unnecessary use of medicines, and insofar as it persuades doctors to chose a cheaper rather than a more expensive medicine if other things are equal. This is achieved in Britain by visits from Department of Health Regional Medical Officers to doctors whose prescribing costs are substantially above average, and by continuous persuasion on doctors as a whole to consider the importance of economy in prescribing.

In other countries, however, more draconian measures have been introduced, under which doctors are either prohibited from prescribing some expensive medicines or else are specifically limited to a list of 'approved' preparations. These measures are a serious barrier to innovation, because they inevitably penalise newer medicines, which tend to be more expensive and less well-established in use. Britain is fortunate in having no such restrictions, and the former Secretary of State for Health and Social Services, the Rt Hon Patrick Jenkin, has specifically said that Britain does not favour such methods.[31] Not only do such measures restrict the doctors' freedom to treat patients as they think best; in addition, they represent a serious threat to pharmaceutical innovation.

Consumer criticism

As in the case of brand names, the role of the consumer movement in relation to pharmaceutical innovation has been fully discussed in a previous Office of Health Economics publication.[32] In general, the consumer movement tends to reinforce the dangers threatening the industry's innovation – for example, in calling for stricter controls on the introduction of new medicines and in attacking the use of brand names. OHE has pointed out that these attitudes tend to ignore the enormous benefits which the free-enterprise system as a whole has brought to countries such as Britain. It has pointed out that nationalisation – one extreme demand of those who want 'consumer' control – acts in reality against consumer sovereignty. The free-enterprise competitive companies in any industry have to be much more responsive to consumer criticism than does a nationalised enterprise such as the Post Office.

The consumer movement, which has grown up over much the same timescale as the research-based pharmaceutical industry itself, has undoubtedly helped to ensure that the industry acts in a responsible way. For example, the misleading claims of which pharmaceutical manufacturers were accused in the 1960s have been eliminated by the operation of the Code of Practice, which was itself a response to consumerist criticism.

Thus in general the objective must be to bring the consumer movement and the pharmaceutical industry closer together in order that they can act in unison to ensure that the community benefits as rapidly, as economically and as safely as possible from the advances in therapy which are to be expected over the next thirty years. If, instead, some consumerists were to accentuate their isolation from the industry and their hostility towards it, they could represent a major threat to pharmaceutical innovation.

31 Jenkin P (1981). Speech to the Annual Dinner of the Association of the British Pharmaceutical Industry. 2 April.

32 Taylor D G (1983). The Consumer Movement, Health and the Pharmaceutical Industry. Office of Health Economics, London.

Conclusion

The pharmaceutical industry in Britain is a victim of its own success. It is accused of developing too many medicines. It is criticised for being too profitable. It appears to have too much money to spend on sales promotion. And it arouses jealousy because it is powerful and influential. On the other hand, its achievements, in terms of the lives which it saves and the suffering which it alleviates, are overshadowed by the occasional disasters which its products cause. There are those working in the industry who are so obsessed by the attacks on it that they doubt whether it can survive into the 21st century.

This paper has analysed the problems facing the industry. They could indeed be formidable unless the social and economic factors necessary for pharmaceutical innovation become more widely understood in the next few years. If indeed the problems were to override the potential, it could be a double tragedy. First, on a worldwide basis, the progress against disease could no longer be maintained in the way that it has been over the past forty years. Victims of cancer and heart disease, and those who suffer from the less common but more progressive disorders such as Parkinson's disease and multiple sclerosis would be the losers. But, second and more parochially, Britain could selectively lose out in the field of pharmaceutical innovation. At present, it is one of five countries in the world with a substantial positive balance of trade in pharmaceuticals. It can only maintain its position among these leaders if the pharmaceutical industry is fully understood and supported in Britain over the next thiry years.

Any country can choose the option of a 'cheap drug' policy. In Britain, as a ball-park figure, this might save the National Health Service £200–£300 million a year – perhaps 2 per cent of the total cost of the NHS. These are the figures quoted, for example, in the Social Democratic Party's statement of health policy. That Party argued that such savings could be achieved by substituting cheap generic medicines for the innovator's original brands and by restricting the introduction of new medicines.[33] Such 'savings' would not just make the industry 'less profitable'. The figure is twice the annual profit which the industry earned from its sales to the Health Service in 1979 and 1980.[34] Such a 'cheap drug' policy would kill the innovation-based industry in Britain, losing its £1,000 million export contribution. The true cost to the nation and the taxpayer would result from this loss of exports and probably eventually from the cost of imports instead. Even in a relatively short space of time, the savings to the NHS would be more than offset by the loss of corporation tax on the profits of the industry's home and export sales. Furthermore, a 'cheap drug' policy would seriously damage the interests of British patients. It would delay their access to the latest available medicines, which could include treatments for cancer and heart disease. It is unrealistic to suppose that a government 'cheap drug' policy could enable the industry selectively to market only valuable medicines and somehow keep less valuable ones off the market. Pharmaceutical innovation is an intensely competitive process, and companies must market a spectrum of medicines from those which represent a major breakthrough in therapy to those which are useful only for a minority of patients. Concentration on patent-expired generic medicines and barriers to the introduction of less important new therapies would slow down the whole business of making new medicines available. Thus a 'cheap drug' policy would be against the health interests of the patients as well as the economic interests of the country.

A more subtle threat comes from those who argue that the pattern of the pharmaceutical industry's innovation could be improved by further regulation. They point to unnecessary duplication of similar pharmaceutical chemical entities, and the risk that doctors may be persuaded to adopt trivial and costly new medicines because of excessive promotion. More especially, they constantly highlight the dangers associated with powerful therapeutic agents. This, of course, is a question of balance. The danger is that such extra regulation would tip the balance against Britain as a base for the international companies.

The problem of an unnecessary multiplicity of similar medicines is, of course, a genuine one in a competitive industrial situation. Every company would like to produce only major breakthrough medicines representing a unique advance in therapy. But the reality of medicinal progress is very different. Given the long timescale of development of pharmaceutical chemicals, all too often a company ends up with an innovation which is similar to several already on the market. These are valuable because individual patients respond differently to different medicines, and the availability of apparently similar compounds benefits these individuals. However, no one could argue that twenty or more similar compounds were all individually necessary. The problem is that any artificial limitation on multiplication of this sort may

33 Council for Social Democracy (1983). Health and associated social services. Policy Document No. 6. Social Democratic Party.

34 Controller and Auditor General (1983). Appropriation Accounts 1981–82; Class XI Vote I. Health and Research Social Services, England; Paragraph 49. Her Majesty's Stationery Office.

prevent a particularly useful medicine reaching the market. More seriously, it would distort the necessary competitive structure of the industry. Companies must often rely on 'me-too' products to keep them in business between infrequent major innovations. A multiplicity of products does not lead to unnecessary usage and can lead to direct price competition. 'The Canberra Hypothesis', in this series of OHE publications in 1975, argued that relatively minor innovations were usually competitively priced to give prescribers an additional reason to choose them in preference to already established alternatives. Apparently unnecessary duplication of medicines is, however, admittedly a market imperfection in Utopian terms. But taking a broader view, it is an economic price which is justified by the overall pattern of therapeutic achievement from the pharmaceutical industry over the past four decades.

Economic analysis of the British industry in the past twenty years has suggested that it is competitive and efficient.[35] The case for further regulation has been made mainly in the mass media. It can be powerfully argued that if Britain is to benefit from the 'second pharmacological revolution' the industry should receive more public support and less harassment by the press and Members of Parliament.

35 See, for example:
Cooper M H (1966). Prices and Profits in the Pharmaceutical Industry. Pergamon Press, Oxford.
Reekie W D (1975). The Economics of the Pharmaceutical Industry. Macmillan.
Reekie W D and Weber M H (1979). Profits, Politics and Drugs. Macmillan.