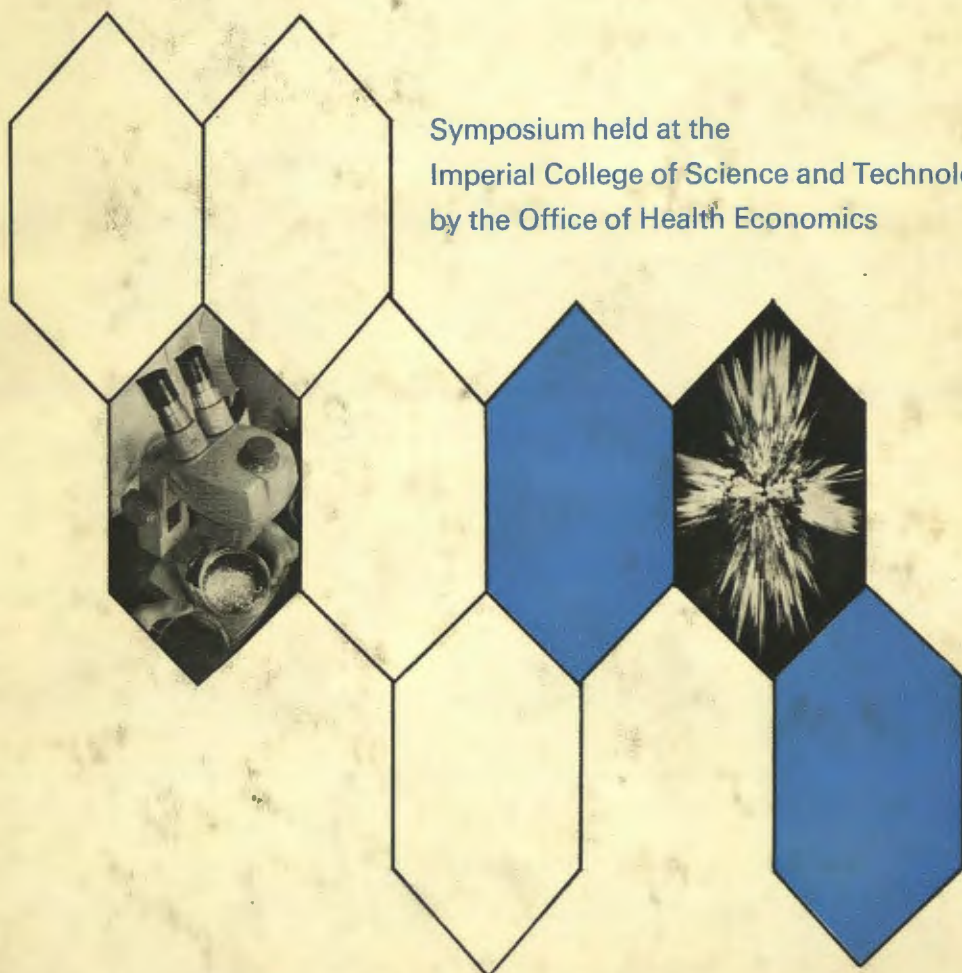


# Innovation and the Balance of Payments: the Experience in the Pharmaceutical Industry

Edited by George Teeling-Smith

Symposium held at the  
Imperial College of Science and Technology  
by the Office of Health Economics



This book is a published version of the second series of evening lecture meetings arranged by OHE. These again deal with questions relating to the significance of science and technology for British industry. This series on

*Innovation and the Balance of Payments:*

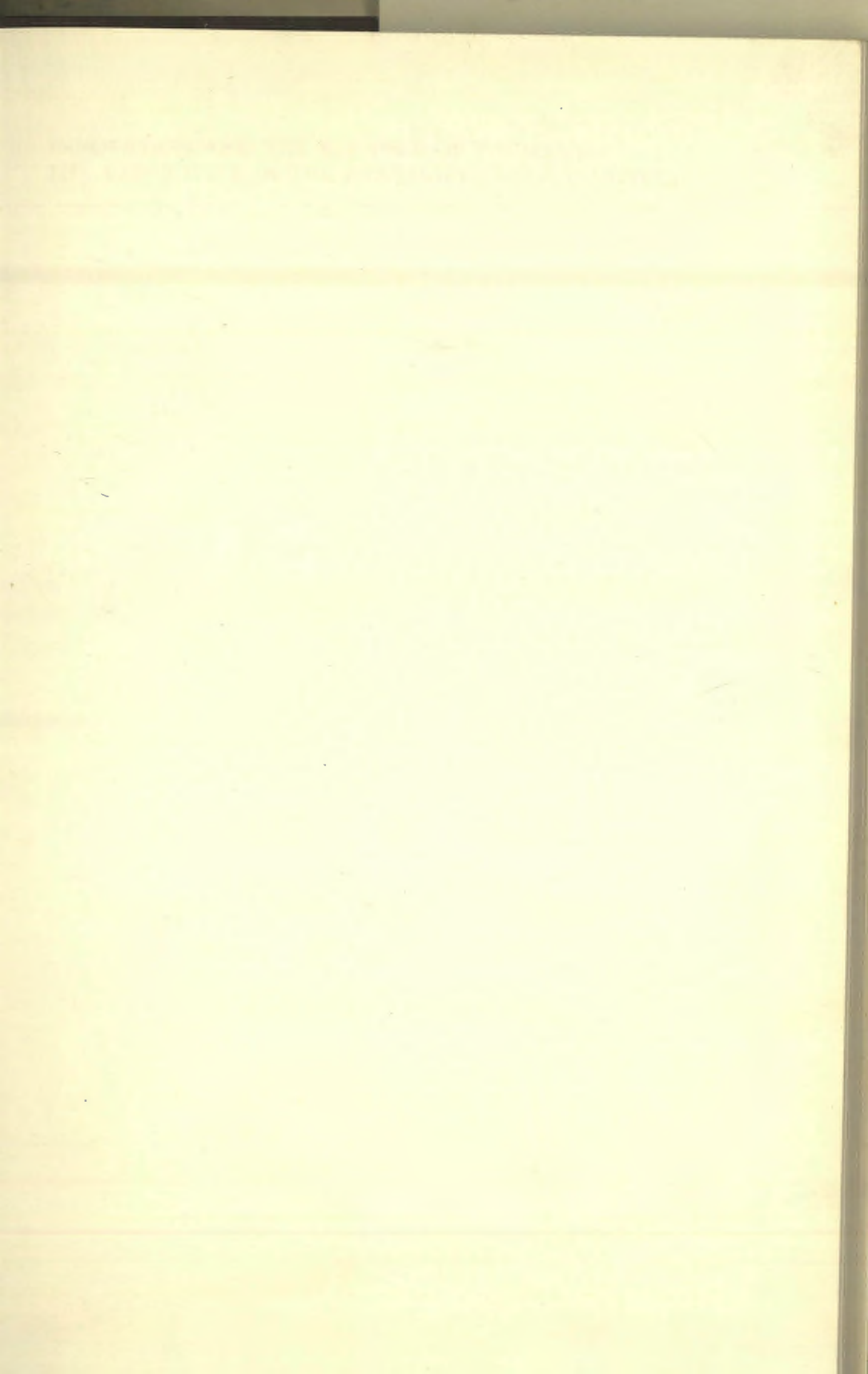
*the Experience in the Pharmaceutical Industry*

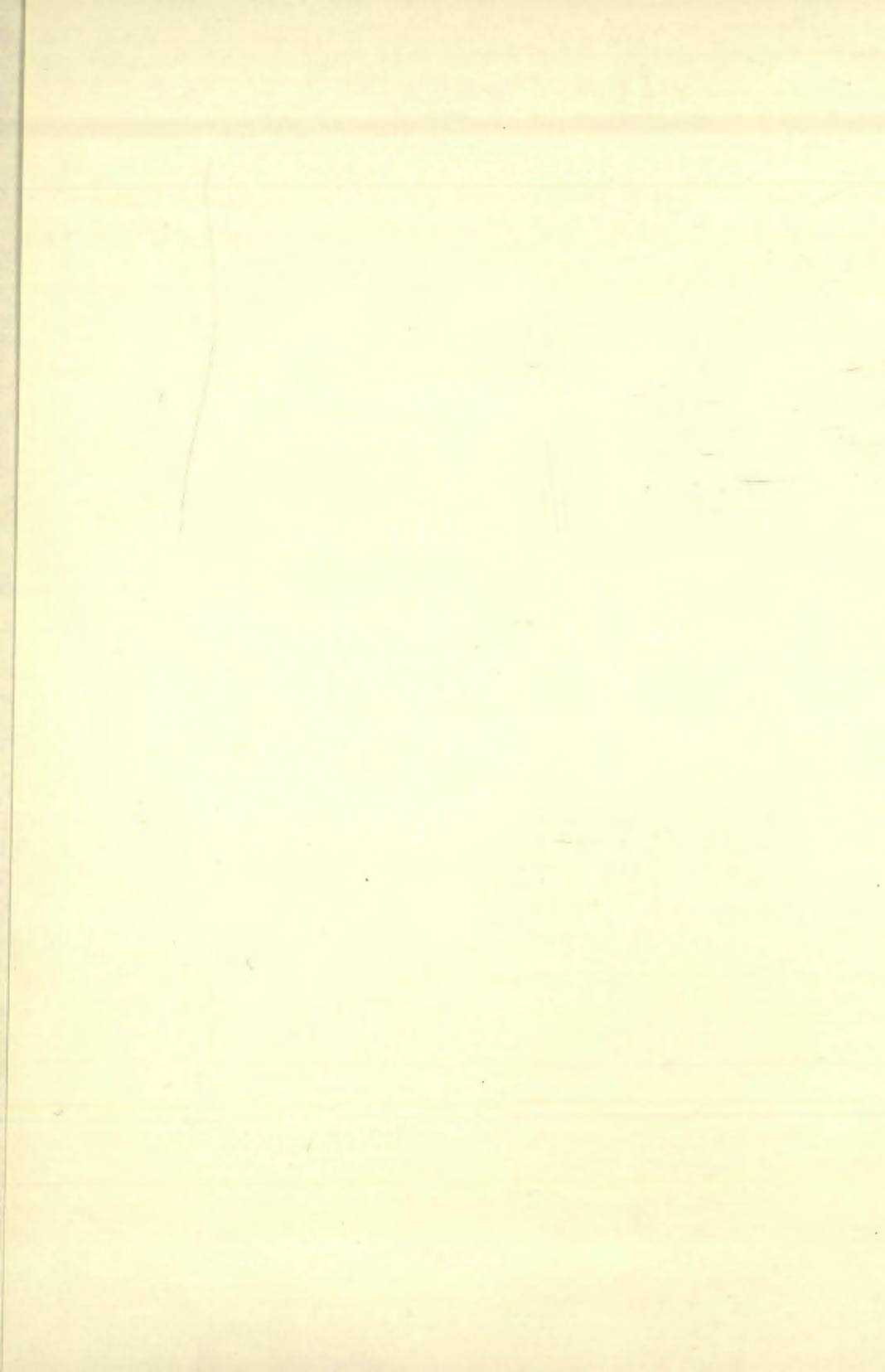
is concerned with practical aspects of the relationship between an industry's contribution to the balance of payments and its pattern of research and innovation. This highly topical subject is of the greatest importance to the British economy. The experience of the pharmaceutical industry, whose research investment and contribution to Britain's balance of trade are both increasing, is used as a case history.

The first two papers describe the experience of two companies, who are both winners of the Queen's Award to Industry. The second two describe the way in which the strengths and weaknesses of the patent system in five countries have affected their pattern of international pharmaceutical trade. The next two papers discuss the commercial considerations, such as profitability, pricing, use of brand names and sales promotion, which also affect an industry's success in innovation. The seventh is concerned with the international financial ramifications of a world-wide science-based industry, and the last with the role of the government as a sponsor of research.

The foreword, by Christopher Freeman, reviews the strengths and weaknesses of the arguments in each of the papers.

The series is edited by George Teeling-Smith.







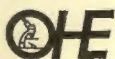
**INNOVATION AND THE BALANCE OF PAYMENTS:  
THE EXPERIENCE IN THE PHARMACEUTICAL INDUSTRY**



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Office of Health Economics 162 Regent Street London W1

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Office of Health Economics

First edition 1967

Innovation  
and the Balance of Payments  
the Experience in the Pharmaceutical Industry  
Presented at the  
Annual Meeting of the Royal Society  
of Medicine, London, 1966  
Edited by George Taylor Smith

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# Foreword

C. Freeman

*Director, Unit for the Study of Science Policy, University of Sussex*

THIS SERIES OF eight papers presented by the Office of Health Economics is of unusual interest and importance, both for the professional economist and for the public. The industry's products have a direct influence on the life and death of every one of us. It is one of the fastest growing sectors of the chemical industry, which is itself a major growth industry. It is an industry of high research-intensity, but unlike the greater part of the chemical industry, it is one of low capital intensity. Its pricing and promotion policies are the subject of intense political controversy and government investigation. It is one of the few British industries in which foreign-owned firms apparently own the greater part of the assets employed and account for more than half the sales, although less than half the exports and less than half the UK-based research and development.

Not unnaturally some of the papers are concerned to justify the policies and practices of the principal firms in the industry. But the ABPI and the Office of Health Economics have been ready to invite independent outside criticism unconnected with the industry and to promote some independent research and inquiry into the industry. It is the function of this foreword to make a critical commentary on the series of papers and to formulate some unanswered questions for further inquiry.

The theme of the 1966-67 Winter Lectures of the OHE was pharmaceutical innovation in relation to the balance of payments, but the papers necessarily covered some of the other related issues confronting the industry. The general sense of the arguments presented may, I think, be not unfairly summarised as follows:

1. The industry is entitled to more sympathetic understanding of its problems and achievements, and especially of its innovations.
2. It has made an outstanding contribution to exports and the UK balance of payments.
3. The export achievements rest upon product innovations, which are

in turn based upon a high level of research and development expenditures.

4. Innovation is risky, expensive and difficult. In a competitive system it will not take place unless firms have special incentives to innovate and the possibility of exceptionally high profits to recover development costs and pay for all the unsuccessful attempts at innovation.
5. This incentive is best provided by the patent system and the monopolistic pricing which this system permits.
6. This system should not be interfered with and countries such as Italy, which have dispensed with patents for drugs, should come into line with international practice.

From the evidence presented and from my general experience of research and innovation in other industries, I accept the first, third and fourth points, but I reject the second and regard the fifth and sixth as unproven, although with certain reservations a strong case is made for them. I shall examine these points in turn.

I am sure that the authors of several of the papers are right in their contention that the problems of drug innovations are little understood. I would go further and contend that innovators in almost all fields are little understood and meet with irrational hostility. It was Machiavelli who long ago pointed out that:

‘... there is nothing more difficult to take in hand, more perilous to conduct, or more uncertain in its success, than to take the lead in the introduction of a new order of things. Because the innovator has for enemies all those who have done well under the old conditions, and lukewarm defenders in those who *may* do well under the new. This coolness arises partly from fear of the opponents, who have the laws on their side, and partly from the incredulity of men, who do not readily believe in new things until they have had a long experience of them. Thus it happens that whenever those who are hostile have the opportunity to attack they do it like partisans, whilst the others defend lukewarmly, in such wise that the prince is endangered along with them.

It is necessary, therefore, if we desire to discuss this matter thoroughly, to inquire whether these innovators can rely on themselves or have to depend on others: that is to say, whether, to consummate their enterprise, have they to use prayers or can they use force? In the first instance they always succeed badly, and never compass anything; but when they can rely on themselves and use force, then they are rarely endangered. Hence it is that all armed prophets have conquered, and the unarmed ones have been destroyed.’<sup>2</sup>

Industrial innovators must rely on ‘prayers’ rather than ‘force’, although some of them must sometimes be sorely tempted. These ‘prayers’ may be more effective if detailed knowledge of the story of actual innovations is much more widely known. Although I would have welcomed more information on costs, I personally found Mr Wilkins’ account of innovation in semi-synthetic penicillins by far the most fascinating of the eight lectures.



I hope that the OHE will commission and publish a whole series of studies of this kind. They should be as frank and detailed as possible, particularly about the obstacles to innovation which had to be overcome, both within and outside the innovating firm. Especially instructive would be a detailed account of the resistance in the medical profession to the introduction of new pharmaceuticals—for example, the case which is quoted by Mr Teeling-Smith of the anti-depressants.\*

Moreover, case studies with disclosure of the *actual* costs of research, laboratory trials, clinical trials, and promotion of new drugs are necessary if the more generalised arguments in papers such as that by Fryers and Lee are to carry conviction. The public undoubtedly appreciate the enormous benefits which have been derived from the sulpha drugs, penicillin and many others, but scepticism about the industry's argument for exceptionally high profits and prices is likely to persist unless much more is known about the actual costs of innovation in a larger number of cases. Fryers and Lee themselves point out that: 'the lack of specific information is alarming', although they believe that this is being made good.

It would be particularly interesting if case studies provided supporting evidence for their extremely interesting suggestion that:

'with the new product which represents only a marginal advance over existing competing products, the research costs are lower but the marketing costs are higher. The difference between development costs is not great.'

I shall return to this in considering points (5) and (6). The point which I wish to make here is only that the sympathetic understanding which the industry receives is likely to be related to the information which it makes available about its operations, and in particular about the costs of its innovations.

Coming to the second and third points, it is regrettable that in a series of lectures dealing with the pharmaceutical industry and the balance of payments, little information was given on the pattern of world trade in drugs, or on the magnitude and rate of growth of drug exports from several of our principal competitors, especially Germany, France and Switzerland. Since 1960 the rate of growth of exports of all our principal competitors except the USA has been much faster than our own. German exports, which in 1962 were less than our own, were 20 per cent greater than the UK in 1965.<sup>2</sup> The achievements of Mr Williamson's company, although remarkable, are quite exceptional as he himself is careful to

\* Perhaps even more valuable would be a series of studies of projects which failed. Some firms in the industry are remarkable for their resolute acceptance of a high failure rate, and their readiness to bet on a statistical probability of success which would be considered far too low in many other industries. An account of the methods of R and D project selection and management in some of the leading innovative firms would be instructive for many of us both outside and inside the industry.

emphasise. The British share in world drug exports (about 13 per cent) is about the same as our share of world exports of manufactures in general, and the proportion of British output exported (about 27 per cent) is substantially lower than for many branches of the engineering industry and for other science-based industries. Whilst it would be perhaps unrealistic to expect the British industry to attain the Swiss ratio of nearly 80 per cent, it seems to me that it is not unreasonable to expect our leading science-based industries to attain an export sales ratio of 40–50 per cent.

It may be objected that, even if the UK *share* of world drug exports is rather disappointing, the balance of trade is extremely favourable—imports have grown more slowly than exports and remain very low. This is true and gives grounds for satisfaction at a time when imports of many products have risen so steeply. However, as Professor Wells points out, if invisible payments are taken into account, the picture is a little less favourable. It is indeed remarkable that the substantial exports of foreign-owned firms operating in the UK are entirely offset by their imports, their royalty payments and remission of profits, so that the net effect on the UK balance of payments is neutral.

The Board of Trade has recently estimated that foreign-owned firms in Britain accounted for 18 per cent of total UK exports in 1965, whereas they accounted for less than 10 per cent of UK assets in manufacturing.<sup>3</sup> Before jumping to the conclusion that foreign-owned firms benefit the British balance of payments more than British-owned firms, it is clearly important not only to examine the distribution of foreign interests, but also to examine the pattern of their payments as well as their receipts. The Survey made by Lee and Jones and quoted by Professor Wells is of exceptional interest because it represents one of the few attempts to do this. At least so far as the drug industry is concerned, it demonstrates quite clearly that British-owned firms account for the whole of the *plus* item in the industry's favourable balance. Furthermore, the British-owned firms did in fact achieve an export/sales ratio much higher than the average ratio of 27 per cent and in addition earned a further £7 million net in invisible income.

These conclusions do not, of course, mean that Britain has derived no benefit from the extensive foreign investment in the British drug industry. On the contrary I am sure that Professor Wells is right when he points to the competitive stimulus of American and European-owned firms operating in Britain and to other indirect benefits from their presence. Imports might have been higher but for the operations of foreign companies. But it does seem reasonable to conclude that British-owned firms are likely to benefit the British balance of payments more than others, and if our main concern is with the balance of payments, then this has important implications for research policy and innovation by British firms.



I personally accept the contention of many of the authors that there is a close connection between innovation and exports, although I would welcome more supporting evidence than has been provided. The trade pattern is complicated by the operations of overseas subsidiaries, but it should be possible to compile statistics on the changing product pattern of pharmaceutical exports which would establish this point conclusively. Elsewhere Cooper has in fact provided some interesting supporting evidence for his view.<sup>4</sup> The export of 60 per cent of output from the Worthing factory of Beecham's, quoted by Mr Wilkins, is the kind of example which I find convincing. An analysis of the pattern of exports in terms of product cycle theory would be illuminating, whether it was based on Mr Williamson's model or on those developed for other industries by Hufbauer, myself and Hirsch.<sup>5</sup>

If we assume that rate of growth in exports depends to a considerable extent on successful product innovations, then the scale and efficiency of UK research and development are obviously of great concern. It is here that the analysis made by Dr Cain in the last paper is significant. The success of drug firms in research and innovation depends not only on their own efforts but also on the 'infra-structure' provided by the universities, by government research institutes, and other non-profit organisations. As Beesley pointed out in his comments on the previous OHE series, it is a commonplace of innovation case studies that success very frequently depends on cross-fertilisation between a number of different types of research organisations.<sup>6</sup> There is further supporting evidence for this view in the case study by Mr Wilkins. He emphasises most strongly that:

'it has always been our policy to have a group of eminent scientists, who are recognised world authorities in their own field to act as consultants to us.'

I shall return to the key role of the NRDC at the end of this paper. I wish now only to emphasise that success in innovation is by no means the same thing as success in research, and that the NRDC is an organisation which can link academic and governmental research workers with industrial firms, and which can help firms to face the risks of innovation.

I accept without reservation the view expressed in many of the papers (the fourth point in my summary) that innovation involves exceptional risks and requires exceptional incentives. It also requires great initiative and independence on the part of management. This applies whether the innovating organisation is publicly or privately owned. We owe the distinction between invention and innovation primarily to Schumpeter and it is very important. In the economic sense innovation takes place only with the first commercial transaction involving the new product, process or technique. In every branch of industry successful innovations demand management qualities of a high order. The innovating entrepreneur

(whether public or private) must not only calculate and assume a variety of risks beyond those of normal business investment, he must overcome many resistances to changes both within his organisation and outside it. He must be prepared for systematic education and training, both of his own staff and those of his customers; he must often provide technical services and assistance far beyond those normally offered; he must deal with quite novel problems of standards, specifications and codes; he must often design and install new equipment to produce a new product; he must cope with the inevitable bugs which attend any major new development; he must deal with security, patenting and licensing problems; and he must co-ordinate closely the work of development, production-engineering, marketing and other staff, who may not easily work together. All these considerations apply in full measure to the innovating entrepreneur in the drug industry. The problems of the public interest in the safety aspect of new pharmaceuticals adds another dimension to the complexity of innovation in this industry.

Does it therefore follow that the patent system is essential as a protective framework for the innovating firm? Kemp and Cooper in their papers make a strong case for this view and it is one which apparently is endorsed by most firms in the industry. It would be interesting to know more about the views of the Italian firms, as one of the difficulties of the whole argument about patents is that no-one knows what *would* happen if the patent system were abolished. Even though only in one or two industries the Italian experience does provide some evidence on this point. The treatment of this experience in the papers presented is not adequate to form any considered judgment. The low level of Italian exports of drugs and the low level of Italian research expenditures are not conclusive evidence. Italian R and D expenditures are low in almost all industries and not only in those without patent protection. Total Italian expenditures on R and D are not much higher than those of the Netherlands and far lower than Britain, France or Germany. By international standards both Italian exports and Italian R and D are low in several science-based industries enjoying full patent protection, such as electronics and scientific instruments.

What the Italian experience *does* show is that it is extremely difficult for one country acting alone to abrogate the patent system, even in only one industry. It is increasingly an *international* system and if the European Economic Community introduces a European patent, it will be even more so. The earlier attempts in the nineteenth century to abolish the patent system in individual countries (Netherlands and Switzerland) also failed to a considerable extent because of international pressures.<sup>7</sup> I believe that Kemp is right in his view that the general trend in patent legislation is towards strengthening the system and removing the exceptions and I would expect Italy too to move in this direction.



Despite all the criticisms from academic economists and despite all its manifest anomalies and shortcomings, the patent system has shown a remarkable resilience. Indeed it now seems possible that the period of patent protection will be extended to 20 years both in the USA and in Europe. Moreover, the Soviet Union and other East European countries, although they have their own internal systems of inventors' awards, have begun to apply the international patent system so far as their external transactions are concerned. We have now reached the curious position where the only consistent abolitionists are the most rigorous and purist defenders of the free enterprise system.

Cooper rightly says that 'the patent has never found an easy friend in the economist' and it is easy to see why. The patent system is based on the deliberate reinforcement of monopoly pricing. For those who believe that the efficiency of the economic system depends entirely on price competition, this is a difficult pill to swallow. Almost all economists (and most of the public too) know that monopoly powers may often lead to higher prices and a lower level of output than would prevail under competitive conditions. Consequently, anti-monopoly legislation of various kinds has been a feature of the industrial scene, especially in the USA. Although it is generally recognised that oligopolistic situations are inevitable in many branches of industry, there is widespread agreement among economists that some forms of countervailing pressure on prices is desirable, whether this comes from the fear of Government investigation, from powerful buyers, from public opinion expressed through consumer organisations and the press, or through the reduction of barriers to international trade. The patent system appears at first sight to fly in the face of this consensus.

Fryers and Lee are probably right in pointing to the significance of competition by innovation as the key to the resolution of this paradox. I think it is a fair criticism of orthodox neo-classical economics that it largely neglected problems of innovation and growth and concentrated on models of competitive equilibrium. There have, of course, always been less doctrinaire economists, from John Stuart Mill through Schumpeter to Downie, who recognised fully the importance of innovation. I accept the view of Schumpeter and Marx and most of the papers in this collection that the innovator is stimulated by the prospect of monopoly profit and a temporary escape from the pressure of price competition. I accept too that this innovative process is essential to growth. Does it follow that a formal legislative protection of the process in the form of the patent system is a necessary condition for its successful operation? I do not regard this point as proven, although I think that the balance of the argument favours this view. It seems to me likely that competitive pressures would in any case compel firms to research and innovate whether they had patent protection or not. It might even be true, as Melman has claimed, that firms in some

industries would strive harder to achieve and maintain a technical lead if they had no recourse to patent protection, as their temporary monopolies would then depend entirely on their own technical progress and not on a legal situation.

However, I recognise that there is considerable force in the counter-argument that absence of patent protection, especially in industries such as pharmaceuticals, might make the hazards of innovation so great as to deter some innovators. Further, it may also be true that there would be less disclosure and greater secrecy if there were no patent system, although I think it is somewhat naïve to believe that the patent system in fact leads to full disclosure. The argument which weighs most heavily with me, however, is the purely pragmatic one that there are no proposals for a better system to stimulate innovation, and that international agreement to abolish the system is extremely unlikely. In these circumstances it seems to me sensible to make the best of the system. To this extent I accept the argument of the fifth and sixth points in my summary.

In my view this does not mean weakening those pressures which may be exercised on firms holding patent privileges. I believe that the dangers arising from monopoly power are real ones and that safeguards are necessary. There are three main dangers: first, the danger of delay in diffusion of major innovations; secondly, the associated danger of unnecessarily high prices for a long period; and finally, the danger that 'blocking' patents may hinder technical progress by competitive firms. I see no case for weakening those provisions of the Patent Law which are designed to deal with these dangers. In particular, it seems to me that the general provisions in the Patents Act for compulsory licensing are essential and constitute an extremely useful form of pressure on innovating firms to diffuse their innovation rapidly and to license widely, where they are not themselves capable of diffusing sufficiently rapidly. The classic case of compulsory licensing of ICI's polyethylene patents to major American chemical firms seems to me to establish this point. It led not only to new applications and a much faster build-up of production, but also to major benefits for ICI and very considerable royalty income. It did not prevent ICI from making very large profits from this innovation. Even if it is seldom used, it seems to me that the threat of compulsory licensing is an essential reserve weapon.

The existence of Section 41, and the use of Section 46 of the Patents Act by Mr Powell in 1961 are more controversial. However, with the latter it seems to me that there was a case for the Minister's action, even if its particular form was misguided. He might have been wiser to use one of the more general provisions for compulsory licensing under which abuse of the patent must be proved. Even the most ardent advocate of a high price, high profit, high technology economy must recognise the need for downward pressures on prices by consumers. Teeling-Smith and others



have given some evidence that these pressures are effective. Buying power should certainly be used to stimulate and reward innovation and in some cases deliberately to commission it, but this surely cannot mean purchase at *any* price. I agree with Beesley that 'we should never underestimate the traditional function of price reductions in spreading the consumption of new products; and even if it is true that demand for particular drugs is often inelastic, there may still be gains by getting drugs cheaper rather than dearer.'<sup>9</sup>

This applies particularly to the developing countries and we must, I think, recognise that there is a certain conflict of interest between the industrialised countries with their near-monopoly of research and know-how and the greater part of the world, dependent on imported products and imported knowledge. Whilst accepting the argument that countries such as India may benefit from investment by large technically advanced overseas firms, we must also recognise that they have a very strong interest in developing their own research and innovative capacity. As Cooper points out, Japan is a particularly interesting case, because she has deliberately used foreign know-how and investment to build up an industry capable of undertaking its own research and development on a large scale. When a country has reached this position, it is enabled to bargain on more even terms. He goes on to argue that the main problem is the 'unequal distribution of world pharmaceutical research' and not the patent system. But it may be necessary to consider special arrangements to enable the less developed countries to acquire licences and know-how on more favourable terms.

Despite my reservations, on the whole I accept the case made by Fryers and Lee for the 'super-innovating' firm, able to make above average profits by its innovations and thereby to finance large-scale R and D, new product promotion and more rapid growth. The reservations I have made are motivated by the fear that the firms which might benefit from excessive generosity in price and patent policy might not be the 'super-innovators', but ordinary monopolists. These fears are not diminished by considering their observations on 'new products which represent only a marginal advance over existing competing products'. Is there not some danger of resources being unnecessarily devoted to the high cost of developing and promoting relatively insignificant advances? The power to influence the prescribing pattern of the medical profession conferred by modern advertising techniques associated with other forms of monopoly power seems to me to make this danger a real one.

It can be lessened by policies designed respectively to influence the promotion of new products and the research-development process. Teeling-Smith in his original research on sales techniques in the industry provides interesting information on the breakdown of promotion costs, and both



he and Williamson provide welcome evidence of rising professional standards in drug promotion. This in itself would be an important safeguard. He suggests that downward pressure on prices automatically tends to 'limit the amount which could justifiably be spent in promoting minor therapeutic advances'. This would seem to imply that this pressure is performing a useful function, as the major breakthrough in a new therapeutic field is not subject to the same pressures at least for the first few years of the patent monopoly. As Fryers and Lee point out:

'The scope for freedom of pricing (of charging what the market can bear) as well as the share of the market captured is, however, set by the degree of uniqueness of the product. The major innovational breakthrough into an entirely new therapeutic field has no competitors offering a reasonable substitute and can thus look to dominance of the whole market in that new therapeutic sub-group.'

Consequently, firms have a strong incentive to become 'super-innovators' capable of achieving a major breakthrough. Whilst not denying the cumulative benefit of marginal advances, 'super-innovators' do need additional encouragement, and innovations of low social value should be relatively discouraged. I am not satisfied that this is in fact what is happening today.

Why are there not more British firms in the 'super-innovator' class? Several of the papers threw light on this question. Williamson and Wilkins both provide evidence on the extremely high cost of making a 'super-innovation' and of marketing it. Although the small firm may make an *invention*, it will have great difficulty in making an *innovation*, and in marketing it throughout the world. It would be very useful to have complete figures on the size, distribution and R and D expenditures of the firms in the industry. Even quite large British drug companies and the NRDC found it useful to enlist the help of American licensees in the final stages of development, production and marketing of major innovations. This is a sensible strategy. Cooper points out that the largest British-owned research company spent only one-fifth of the average research expenditure of the leading American companies. The leading American firm (Merck) spends more each year than all British and foreign-owned companies in the UK put together.<sup>10</sup>

Obviously Britain cannot match the USA in *absolute* level of resources, but individual British firms can be in their league. Cooper points out that:

'the same three firms led the British-owned companies sales and research ladders, had the most new products and were the most profitable companies.'

The Swiss drug firms provide an instructive example of concentrated R and D effort over a long period by a few firms. I agree with Beesley that from a world point of view a shift of resources from military to medical research is overdue, but unlike him I *do* take it as axiomatic that British pharmaceutical research activity must grow. Our factor endowment, principally in skilled manpower, fits us for this role and, though the scientific expen-

ditures required are large, they are by no means beyond our resources.

I differ from Beesley too in his sympathy with Nelson's 'research firms' as a way of 'disintegrating' the research function from the production and marketing functions of the drug firms. I believe on the contrary that there is a need for a greater *integration* of the research, production and marketing functions. The excessive separation of these functions has been one of the principal weaknesses of British industrial innovation. The whole history of penicillin is a copy-book example of this weakness. (I am not, of course, referring here to the Beecham semi-synthetic penicillin but to the original breakthrough.) The example of cephalosporin, quoted by Dr Cain, encourages me to believe that the penicillin story need not be repeated and that we have in the NRDC a valuable British social innovation which can do a great deal to promote the mutual cross-fertilisation of university, government and industrial research. I am very much in agreement with him that it seems doubtful whether the scale of government medical research or industrial research is yet adequate and with his proposals for increased government and NRDC sponsorship of research and innovation.

I would emphasise finally the importance of the distinction between 'research' and 'development'. The possibilities of a major breakthrough depend on fairly large-scale *research* (as opposed to development), as the Beecham example makes clear. Firms need to undertake this research in order to assimilate the results of MRC and university laboratories, as well as to make their own discoveries. At a time when it has become fashionable to talk of 'too much' research in Britain in relation to development, this is an extremely important conclusion.

Many of the views which I have expressed are, of course, personal judgments, which I hope will be criticised in a continuing debate. The most valuable function which the OHE has performed in starting this series of lectures and publications is to stimulate the public debate and to make it better informed.

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# Exporting Pharmaceuticals

C. R. B. Williamson

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'PHARMACEUTICALS' IS NOT a particularly precise definition for the products I will talk about tonight. I have used it, in the title of this paper, because it is the least *emotive* of the possible descriptions. *Drugs, proprietaries, specialities, patent medicines, 'ethicals' even pills*, all predispose the mind to passion rather than logic. They do so perhaps because it is difficult to consider a pharmaceutical, without thinking about its use. The use of any drug constitutes an interference with nature. Such interferences can have happy or unhappy results. Even the cost of pharmaceuticals evokes strong emotional reactions—no doubt because it is widely felt to be distasteful to profit out of happiness or unhappiness.

Tonight I am to talk about exporting pharmaceuticals. Exporting is necessarily a commercial activity involving purchasing power, salesmanship, advertising and the making of profits. We should, therefore, try to switch off our emotions and concern ourselves with the facts as they are, rather than as we feel they ought to be.

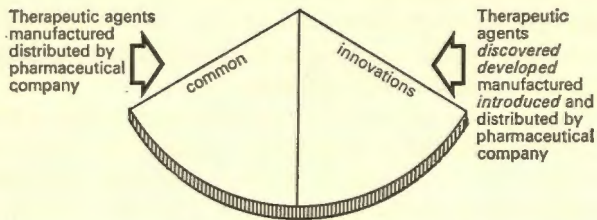
There are three principal classes of pharmaceuticals (Fig. 1). I will be focusing upon those which are often referred to as *ethicals*, because of the manner of their advertising, and are, in the main, available only via a physician's prescription. In Britain, the degree of freedom the public has to purchase 'ethicals' is determined variously by the Poisons Rules, The Therapeutic Substances Act, The Dangerous Drugs Act, the attitude of the dispensing pharmacist and the recommendations of the manufacturer. Distribution restrictions in other countries vary according to local law and custom but are broadly similar.

Ethicals as a group can be further subdivided (Fig. 2) into standard, unpatented or *common* pharmaceuticals on the one hand and pharmaceutical *innovations* on the other. The common pharmaceuticals are manufactured and distributed; occasionally under brand names they are also advertised. The innovations are discovered, developed, manufactured, introduced, always under brand names and are the subject of vigorous

FIGURE 1  
Pharmaceutical Preparations



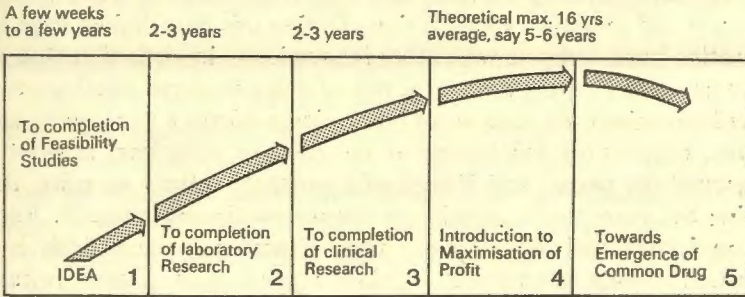
FIGURE 2  
Therapeutic Agents Advertised only to Physicians (Ethicals)



advertising. The two classes—common pharmaceuticals and innovations—present distinctly different exporting possibilities and manufacturers tend to specialise in one or other.

Many of us have a biological orientation of mind and therefore to depict a pharmaceutical innovation as having a *life cycle* provides a familiar perspective. Indeed a great many of the exporting facts of life relate to this life cycle (Fig. 3). The first stage involves practically nothing else but *thought*. It is concerned only with the feasibility of the idea. The second stage comprises chemical synthesis or formulation, stability or compatibility, activity, toxicity, metabolism—and all these studies are undertaken experimentally in the laboratory. The third stage begins when the innovation is first administered to volunteers who are usually company personnel and continues to the satisfactory completion of large-scale clinical trials. The fourth stage begins with the decision to introduce the innovation to prescribers. It proceeds through advocacy of its use where indicated,

FIGURE 3  
Life Cycle of Innovation



promotion to obtain the largest practical sales volume, to the attainment of the maximum profit return. The fifth stage covers that period during which the innovation *declines* in popularity or usefulness, or having become a *common drug* is promotionally abandoned as its profit earning capacity is eroded.

Additional perspective is obtained by applying a time scale to this life cycle. Stage one can last a few weeks or maybe a few years. The vast majority of ideas, like frog's spawn, never survive this stage. In our experience, the laboratory stage averages two or three years. It is during this stage that an attempt is made to obtain a patent—a very important factor in ultimate exportability. In return for making public knowledge of his invention, the manufacturer is granted a theoretical maximum of sixteen years' exclusivity. The clinical stage, in our experience, also lasts about two to three years though it can be much longer.

The stage of active commercialisation lasts no longer than the remaining life of the patent at its beginning. The *earlier* a manufacturer applies for a patent the *greater* is his chance of obtaining one. The *earlier* he obtains one the *shorter* is the time available for its commercial exploitation. You will see that if stages one, two and three take respectively, one, two and three years, the period of active commercialisation remaining at the commencement of stage four is reduced to ten years.

At every stage the hazards are numerous. In our experience the chances of an innovation completing stage two are at least 200: 1 against. An innovation which reaches stage three has a chance of about one in twenty of reaching introduction. It is these hazards which determine the high cost of innovation. Research expenditure must be paid for out of current profits. It is very important that profits which are sizeable enough to finance continuing research are earned as soon as possible in the time-limited stage four.

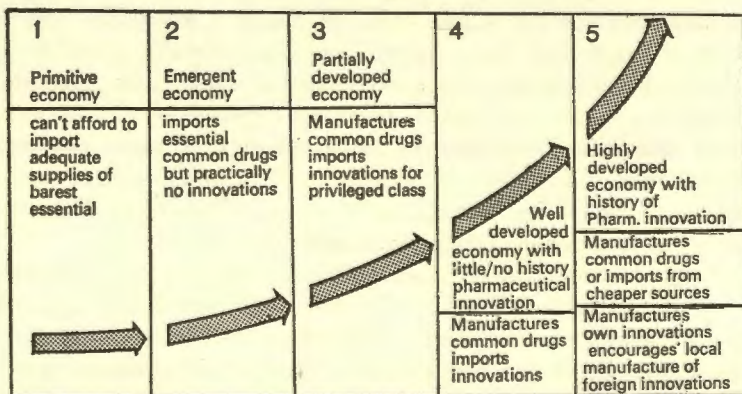
But having reached stage four, too dogmatic a claim or too high a



volume of advocacy can evoke criticism from which the innovation may never recover. In export markets, foreign experimental and clinical data may be chauvinistically set aside and local duplication of work is often expensive and consumes valuable time. During this time-limited stage the innovation must compete with other innovations—by definition they are *all* recent—and runs the additional risk of being rendered obsolescent by newer innovations. As soon as an innovation achieves a worthwhile sales volume, competitors functioning at the *common* drug level attempt to get around the patent, and if successful, compete entirely on price, thus eroding the innovator's capacity to finance continuing research. Rapid communication and advocacy are vital. Expertise in these fields is as important to corporate survival, let alone expansion, as scientific research and development.

Foreign markets for pharmaceuticals can also be said to undergo a development cycle. This cycle also consists of five stages (Fig. 4). Countries

FIGURE 4  
Development Cycle of Export Markets



in stage one cannot be regarded as markets for common drugs or innovations. Countries in stage two development represent markets for common drugs but shortages of foreign currency make selling difficult and contribution to profit meagre. Stage three countries, which have begun to encourage local manufacture, are difficult markets for common drugs and few of their people can afford innovations. Stage four countries are potentially good markets for British innovations but are equally attractive to all innovating pharmaceutical companies. Competition is therefore strong. Such markets also possess relatively highly developed pharmaceutical manufacturing capability even if they do not have a history of innovation.

Importation of innovations is discouraged and manufacture under licence encouraged. Stage five countries, like our own, have a history of pharmaceutical innovation, and whilst undoubtedly representing the most valuable export markets for UK innovations, are highly competitive. All international innovating companies compete for a share of such potential. All countries in stages four and five have well developed social security systems, and consequently pressure on prices and some degree of restriction of prescribability exists, whether it be governmentally engineered or exerted by private or semi-private health insurance organisations. It is perhaps paradoxical that having at last reached the economic position where they can afford advanced therapeutics for all, such nations attempt in a variety of ways to curtail the franchise.

The simplest method of market categorisation does not rely for its tenability on import statistics nor health expenditures. By definition ethical preparations are prescribed by physicians. Physician density is therefore a basis of classification. The more advanced the country the greater is its surplus of physicians over the number directly involved in patient care and therefore capable, directly, of influencing prescribing. Such margins

FIGURE 5  
Physician Density; Patients per Doctor

USSR	510
Germany	650
New Zealand	670
United States	690
Australia	730
Switzerland	760
United Kingdom	840
France	870
Canada	890
Japan	920
Sweden	960
China	2400
Korea	3000
Turkey	3300
Brazil	3600
Iraq	4800
India	5800
Pakistan	7000
Guinea	21000
Sudan	29000
Afghanistan	32000
Indonesia	41000
Nigeria	50000
Nepal	72000
Ethiopia	91000

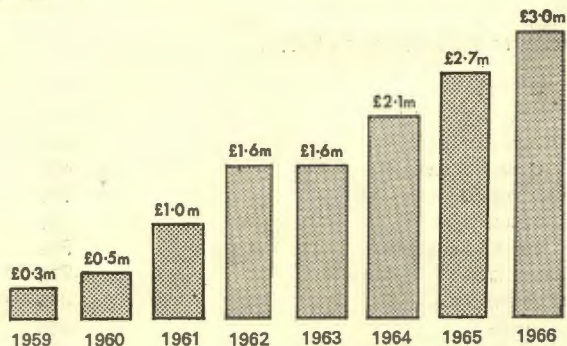


introduce a fine degree of error into available statistics but not so as to invalidate them for this purpose. Inspection of a complete table of international physician density statistics enables one to classify markets with a fair degree of accuracy regarding their export potential (Fig. 5).

Statistics about importation of innovations are hard to come by but figures concerning the use in various markets of branded as opposed to unbranded preparations can be obtained. These data, plus the other intelligence that is available, confirm that it is in the field of innovations rather than common drugs that substantial export potential lies. And as we have seen, and as we would expect, it is in the highly developed countries that there exists not only the greatest potential but also the most severe competition and the highest risk of early obsolescence.

The Winthrop Products Company exports to 134 countries from its British factory in the Newcastle-upon-Tyne development area. In 1959 exports were worth £300,000. By 1966, £3 million (Fig. 6).

FIGURE 6  
Direct Exports of Winthrop Products Company and Associated Companies 1959-66



The British Pharmaceutical Industry of which Winthrop is a part has an above average exporting record (Fig. 7), but Winthrop has done rather better (Fig. 8). It was for these results that we were honoured with one of the first Queen's Awards to Industry.

Our greatest successes have, however, been scored in the continental markets of Europe. It was there in recent years that we decided to concentrate our efforts, precisely because of the potential which existed. All these markets, except those in Eastern Europe, are markets in stage four or five of development. In fact, it was in Germany that innovating pharmaceutical industry had its beginnings and it is in Switzerland that there exists the greatest concentration of innovating pharmaceutical industry on Earth.



FIGURE 7

## UK Pharmaceutical Industry Exports 1959-66



FIGURE 8

## Index of Export Performance 1959-66



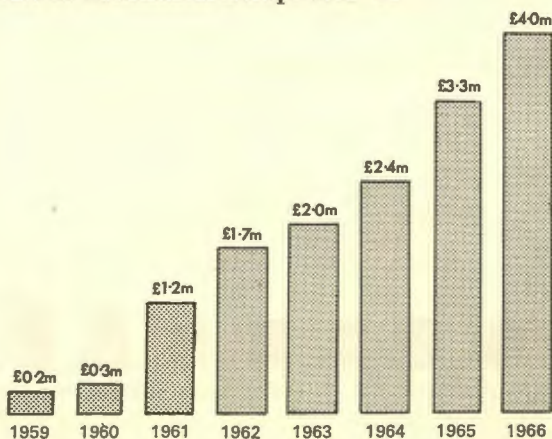
France is also high amongst stage five markets and Sweden, Denmark and Belgium have all contributed some therapeutic innovations from their well developed pharmaceutical industry (Fig. 9). Not surprisingly, markets of this type deter the importation of finished pharmaceutical products. They take the view, as does the UK., that domestically they are quite capable of putting tablets into bottles or even making the tablets. Consequently, considerable persuasion is often exerted upon foreign manufacturers to encourage them to undertake local manufacture or to restrict

FIGURE 9  
Examples of Pharmaceutical Industry Research Expenditure 1965

	<i>£ million</i>	<i>Per capita shillings</i>
USA	140	12s. 0d.
UK	12	5s. 0d.
Switzerland	12	40s. 0d.
Germany	10	4s. 0d.
France	9	4s. 0d.
Japan	20	4s. 0d.
Canada	1.5	1s. 6d.
India	0.5	under 1d.

importation to chemical substances. We have resisted these pressures on economic grounds wherever we could do so. We have learnt, however, that to comply in some cases even where it was partially disadvantageous has locally been a political desirability. Simple export statistics therefore understate the Winthrop continental growth. Expressed as sales in the markets at net sales return, our growth over seven years has climbed from £200,000 to £4 million (Fig. 10). We have not obtained comparable

FIGURE 10  
Winthrop Sales in Continental Europe 1959-66

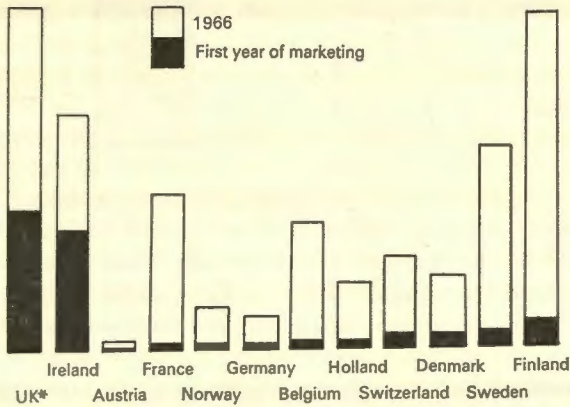


results in all markets. I would rather not provide individual territorial sales because I am conscious that some of our competitors are represented here tonight. A way of illustrating comparative results, however, is to compare 1966 sales with the sales in each market in our first year of marketing, which business was mainly conducted through agents (Fig. 11). Austria is an interesting case because there we still export through an agent rather than through a branch of our own company. The UK position

FIGURE 11

## 1966 Per Capita Sales Compared to first year of Marketing

\*UK compared to sales in 1959



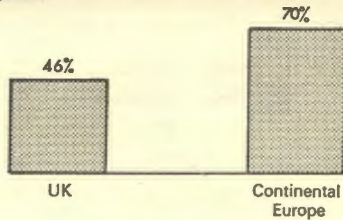
in 1959 and 1966 is included to dispel over-simple explanations. Clearly in some countries we have been relatively more successful than in our own home market.

Looked at from a national standpoint 62 per cent of our total production of ethicals is now exported in one form or another. The net annual contribution to Britain's balance of payments is currently in excess of £1 million per annum. Such a computation takes no account of the fact that the equivalent of 475 people earn their living out of our export business quite apart from our continental employees who number an additional 500. It also ignores a wide variety of other benefits to Britain and her people. At this point I should perhaps add that all this represents an interesting example of how a commercial enterprise whose share capital is largely in foreign hands can contribute to the profitability of the United Kingdom.

Reverting to the life cycle of a therapeutic innovation we must record that we have been far less successful in our attempts to export unpatented products than patented ones (Fig. 12). Our attempts to market unpatented products have been met by price competition from copy products only after we have introduced the product and managed to obtain a share of the market for its particular therapeutic indication. It is difficult in such circumstances commercially to justify continued promotional investment. We have learnt the hard way that it pays to obtain patents in every country where there is likely to be a potential for export sales. Such patents have to be applied for long before a product has successfully emerged as a marketable innovation and consequently the wasted expenditure on patent filing costs is a not inconsiderable expense factor.



FIGURE 12  
Sales Covered by Patents



Whilst a valid patent confers some degree of protection insofar as it helps to delay the early introduction of cheaper copies it by no means eliminates price competition from elsewhere. Most innovations have but marginal advantages. The introduction of a so-called 'winner' is an unusual event. When pricing an innovation it is necessary to take into account the prices charged for competing products in the appropriate therapeutic group. Qualitative advantages have to be set against quantitative ones in arriving at the price that will attract prescribers. Unrealistic price setting cannot necessarily be corrected if a high price image has been gained. In these circumstances the maximal profit earning potential of an innovation can be lost. Conversely, if a price is set too low it can seldom be increased, and even if the innovation is spectacularly successful one can fail to earn sufficient profit to make a significant contribution to current research expenditure.

I mentioned earlier that markets in stages four and five of their developmental cycle had advanced social security systems. In all our western continental markets pressures to reduce prices exist in one form or another. It is not surprising, therefore, that when the Ministry of Health at home manages to depress the price of an innovation in the interests of domestic prescribing economy, foreign authorities bent on the same endeavour, press for similar satisfaction. In some cases—and this will become the rule in time—the saving to the NHS achieved by such measures will be *less* than the *loss* of foreign currency which results. Arbitrary classifications of the cost of particular innovations in relation to efficacy—again frequently made at home in the interests of NHS prescribing economy—can have similar adverse effects abroad. It is extremely undesirable from the export standpoint that such classifications should be given an official status. In one particular case of ours a reduction in price to the NHS of 10 per cent could, if extended to our continental markets alone, result in a greater loss of foreign currency earnings than the total NHS sales of the product.

I would now like to turn to the important subject of communication. There are three principal conventional methods of bringing innovations to the attention of prescribers—direct mail, professional journal adver-

tising and technical representation. Journal advertising is theoretically the cheapest per doctor reader. But very big allowances have to be made for the fact that placing an advertisement in a journal does not automatically result in the same readership for the advertisement as is claimed for the journal. Taking this factor into consideration direct mail, despite its undoubted element of waste, has a higher certain readership at lower cost than journal advertising. The technical representative's personal discussion with a prescriber is considerably more expensive per exposure but is of such a different quality that pound for pound it is infinitely superior. Moreover, it has an element of feed-back which does not apply with other media.

Prescribers in continental countries are no less victims of the information explosion than their counterparts in Britain. In our experience there are few countries on the Continent where the prescriber receives less direct mail, is faced with less journal advertising or interviews fewer representatives. In many of these markets the volume of pharmaceutical communication is greater. It is well known that the physician is probably by nature, and certainly by training, conservative. Whilst the therapeutic revolution, which has resulted in the innovation having an average life of about five years, has accustomed him to change he does not actively seek it. When entering the continental markets where our company was quite unknown, we were immediately at a disadvantage compared with locally established companies. Our earliest ventures convinced us that to break through the communication barrier we would initially have to undertake many times the volume of direct mail, journal advertising and representation that was currently being carried out by competitors. As we did not have the funds for such investment, alternative approaches had to be devised. We submitted all conventional communication techniques to rigorous analysis. As a result, we postulated that our journal advertising would have much greater readership if it were contained in a new medium which of itself had superior reader attraction. If we could limit the amount of competitive advertising with which our advertisements competed for readership, so much the better. If a useful new medium could be devised which was closely identified with Winthrop we would, by having provided it, overcome our unfamiliarity as well.

We found our answer in *Pulse* a newspaper for doctors which catered for the non-clinical aspects of their vocation. It was introduced in one market after another in the early sixties. Knowing a good deal about physicians from long association with them in other markets it was not difficult to predict the para-medical subjects which would interest them. Rapidly, *Pulse* editions, a separate one for each market, gained high readership and as the months went by strong prescribing responses to our advertisements were recorded. The cost of producing *Pulse* per prescriber-reader



FIGURE 13  
Communication—Cost per Doctor

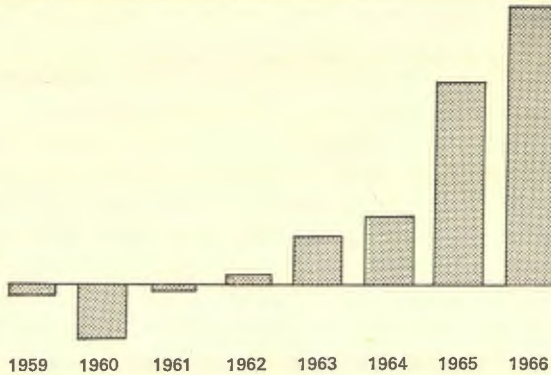
	<i>Pulse</i>	<i>Direct Mail</i>
France	7d.	5d.
Germany	8d.	4d.
Belgium	6d.	5d.
Sweden	1s. 2d.	8d.
Finland	1s. 2d.	11d.
Denmark	1s. 0d.	9d.
Holland	11d.	10d.

was marginally greater than the average costs of direct mail—but the sales response was many times greater (Fig. 13). Within a year or two the *Pulse* network of newspapers became the vehicle for so much comment and debate on matters affecting the practice of medicine that we considered it was no longer appropriate that a pharmaceutical company should have editorial control. Consequently, we sold our interests one by one to an independent publisher. Today we are not alone in purchasing advertising space in *Pulse* editions but we take a good deal of pride in having provided a medium of communication which by its success was clearly needed. Our own need was also satisfied.

Analysis of the interrelationship between the technical representative and the prescriber pointed up an essential barrier. A single representative, working in the conventional manner, could interview but five or six prescribers per day. An increase in this exposure rate could from theory only be obtained if prescribers could be persuaded to visit representatives rather than representatives prescribers. Needless to say, if this were to happen there would have to be considerable advantages to the prescriber. Further, research indicated that a meeting of several doctors and one representative could reduce costs, permit, by use of film or filmstrip, an incomparably better presentation, allow collective debate, enable the prescriber to meet his colleagues and local consultants and lead to an altogether more thorough and balanced examination of our products and their uses. Of course there were teething troubles, but over the past five years we have recorded nearly 200,000 physician attendances at our clinical meetings from Lapland to the Côte D'Azur and from Bordeaux to Berlin. Needless to say, the outlay on such activity is greater than that of conventional representation but the larger numbers of prescribers seen brings the unit cost down to £3 12s. 0d. per doctor compared with £3 16s. 0d. for a conventional surgery visit. The costs of both are of course greater on the Continent than in the UK because of the higher salaries and costs which rule in many of the continental countries. The results in terms of sales have been greater and the acceptance by physicians considerably



FIGURE 14  
Winthrop Profit History in Europe 1959-66



higher. These two examples from many illustrate the importance of innovation in the field of marketing practice to exporting economics.

Finally, I must answer the question—has our exporting activity been profitable? The answer is that it has. Taken as a whole our Continental European operations broke even and began to make profits after two years and eight months. Since then the contribution to profit has increased sizeably each year (Fig. 14). Almost without exception our prices in these markets are higher than they are in the UK despite the fact that only at home does the State pay all. Without exception, the cost of communication as a percentage of sales, though consistently being reduced is higher than the 13 to 14 per cent which we spend at home. This will remain so until all our markets are out of the development phase. We have not been equally successful in all territories. Some are already making a similar or greater percentage profit to sales as we do at home, but others have yet to reach this level. Until we achieve the same sales per head of population for the same or lower cost throughout the Continent, as we achieve in Britain, we shall not be satisfied. Whilst in some countries we are now within a short distance of that target in others we have a long way to go.

In little more than half an hour one can but skate over the surface of what is a complex and many-faceted subject. For my part, I would have preferred to dwell on the management factors and inter-personal relationships involved in building a foreign business in pharmaceuticals. But such an assignment would hardly be within the scope of the Office of Health Economics.

# A Record of Innovation and Exports

G. J. Wilkins

*Chairman, Beecham Research Laboratories Limited*

MR WILLIAMSON EXPRESSED his gratitude for being asked to speak this evening and I should like to add mine. However, I feel that I should explain at this early stage that the choice of subject does impose some limitations. Of necessity, what I shall say to you can only deal with two aspects of the total operation of an international pharmaceutical company and therefore does not represent an overall picture of my company. I would ask you to bear this in mind so that you will understand that actions, decisions made and results must be looked upon and considered as part of a larger business and not complete in themselves. In some ways it is unfortunate that both Mr Williamson and I have the common item of 'exports' in our subject matter. I have tried to make sure that there is not too much duplication and consequently I propose to spend most of my limited time dealing with the 'innovation' part of my subject matter.

The way Beecham has set about expanding its prescription pharmaceutical business is not precisely the same as any other company because of circumstances. I should emphasise that like Mr Williamson I am only talking about products which are prescribed by the medical profession, in hospital or in general practice.

To put our current successful 'innovation and export achievement' in perspective I have to go back some way. The Beecham Group was formed by an amalgamation of a number of proprietary medicine businesses and by the acquisition of several toiletry, food and proprietary medicines companies. At the end of the war the management of Beecham realised that we were about to enter a technological era and that products which had been accepted, and considered successful and scientifically adequate before, and during, the war, might not be good enough to meet the challenge of the post war era. Clearly, in due course, consumers were going to become much more sophisticated and demand new or improved products.

After much debate, and largely due to the determination of our present



Chairman, Beecham decided to set up a group research laboratory where, as a first task, the existing products would be carefully examined and modernised and improved where possible or appropriate. In 1946 the company purchased Brockham Park, a large country mansion in extensive grounds not far from Dorking and converted it into a series of research laboratories. A team of research scientists was chosen and the work of improving the existing products was begun.

The next event which had a major effect on policy was the introduction of the National Health Service in 1948. At that time, Beecham was very largely dependent on its proprietary medicines which are both sold, and advertised, direct to the public for self-medication. It was thought (wrongly as subsequent events have shown) that the market for these advertised proprietary medicines, or home remedies as we prefer to call them, would decline very quickly. Therefore, a decision was taken that Beecham should enter the field of prescription pharmaceuticals. C. L. Bencard, a small company specialising in diagnostic solutions and treatment of allergic disorders, was purchased to serve as a nucleus for future growth. Nevertheless, it was realised that significant progress could only be made from new inventions, and with products of original research.

At about this time the function of Brockham Park and its laboratories was changed drastically to become a research station devoted to original research aimed at discovering new ethical or prescription pharmaceuticals. Although research into allergic disorders and their causes was our main project, others based on synthetic organic chemistry were initiated. Many hundreds of interesting and promising compounds were made, tested, and generally followed up, but all except one proved to be disappointing either due to lack of activity in man, or too many side-effects or no improvement over existing products. The exception was Nacton, an antispasmodic acting on the alimentary canal and which reduces the secretion of gastric acid by up to 50 per cent.

The most important decision was made in 1954. During that year it was decided to undertake a major research effort into penicillin. Most people thought that there was very little possibility of any significant improvements over the then existing penicillins G and V. However, our management and its advisers were aware of the fact that antibiotics constituted one of the largest individual segments of the prescription pharmaceutical market and successful research which would enable us to get into this sector of the market would open up to us an area of great commercial potential.

At this point I should stress that it has always been our policy to have a group of eminent scientists, who are recognised world authorities in their own field, to act as consultants to us. This particular policy has been, and I consider is, one of the strengths of our research effort in that



it gives our research scientists the opportunity of discussion and debate of their ideas and proposals with world renowned experts. Over the years prior to 1954 we had built up a research group at Brockham which was very strongly orientated to organic chemistry. Therefore, when it was decided to start research into penicillins it was a natural decision not to follow the existing usual pattern of screening hundreds of soil samples to see if any micro-organism or mould would produce an antibiotic under appropriate conditions. It was suggested that a particular penicillin, if it could be produced by the usual fermentation techniques, could probably be modified by the application of organic chemical processes. This type of chemical manipulation and change seemed a natural approach for us. The decision was taken to proceed and we started.

This meant an increased rate of research expenditure and was a considerable act of faith. It is not often realised that a company making a determined and realistic effort to enter the pharmaceutical industry must be prepared to make a substantial and long continuing investment in research with no guarantee of a successful outcome. No company without substantial profits from its other activities could hope to sustain the necessary effort and continued losses. We could do it only because the profits earned on the advertised Beecham Group products, such as Lucozade, Brylcreem and Phensic were sufficient to offset the early losses.

A research budget is a major financial and organisational item. It cannot be varied up and down at short notice. In a research budget, salaries amount to about 60 per cent of the total cost. Successful research cannot be achieved with a widely fluctuating number of research workers and once embarked on a scale of operation and expenditure it would be disastrous to reduce the effort at short notice. Research is a team effort and the two most important aspects are to build up a good team and to provide them with the correct environment in which to work. Appropriate laboratories and surroundings are essential to achieving this correct environment; but equally important is the desire to succeed and the stimulus to people of knowing that they must succeed. This is an extremely complex subject which is difficult to define. However, to have a successful research group the environmental balance must be right.

It is essential that research into new medicines should be carried on in both the academic institutions and in the laboratories of the pharmaceutical companies. However, there is a major difference between them. In the academic institutions, adding to the pool of knowledge is the important parameter. In industry, there is the added necessity of being able to apply the knowledge and discoveries where they will represent an improvement over existing medicines or therapy. This is achieved by close liaison between the scientists and commercial executives in the company and by the control of the research itself. It is difficult enough to choose an appropriate new

research project, but much more difficult to stop it or change its direction if the original idea is obviously leading nowhere.

To return to Beecham's own business, we set out to make a particular penicillin (-para amino benzyl penicillin) which was thought by our scientists and consultants to be capable of chemical manipulation which should lead to being able to make other different penicillins. During the assay of the fermentation broth made in our experiments to produce this penicillin our scientists observed the different results obtained by chemical analysis and microbiological analysis. This discrepancy had also been observed by others. However, our scientists started questioning why there should be this apparently regular difference rather than merely accepting that it always occurred. A group of our chemists, biologists and microbiologists postulated a theory that since the chemical analysis always gave the higher result there must be a material present which was chemically like a penicillin but which had no biological activity. They suggested that this material might be 6-aminopenicillanic acid (6-APA) which is the nucleus common to all penicillins. If this could be shown to be so and the 6-APA could be isolated, then an infinite variety of different chemicals could be added as side chains to make large numbers of penicillins which could not possibly be made by known conventional biological means.

It took many months of painstaking and costly research but eventually the theory was confirmed and we were able to publish our findings in *Nature* in January 1959. This breakthrough, achieved after years of research and at a cost of almost £2 million in research expenditure, was of course only the beginning since 6-APA itself has no biological activity and no therapeutic properties. *The discovery was only of importance if new therapeutically active penicillins could be made from it and produced on a large scale and at an economic price.* The problems facing us could be stated as simply as that, but solving them presented a tremendous challenge to a company with limited research facilities and no experience in either the commercial manufacture or handling of antibiotics.

Pharmaceutical chemistry is a rapidly changing science—the desire for health and for new medicines which are shown to have advantages, is so great that if a company is to reap reasonable financial rewards from its research then speed is essential in getting fully tested products on to the market. We realised that as a company we should probably require some help and therefore decided to obtain this from other companies in return for restricted licences to the other companies to market any successful new penicillins. Our first licensee was an American company which agreed to conduct a joint research programme for a limited time and also help us in the design of an antibiotic factory. In return the licensee had the right to sell our new penicillins in the USA and many other overseas countries. We also licensed one manufacturer in each of Italy, Germany,



Scandinavia, Japan, Brazil and Australia. In every case we retained the right to market our own brands in each market. From these licensees we have obtained valuable help, in particular in the design of our factory at Worthing. Whilst we could probably have done this ourselves and developed fermentation know-how there is no doubt that obtaining it in return for royalty bearing licences saved us much time and effort.

To return to our research scientists. They were given four areas to concentrate on, where improved or new products would be an advance:

1. An oral gram-positive penicillin superior to penicillin V or the injectable penicillin G.
2. A penicillin with broad spectrum activity which would greatly extend the range of diseases against which penicillin is effective.
3. Compounds which would destroy the lethal penicillinase producing resistant staphylococci which were then menacing hospitals.
4. Penicillins having no sensitising properties—a phenomenon possessed by penicillin G and causing allergic reactions in a small number of patients.

Work was intensified and in October 1959 we marketed Broxil which was the first of the new semi-synthetic penicillins from the 6-APA nucleus.

During the period 1959 to 1967 we have more than doubled the number of scientists engaged in research and development. Of the more than 2000 compounds discovered and tested we have marketed four other new semi-synthetic penicillins which provide outstanding new products to cover the first three target areas we had set. Several of these products—particularly Penbritin, Orbenin and Celbenin were hailed by the world medical press. I will not bore you with a lot of words of my own, in praise of these products since you might think that I am biased. However, I will quote you what the *Lancet* said in 1960 about Celbenin:

‘A new penicillin has been prepared which is active against the usual penicillin-sensitive micro-organisms and yet resists staphylococcal penicillinase. This is a major event in chemotherapy. From the information given in the *British Medical Journal* last week and in the three papers appearing in our present issue there is good reason to hope that the new BRL 1241 (CELBENIN, Beecham Research Laboratories) will be a means of controlling the staphylococcal infections which have plagued hospitals throughout the world during the past ten years.’<sup>1</sup>

Finally a comment from the *British Medical Journal* in 1961 about Penbritin when the results of clinical trials were published:

‘Whatever may prove to be specific indications for PENBRITIN, it is assured of popularity both by the wide range of its activity and by its ease of administration. The bactericidal nature of its action and its very low toxicity and freedom from

1. *Lancet*, 1960, ii, 585.



side-effects—assuming that this is confirmed by further experience—are two further solid advantages. For some purposes at least it may well prove that the earlier broad-spectrum antibiotics are now out of date.<sup>2</sup>

I can confirm to you that the comments of these two medical journals have been completely borne out by clinical usage of these new semi-synthetic penicillins throughout the world.

Whilst all of the activity to discover new derivatives of 6-APA was going on in our research laboratories great changes were taking place in other sections of the business. A large new antibiotic manufacturing unit was being built at Worthing. To a large extent this was another act of faith and pre-supposed that we should discover commercially useful products. To give some idea of the investment at risk I can tell you that before we knew that we should discover *one* compound that would be worth marketing we had spent over £2 million on research as mentioned but also irrevocably committed ourselves to building a factory at a cost in excess of £3.5 million.

At the same time we had been examining and building up our marketing and commercial teams. In 1959 at the time of the 6-APA discovery we had a small organisation in the United Kingdom and nothing but a very fragmentary commercial organisation to cover the rest of the world. It takes time to build up an organisation and to ensure the rapid development of the new products overseas we embarked on a programme of selective licensing, always of course retaining the right to market ourselves in every country. This ensured that the new medicines were available to the medical profession overseas and in return we obtained a rapid build up of earnings of foreign exchange from the royalties we received. Our royalty income is substantial and still increasing; in our last complete year it amounted to more than £1.5 million.

Although royalties are useful and acceptable they are no substitute for the profits arising from the sale of a company's own brands. Commercially, therefore, our target was to build up as quickly as possible, a network of arrangements whereby our own products under Beecham trademarks were available overseas in competition with royalty bearing equivalents marketed by Beecham licensees. Mr Williamson has referred to the tedious, complex and almost infinitely varied health registration requirements in Europe; additionally there are the usually separate pricing, Health Service and reimbursement formalities. Negotiations of all of these—which have to be completed before a product can be marketed—often take months and sometimes even years to complete. The formalities are possibly even worse and more complex in some non-European countries. However, we have made very substantial progress and Beecham brands are now actively marketed in seventy-four different countries. Progress is also

2. *British Medical Journal*, 1961, ii, 191.

reflected in our sales figures and direct exports from this country now account for 60 per cent of the antibiotic manufacturing capacity of our Worthing factory.

As you have heard, the Pharmaceutical Division of Beecham was honoured by one of the first of the Queen's Awards to Industry. It was specially important to us to receive it on two counts, namely for Technological Achievement and also Export Performance thereby confirming that we have been successful both in *innovation* and *exports*. However, this award merely marks a milestone in our progress. The important thing is where do we go in future and what do we achieve in the coming years? Our own company's objective is clear, but whether we shall be able to achieve it depends not only on our own ability but also upon freedom from Government interference of many kinds. We must be allowed to continue to carry out successful research and to exploit our inventions. We cannot do this if unnecessary restrictions are put on us in marketing our products in this country.

Let me illustrate what I mean. At the present time we have achieved success in one section of the prescription pharmaceutical market—namely in the antibiotic section with our new penicillins discovered in our research laboratories. We estimate that, excluding the Iron Curtain countries where it is impossible to make any reliable estimate of the size of the markets, the remainder of the world antibiotic market is about £300 million per year. Of this only £22 million or at most 7 per cent is in the United Kingdom. Therefore there is a much greater potential market for us overseas and we should be able and expect to build up our overseas business to be many times the size of our United Kingdom business.

However, overseas governments and authorities watch very carefully the position in the United Kingdom and if we are *forced* by Government or other action to reduce our prices here, then there is inevitable pressure, or sometimes legal obligation, to reduce prices overseas. We accept the desire of the Ministry of Health to obtain the lowest possible prices for medicines under the National Health Service and we have voluntarily reduced the prices of our products. As an example take Penbritin which is our largest product, we have voluntarily reduced its price six times since it was first marketed in 1961 and it is now only 40 per cent of its original selling price in 1961. However, the necessarily limited aims of the Ministry of Health should not be allowed to over-ride the greater national need of our country, which is to earn the maximum foreign exchange. The potential value of Beecham's exports and sales overseas are many, many times as great as our sales to the National Health Service. So far the pharmaceutical industry has a remarkably good export record. It can continue to improve this if allowed to do so and make an even greater contribution to the future balance of payments.



Similarly any unreasonable restrictions on our sales promotion activities in the United Kingdom would mean that we should not have experience of a fully competitive home market. This could seriously damage our expansion overseas since we should not be able to apply the knowledge and experience gained in our home market to our business overseas. In this country there is a great deal of criticism of sales promotion; much of this stems from people who do not understand the subject. There is always room for improving the standards of advertising and sales promotion and much has been achieved in the last few years. Constructive criticism will always be welcomed and acted upon and I firmly believe that this is the way to better advertising rather than trying to improve it by the introduction of restrictive legislation.

My company has made some important discoveries, which have been recognised by the Queen's Award. We know that these products would not have been used unless we had used our skill and knowledge of sales promotion. It is only in those countries where we have told doctors of our products and their benefits that the sales or usage have increased. Conversely, where we have not yet been able to develop an organisation for one reason or another then the usage of our products is either negligible or nil. From our experience we can conclusively show that medicines which are acclaimed in the medical journals as important therapeutic advances are used to treat patients only when their sales are actively promoted to the medical profession.



# Pharmaceutical Patents

in Britain, India, Italy, Japan and the United States of America

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AS THE TITLE of this paper indicates, the intention this evening is to deal with the practical differences of approach adopted in the stated countries to the patenting of pharmaceutical inventions. However, to be realistic, such a comparative appraisal must take into account at least certain historical aspects of the patent system, as well as current views and trends, both national and international (and, if one may say so, rational and irrational).

In one form or another, patent systems have existed in the western world for a number of centuries and most have followed the basic British patent system as set forth in the Statute of Monopolies of 1623 which abolished the right of the Sovereign to grant monopolies at his pleasure except with respect to 'any letters patent . . . for the term of fourteen years or under, . . . of the sole working or making of any manner of new manufacture within this Realm, . . . so as also they be not contrary to the law or mischievous to the State, by raising prices of commodities at home or hurt of trade, or generally inconvenient. . . .'

When in the period 1944 to 1947—the last occasion on which the British Patent Law was subjected to an impartial scrutiny—the Swan Committee analysed the history and fundamental character of that law, they emphasised that the philosophy underlying the original Statute of Monopolies and subsequent patent legislation in this and many foreign countries has been to encourage technical development and progress in four different ways: firstly to stimulate research and development (this obviously including competitive effort triggered off by a successful patent to circumvent it or improve it); secondly to induce an inventor to make his invention available to the public instead of keeping it as a trade secret; thirdly to offer a financial reward for the expense of developing inventions to the commercial stage of earning a profit; fourthly, and perhaps most important, to provide an inducement for the investment of risk capital in the development of new industries within the Realm.

The Swan Committee compared the British patent system with the author certificate system of the USSR, under which an inventor receives a direct monetary and/or other compensation, but concluded that 'Soviet experience can have little bearing upon the problems of a country in which technical progress largely depends upon private initiative.' Being designed not only to encourage research but also to reward successful commercial development of an invention, the patent system is concerned with the trinity: inventor, entrepreneur and investment of risk capital. Under it, the offer of reward clearly necessitates the bringing together of the three and the successful completion of three stages—(a) conception of invention, (b) technical development of the invention from the viewpoint of manufacture, and (c) successful launching on a commercial scale. Under the Soviet and like schemes of simple monetary reward, the inventor presumably qualifies solely with respect to the part he played as the first to conceive the invention. These schemes are in fact comparable to the so-called 'suggestion scheme' awards made in many western companies as a recognition of a personal contribution by an employee.

Speaking from another country and twenty years later, in December 1966, the President's Commission on the Patent System in the United States expresses substantially the same view as the Swan Committee concerning the patent system but additionally emphasises that it promotes the beneficial exchange of products, services and technological information across national boundaries by providing protection for industrial property of foreign nationals. The members of the Commission were unanimously agreed 'that a patent system to-day is capable of continuing to provide an incentive to research, development and innovation.' They discovered 'no practical substitute for the unique service it renders.'

From time to time it has been alleged in one quarter or another that the patent system, as typified by our own, operates against the public interest, that is it fails to fulfil the primary requirements of 'the good of the Realm', to use language of an English decision of 1602 (*d'Arcy v. Allen*). However, any fault appears to lie not with the patent system in general but in the way that system is applied nationally. The only logical justification under the patent system for the grant of a monopoly of limited term is the possession by the patentee of a valid patent, worked under conditions that take account of the public interest. A valid patent does not subtract from the public domain; it does not prevent anybody doing anything they were entitled to do before the application for patent was made, but rather adds to the public wealth of knowledge. It is, for example, implicit in Section 6 of the British Statute of Monopolies that the patentee shall not use his monopoly rights in a manner such as unreasonably to affect the public interest.

The quality or standard of a national patent will depend not only upon



statutory requirements for patentability but also upon the existence of a pre-grant examination system and the resources of the Patent Office whose duty it is to administer it. The measures taken in the public interest to correct so-called abuse of monopoly rights will reflect a variety of factors which do not stem or derive from the patent system itself. Such factors are first the general attitude of a Government towards encouragement of development of its country's indigenous technological resources, whether with or without the aid of technical, managerial and financial skills and resources from abroad, second, the strength and potential of local industry in the important fields of technology, and third, adequate Governmental controls on restrictive practices, balance of payments burdens, and the like.

These various reasons alone account for significant, indeed major, differences of approach to the patent system, not only as between highly industrialised nations and developing countries but also amongst the industrialised nations themselves. They also perhaps account for many examples of amendments to national patent legislation, ostensibly carried out for the purpose of solving some problem connected with but not necessarily directly due to the patent system but which, in the outcome, resulted in unjustified emasculation of the patent system.

The five countries with which we are particularly concerned in this present study are, of course, at different stages of technological development and, furthermore, are at different stages of appreciation or encouragement of technological development within their own boundaries. All but one have for a long time been faced, and are still faced, with a statistical situation, namely that their national patent systems attract, to a very substantial or preponderating degree, applications from foreign nationals. In the United States, according to a United Nations review, the percentage of patents granted to foreigners over the period 1957 to 1961 was a mere 16 per cent; in Great Britain the comparable figure was 47 per cent; in Japan it was 34 per cent; in Italy 63 per cent and in India as much as 89 per cent. Where, in any of the five countries concerned, there have been or still are imposed upon pharmaceutical inventors restrictions either as to scope of patent or as to erosion of exclusivity rights, it may not have appeared—at first sight—as involving discrimination against the foreign inventor. Nevertheless the cardinal factor in establishing either form of restriction was a defensive measure; that is, in truth it was a discrimination against the foreign inventor.

Fully to appreciate this point and, therefore, to understand current restrictions or possible future restrictions in any of these countries, it is useful to consider British history and attitudes adopted in the light of different levels of indigenous technological development, more particularly since the outbreak of the first World War. In this period, our patent



system has been reviewed by the Parker Committee in 1916, the Sargent Committee in 1931 and the Swan Committee in 1944-47, and amending legislation ensued in 1919, 1932 and 1949 respectively.

Prior to 1919 there were in existence comprehensive provisions to minimise abuse of patent monopoly rights (including provision for revocation of patent if the invention was not the subject of manufacture in this country) but there was no clear embargo on patent protection for a chemical substance (including a therapeutic agent) *per se*.

The 1916 Committee indicated that most cases of abuse of monopoly rights were cases of foreign patentees failing to supply the United Kingdom market by local manufacture and re-drafted the applicable provisions of the 1907 Act with the declared concept of preventing such abuses in the future, of tending to bring inventions into early use, and of developing manufacture within the Realm 'without unduly interfering with any patentee or financier where the patent rights are being legitimately used.' Finally the Committee advocated in the case of chemical substances restriction of protection to special methods of manufacture and to the product when so made, and recommended, for the first time, special compulsory licensing provisions for food and medicines. These recommendations were carried into effect in the Patents Act of 1919.

The Parker Committee apparently heard no evidence and its report (publicly available only recently) gives no explanation for its recommendations concerning chemical substances, food and medicines. Some guidance, however, is afforded by the 1931 report of the Sargent Committee which, commenting upon the work of the Parker Committee observed that there was doubt whether under the 1907 Act product claims were valid and it was considered desirable to remove this doubt 'particularly in view of the numerous claims of this class made in the British specifications of German inventors in relation to dye-stuffs.'

They also observed that as to Clause 11 of the 1919 Bill [ultimately Section 38A(1)] the explanation given when the Bill was introduced into Parliament was that 'This clause relates to chemical products and substances intended for food or medicine; and confines the patentee in his specification to claims for what he has actually invented, namely the substance as produced by the process he has discovered; and not the substance generally by whatever process it may be made. This amendment will bring the law of England into greater agreement with the law of the majority of foreign countries (including Germany) and prevent our giving a wider protection to foreign chemists than our own chemists receive.' It is significant that no consideration was apparently given by the Parker Committee to the United States system which recognised that patentability could extend to a chemical substance *per se*, that is without restriction to a specific process of manufacture.

Regarding Clause 12 of the 1919 Bill [ultimately Section 38A(2)—providing for special compulsory licensing of patents relating to food and medicines] the Sargent Committee commented as to occasion and origin of the clause ‘During the War it became apparent that Great Britain was suffering from a lack of medicine and drugs, many of which were the subject of patent rights in this country. On the other hand, it was found that in many European countries (e.g. France, Germany, Switzerland) such substances were not capable of protection under the patent laws of those countries. In this state of things it was considered expedient to modify to some extent the monopoly consequent on the existence of patent rights in regard to such substances.’ It was not true that in Germany medicines and drugs were not capable of protection in 1919 since, under German Law, it was recognised as long ago as 1888 that a patent for a process of producing a chemical substance covers also the product when made by that process even if the product is a drug.

Finally, the Sargent Committee commented that the restriction on claims to chemical substances imposed by the 1919 Act appeared at the time to have been regarded favourably by the industry.

The inference may be drawn that the root causes of the introduction of the two inter-linked provisions of Section 38A were:

(a) That the compulsory licence provisions of the 1907 Act and the manner in which they were administered had failed to safeguard the public interest in failing to ensure the social and economic benefits which working of foreign-owned (essentially German-owned) patents in this country would have provided, and

(b) That the British chemical industry lagged far behind its European competitors in contributing towards technological advance.

A study of the history of the dyestuffs industry in Europe from 1856, when the pioneer chemical technologist W. H. Perkin first discovered the synthetic coal-tar dye mauveine, to the outbreak of the first World War is revealing. By 1862 the eminent German chemist Professor A. W. Hofmann was able to declare ‘Britain is the greatest producer of coal-tar and Britain is destined to build up the world’s biggest dyestuff industry.’ And yet by 1913 Britain, like the rest of the world, was dependent upon German dyestuffs. In this regard it is well to recall the comment of Raphael Meldola in the conclusion to his Presidential Address to the Society of Dyers and Colourists in 1910. He said:

‘It has often been argued that the British colour industry suffered from the imperfection of our patent laws—there is some justification for the view, and they are by no means perfect now, but that is a very different thing from the assertion that the imperfection of the patent laws was the main cause of our decadence. . . . The history of the fifteen year period refutes it . . .



'It was principally our neglect of science which was responsible for our stagnation, just as it was the appreciation of science which was the cause of the progress of our competitors. Had our factories been creative centres as were the continental factories, had discoveries of great industrial value been pouring out of research laboratories here, I cannot but believe that pressure from within would have brought about an amelioration of the patent laws years ago!

'Instead of attributing the decline of our colour industry to the imperfections of our patent laws, the argument, it seems to me, may fairly be inverted—it may be said that the imperfection of our patent laws was largely due to our want of initiative in colour chemistry.'

This want of initiative spilled over into the youthful field of chemotherapy, which was a development of organic chemistry fostered by the successful producers of synthetic dyestuffs. The conclusion may then be drawn that the 1919 provisions relating to chemical substances (including therapeutic agents) were essentially designed to encourage the copyist manufacturer rather than research and development.

We now turn to the Sargent Committee of 1931. Representatives of the Medical Research Council in evidence 'expressed their conviction that in the medical field the Patent Law does not achieve its purpose of stimulating discovery, because it is in fact relatively little used and the incentives to research are other than pecuniary; that in practice the Patent Law here works mischievously because of the undue advantage obtained by the few, mainly foreigners, who resort to it; and that this situation, if not remedied, is very likely to have a very harmful effect on research work.' Fortunately, this astonishing lack of appreciation of the fundamental concept of the patent system and the proposals supported by the Medical Research Council and others for compulsory dedication of pharmaceutical patents did not receive the support of the Committee which commented:

'We fully recognise the importance of the interests involved and the *prima facie* desirability that any important invention in the medical field should be available as speedily and freely as possible for the relief of human suffering. But a corresponding importance attaches to the encouragement of industry and invention for the purpose of discovering methods of alleviating this suffering. And if, in general, the disadvantages of monopolies granted by a patent system are more than counterbalanced by increased stimulation of industry and invention, we see no reason for thinking that the same result should not equally obtain in this particular field.'

Research-minded British chemical industry was by this time in a stronger position and its evidence to the Sargent Committee obviously persuasive. The Patents Act of 1932, however, imported no major change, in relation to pharmaceutical patents, over the 1919 proposals.



By the time the Swan Committee commenced its enquiries in 1944-45 the technological climate in the United Kingdom had undergone further, indeed radical, change. In these circumstances, it is not surprising that the Swan Committee did not appear to require much persuasion to recommend restoration of the pre-1919 position with respect to the patentability of chemical (including pharmaceutical) products *per se*. Indeed, this recommendation became law (the Patents Act 1949) with singularly little comment, discussion or argument. The Committee had considered additionally strengthening the position of inventors of pharmaceutical inventions by recommending elimination of the special provisions for compulsory licensing applicable thereto but finally decided against this.

This history has a bearing on appraisal of the essential differences and trends of approach to pharmaceutical inventions in the five countries concerned. It shows, moreover, that restrictions peculiar to pharmaceutical inventions either in terms of erosion of subject matter (that is, restriction of scope of monopoly) or erosion of exclusivity (that is, special compulsory licence or special application of Governmental powers) have arisen essentially on short-term grounds of expediency or emotional appeal. Since the pharmaceutical field, considered as an area of technology, is of interest to a country not only from the viewpoint of the health of the nation but also of economic growth, it surely merits encouragement rather than discrimination. We shall be considering in a moment current trends on this issue in the five countries selected for study.

In order to highlight the essential differences of approach in the five countries concerned with respect to pharmaceutical inventions, attention will be directed to the following major factors:

1. Patentable Subject Matter (relative to pharmaceutical inventions).
2. Criteria for Novelty.
3. Examination by Patent Office.
4. Sanctions for Abuse of Monopoly Rights in the Public Interest.
5. Trends *qua* Possible Changes in the Patent Law.

In the following comments various qualifications have been omitted where they are not germane to the subject of this paper. Moreover, emphasis has been directed more to the questions concerning the grant of a patent by the Patent Offices rather than to the ultimate criteria of validity imposed by the Courts. Thus, for example, in the United States patent protection is obtainable for methods of medical treatment which depend for their novelty and utility upon the physiological reaction of the body to the substance in question; the United States Patent Office customarily allows claims of this type at the present time but there is room for serious doubt as to whether the Supreme Court would approve of claims of this type as being in conformity with the statutory requirements for patentability. With this reservation in mind we will turn to a comparative study

of patent law and practice in the five countries with respect to factors 1 to 4 and thereafter consider, as a separate issue, trends *qua* possible changes not merely in national patent law but internationally.

#### 1. PATENTABLE SUBJECT MATTER

The broad statutory requirements for patentability are essentially the same in all five countries. They are aimed at protection of discoveries which have industrial application, and protection is normally restricted to industrially recognisable forms of those discoveries. The majority of pharmaceutical 'inventions' are based upon the discovery of a therapeutic property of a substance, itself new or old. There are then the following possibilities for patent protection (subject to national differences as to scope and type of claim permitted):

- (a) The substance itself;
  - (b) Pharmaceutical formulations containing the substance; that is, mere admixtures;
  - (c) Processes for making the substance, the individual process being either the mere application of a known process and, therefore, obvious or non-inventive once the chemist knows the chemical structure of the required product (the so-called analogy process) or being of itself non-obvious and therefore inventive;
- and (d) Methods of medical treatment, the novelty and utility of which derive from the therapeutic property of the substance.

If in any given country all four possibilities of patent protection are available, then the likelihood of adequate protection for the practical application of any new and significantly important advance in chemotherapy is at optimum. More especially, patent protection [in terms of category (b) or (d)] will still be available even if the substance turns out previously to be known *per se* either merely as the result of an academic laboratory exercise in chemical synthesis or as an ingredient of say a paint or lubricating oil.

As to the law and practice in the five countries in question, we can discount Italy which denies any form of patent protection in the pharmaceutical field. As to the remaining four countries, it can broadly be said that:

(1) In respect of compounds new in themselves, only the United States and Great Britain permit optimum protection [category (a)]; in Japan and India only process protection in terms of category (c) is available—extending to the product when so made—although in India the onus of proof of infringement lies with the patentee.

(2) In respect of substances known *per se*, protection of type (d) and possibly also type (b) is available in the United States, in terms therefore of a method of medical treatment and possibly also of pharmaceutical



formulations; in Great Britain methods of medical treatment are deemed unpatentable but protection of type (b)—for pharmaceutical formulations—is possible; in India the patent law, taken by itself, permits protection of type (b); in Japan no protection is obtainable except in the terms discussed under the next head.

(3) In respect of new processes for the manufacture of therapeutically active chemical compounds (old or new) protection is obtainable in all of the four countries where the process of itself constitutes an un-obvious technical advance.

(4) To the extent that the foregoing comments on product protection apply to India, they must be qualified because of the current attitude of the Indian Patent Office.

*To sum up*, the five countries concerned can be arranged in order of the scope of protection they afford to pharmaceutical inventors as follows: the United States, Great Britain, India (but see the comment under the heading of Trends), Japan and Italy.

## 2. CRITERIA FOR NOVELTY

As a general proposition Great Britain and India recognise novelty of an alleged invention if it has not been the subject of prior disclosure or public use within the national boundaries. This rule, which can be loosely termed 'domestic novelty', is extended in the United States and in Japan to include prior publication (though not public use) anywhere in the world. In the case of Italy prior disclosure or public use anywhere in the world invalidates; this is termed 'absolute novelty'.

## 3. EXAMINATION BY PATENT OFFICE

The basic requirements for validity of patent, additional to the statutory exclusions from patentability, are novelty, utility and lack of obviousness. In the United States it is a function of the Patent Office to review all three criteria; the novelty search is thorough at least with respect to US and foreign patent literature available in Washington DC and in some areas of technology, extends also to technical literature. It also functions to screen, in a preliminary fashion, the other two criteria for validity, and whilst its practice is open to objection on a number of grounds it is at least effective in causing rejection of patent applications manifestly weak in patentable subject matter and/or containing claims of excessive breadth. In short, the United States Patent Office examination is strict and ranges over all of the essential criteria for patentability.

The Japanese Patent Office functions similarly although its requirements, as well as the scope of the official search, are of a lower order than those of the United States Patent Office. In Great Britain the function of the Patent Office extends only to considerations of form of specification and



claims and novelty, based upon a very limited search (in general restricted solely to British patent specifications published within the past fifty years). In India examination by the Patent Office is essentially restricted to formality matters and a novelty search is the exception rather than the rule. In Italy official examination is restricted to formality issues.

*To sum up*, in terms of efficacy of the respective Patent Offices in screening patent applications as to novelty, utility, obviousness and excessive scope of claim, we can arrange the five countries in the descending order: the United States, Japan, Great Britain, India and Italy. In general parlance, only the United States and Japanese patents are regarded as 'strong' patents.

It should, however, be noted that in three of the countries concerned, namely Great Britain, Japan and India, there is provision, after official examination but before grant of patent, for opposition by interested third parties and that this procedure, in at least Great Britain and Japan, is made use of by industry and tends at least in certain technological areas to act as a reasonably effective second screening stage before grant.

#### 4. SANCTIONS FOR ABUSE OF MONOPOLY RIGHTS AND IN THE PUBLIC INTEREST

Three of the countries with which we are concerned can conveniently be grouped together: the United Kingdom, India and Japan. In each of these countries there is provision for the grant of a compulsory licence if it is shown that the invention has not been 'worked' in the country in question. In the United Kingdom and in India the provisions as to non-working are extended to include a number of other conditions, for example failure to supply the market requirements on reasonable terms, all of which are grouped together under the general term 'abuse of monopoly rights'.

In addition, these three countries provide for the grant of licences almost 'as of right' in fields of particular public interest even when there is no 'abuse' or lack of working. In Japan such field is left in generally broad form; in India it is defined as applying to inventions concerning food, medicine, insecticides, germicides, fungicides, or surgical or curative devices or the like. In the United Kingdom the field is that relating to food or medicine or surgical or curative devices or any invention required for the services of the Crown.

Caution must be exercised in trying to draw a precise line of demarcation between compulsory licensing in the public interest and compulsory licensing for abuse of monopoly rights. Thus failure to supply a commodity of vital need to the public at a reasonable price and in reasonable quantity might well be argued to be either a criterion of public interest or an example of abuse of monopoly rights by the patentee.

The position in Italy is substantially different from that in the other

three countries in that there is no provision in the patent statutes for compulsory licensing. On the other hand, a patent can be annulled if there is evidence of non-working and it can also be expropriated (subject to compensation to the patentee) in the interests of the national defence or for other reasons of public utility. There are, of course, no special provisions as to compulsory licensing in the pharmaceutical field for the simple reason that patents are not being granted in that field.

Finally, in the United States there are no provisions at all in the patent laws as to compulsory licensing either on the ground of abuse or on the ground of public interest. Nevertheless, although a patent is a lawful item of property and may be used lawfully to enforce a monopoly, there are circumstances in which mode of use, or non-use, of a patent could give rise to an offence under the anti-trust laws and might result in a form of compulsory licensing by order of the Court.

##### 5. TRENDS QUAE POSSIBLE CHANGES IN THE PATENT LAW

*Generally*, that, despite the advances made in the past thirty years, the use of chemistry as a corrective agency for the treatment of illnesses related to body chemistry is still in its infancy and that the pharmaceutical manufacturers, who have made a great contribution to progress to date, can be expected to play a vitally important part in further technological progress appears to be generally accepted. In recent years, however, two opposite trends have been developing in relation to the continued application of the patent system, as an incentive to private enterprise, to the field of chemotherapy, no doubt due to the special political, emotional and economic considerations involved.

On the one hand, enquiries are being or have recently been conducted in certain countries for the purpose of determining whether or not some restriction should be placed on the extent of monopoly afforded by present law because, so it is argued, patent monopoly of itself engenders price levels and other conditions of sale or supply of drugs that are harmful to the public interest. Enquiries of this kind have occurred, for example, in the United States, Canada, South Africa, India and New Zealand.

On the other hand, there has been active progress, involving countries where the scope of patent protection for pharmaceutical inventions has been either limited or non-existent, towards the removal, or minimising of, such restrictions. In short, there is on foot a trend towards product claim protection for new chemicals having therapeutic activity even in countries traditionally opposed to such form of protection; for example, Germany and Holland. Thus, under the aegis of the Council of Europe a Convention for the harmonisation of national patent laws has been concluded amongst the principal countries in Europe which will provide for product claim protection for new pharmaceutical chemicals. This trend,



accepted at least in principle by, for example, Italy, is but a facet of earnest endeavours being made in interested circles, including national Patent Offices, to ensure that the patent system shall, with increasing efficiency despite the ever-increasing pressure of technological development, continue to play its role of encouraging technological advance.

It is not the intention in this paper to deal with political and economic aspects of the patent system; nevertheless, it may be noted that with respect to those countries in which indigenous technical resources require, or could be helped by, foreign resources, a draft Model Patent Law has been produced by the International Bureau at Geneva in the light of historical development of patent laws in the more highly industrialised countries and of the special needs of developing countries. In that draft Patent Law no special restrictions have been placed on the patenting of pharmaceutical chemicals and, whilst close attention has been paid to the inclusion of provisions designed to safeguard the public interest, the special Committee responsible for the production of the Model Law has emphasised that any express power of a national Government to interfere with the right of a patentee to exploit his limited term of monopoly, with due regard to the over-riding requirement of exploiting his invention by actual manufacture in the country concerned as and when economic conditions enable this reasonably to be done, should be exercised with due caution since, in these extreme circumstances, the advantage to the community of attracting technological development by means of the patent system will be jeopardised. In this sense, the Committee has appreciated not only the value of the patent system to developing countries in thereby promoting across national boundaries the fruits of technological development but also the encouragement of foreign sources of technological development to tackle problems of particular importance to the developing countries themselves. In this connection, it must be remembered that many developing countries, such as India, have—in relation to public health—problems, the incidence and magnitude of which are peculiar to their own environment and that the existence of an acceptable national patent system is at least one of the ways in which a developing country can expect private enterprise in other countries more fortunately placed in technological resources to devote those resources to the special problems in question.

In the *United States of America*, since at least 1912 a number of Bills have been put before Congress proposing one form or another of compulsory licence provision for restraint of abuse of patent monopoly rights. For example, following the Report of the Kefauver Committee an attempt was made in 1961—without success—to secure a restriction of term of pharmaceutical patents with provision for compulsory licensing.

Only as recently as December 1966 a Commission appointed by the President to consider the Patent Laws issued a Report. It contains no

recommendation for discrimination against the pharmaceutical inventor, no proposal for compulsory licensing or public use of pharmaceutical inventions, but is mainly concerned with ways and means for strengthening the quality and effectiveness of US patents, of assisting the Patent Office more efficiently to carry out its work, and in general to improve the system to cope with exploding technology in the foreseeable future.

In *Japan*, the present law provides no protection for the practical applications of the discovery of therapeutic properties in a chemical known *per se*. At the present time, there appears to be no significant pressure from within interested Japanese circles either to follow the current trend in Europe for improving the lot of the inventor in this regard or to impose special restriction upon patentees in the pharmaceutical field.

In *Great Britain*, the Report of the Sainsbury Committee, appointed to consider amongst other things the Patent System in relation to pharmaceuticals, is awaited. It will no doubt comment upon the use made by the Minister of Health in the last Conservative Government (Mr Enoch Powell) in invoking the aid of Section 46 of the Patents Act to permit the importation of patented drugs required for the National Health Service; also upon the significant erosion into exclusivity of patent rights that such an action brings about. Similarly there is the issue of application for compulsory licence under the special provisions of Section 41, especially as to whether there should be power to permit the licensee to import the patented product into this country.

Comment from some circles has been curiously in line with aspects of the view expressed in Medical Research Council evidence to the Sargant Committee in 1931 and has revealed serious confusion of thought on the interrelationship of economic and other problems posed by the availability of drugs in the war against disease and the rights afforded by grant of patent. Thus, Mr Enoch Powell, who when Minister of Health presumably had access to expert knowledge on the Patent System, commented in the *Observer* of 25 July 1965 'Are we so sure that, in the field of drugs at least, it [the patent protection] cannot, and should not, be dispensed with?'

It is to be hoped that the Sainsbury Committee is approaching the problems of pharmaceutical patents in a more impartial fashion. Some twenty years have elapsed since the last general enquiry on our patent system by the Swan Committee and it is perhaps time for a further Committee to be appointed to consider that system along the lines adopted by the United States President's recent Commission on the US system. As to the special restrictions on pharmaceutical patentees peculiar to the British System, many interested circles maintain that: first, Section 46 of the Patents Act dealing with Crown use should be amended to abolish the power of the Ministry of Health to import drugs covered by British patents; this on the ground that such action is contrary to the fundamental



concept of the Patent System, that is of encouraging new industries within the Realm; second, that Section 37, dealing with general provisions for abuse of monopoly rights, already gives the Ministry of Health a remedy for dealing with excessive prices for patented drugs; third, that Section 41, providing for special compulsory licence provisions for patents concerned with foodstuffs and medicines, is an out-moded and detrimental form of discrimination against pharmaceutical inventors and should be abolished on the ground that any advantages it might have had in the public interest as compared to the general provisions of Section 37 are now illusory.

The Government is actively engaged, through the Committee of Experts at Strasbourg and otherwise, in the negotiation of conventions designed to harmonise the patent laws of the countries concerned and to improve the strength of the patent system. There is, however, little sign that, despite its alleged preoccupation with the encouragement of technological development, the present Government attaches adequate importance to the function of the Patent Office and the augmenting of its resources to improve its efficiency and standing.

In *Italy*, attempts have recently been made to secure amendment of the Italian Patent Law to provide for the grant of patents on pharmaceutical products and processes for their production, albeit of very narrow scope, and for the grant of compulsory licences in respect of patents in the pharmaceutical field where such would, broadly speaking, be in the interests of public health. A current proposal has reached the stage of a draft Bill providing for the allowance of patents with claims of narrow scope for processes for producing pharmaceuticals, with a shortened term of ten years and subject to grant of compulsory licence when such would achieve a reduction in price or otherwise be in the interest of national health. This proposal is part of a wider proposal for a five year plan for economic development shortly to be debated in Parliament.

In a report to the Secretary-General of the United Nations Economic and Social Council in 1964 the Italian Government stated: 'Italy is primarily a recipient of foreign inventions. Access to foreign inventions is helped by the patent system in force in Italy. Access to foreign inventions relating to medicines and to processes for their production is hindered because such processes and products are not yet patentable in Italy. However, the present law is being changed to extend patentability to both pharmaceutical processes and their products. When these amendments come into force, access to foreign inventions in this field will certainly be easier.'

In *India*, under Defence Regulations of 1962 consequent upon outbreak of hostilities between India and China, the Patent Office was apparently empowered to withhold from grant all patent applications containing claims to either pharmaceutical chemicals when made by the claimed process or pharmaceutical formulations.

There then followed a Patents Bill (1965) in respect of which a Joint Select Committee, after hearing evidence from interested parties, submitted a report in October 1966. It proposed limitation of term of pharmaceutical patents to ten years and approved far-reaching and drastic provisions for compulsory licensing and unrestricted use of patented inventions by Governmental agencies inclusive of the right to import. In an editorial the *Economic Times* of Bombay (3 November 1966) commented: 'But for a few marginal concessions, the report of the Joint Select Committee of Parliament on the Patents Bill is unlikely to promote an orderly and vigorous development of the industries affected by it. The character of the Bill is such as to abrogate virtually pharmaceutical patents, and to the extent that the report does nothing to allay this apprehension, it is far from helpful to this industry. The ostensible purpose of the Bill is to stimulate invention and to encourage research and development for industrial and technological progress. Unfortunately, the amended Bill not only militates against these laudable objectives but is likely to jeopardise the flow of foreign aid and investment.'

The proposed Bill was not dealt with by the Indian Parliament in the last session now ended and it remains to be seen whether it will be acted upon next month.

(Since the paper was read it was learned that the Bill was not acted upon and at the time of printing it was not known whether it would be revived and, if so, in what form.)



# Patents and Innovation

in Britain, India, Italy, Japan and the United States of America

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PATENTS ESTABLISH PROPERTY rights in ideas. This 'intellectual property', however, is far from easy to fit into economic analysis and as such has never found an easy friend in the professional economist. In the absence of patent legislation, an idea, unlike the normal 'economic good', can be used without limit and its stock remain in no way diminished. Further its use does not imply any sacrifice of other goods and services, whilst it can be transferred from person to person or company to company without incurring any cost apart from that of any search which may be involved;\* any attempt to market an idea would rapidly reduce its price to something approaching zero as, once sold, it would inevitably be freely reproduceable. Information can thus be argued to be a 'free good', and according to the dictates of economic theory should be freely exchangeable at zero price in order to achieve an optimal distribution of resources in the economy.

This is, of course, a purely static view. In a dynamic state patents can be justified on the grounds that whilst the distribution of ideas is relatively costless, additions to the existing stock are not. Once private property rights in ideas are established, information becomes an economic good and exchangeable at a price equal to the discounted value of the expected returns from its employment. Patents can thus be thought of as the incentive which society offers to individuals and companies to search for new discoveries.

There exists, however, no general agreement as to the precise link between patent protection and research effort. It can be argued that it appears highly unlikely that the actual inspiration and discovery of, for example, a new pharmaceutical preparation, is in any direct way related

\* This is not to imply that the intellectual property so gained as a 'free good' could be profitably employed with other factors without cost. A company may have free access to a formula but the ability to understand and develop it into a consumer good may well be very costly.

to the existence or otherwise of patent legislation. Few research workers either as individuals working on their own behalf or as members of a company team are driven solely, or even mainly, by considerations of commercial profit. Indeed as over 70 per cent of all patents are filed by companies, the inventor usually has no stake in the eventual commercial outcome of his discoveries, save for the possibility that they may enhance his future career prospects. Further the individual operator probably stands to gain little from the patent law. Usually he has neither the funds to develop his invention nor the funds to protect it in the courts. Indeed patents are often regarded as little more than licences to sue.

Nevertheless the fact is that companies only employ research workers in anticipation of an eventual profit return. The establishment of a legal right to the fruits of research must enhance the possibilities of that return and therefore provide a strong incentive. Similarly, the individual research operator has open to him at least the possibility that a company will consider his discovery worth developing in exchange for a fair royalty payment as compensation for relinquishing some part of his exclusive ownership rights. This is not to claim, of course, that companies would cease to search for inventions in the absence of patent protection. Being first in the field would always, in the short run at least, carry the promise of an extra profit return. In these circumstances the firms would, of course, have every incentive to keep their discoveries secret as long as possible.

Perhaps the strongest incentive is not so much towards the acquisition of intellectual property as it is towards the development of such property into useful end products. It is at the point where a firm has to decide whether or not to attempt to develop a discovery into a marketable commodity that patent protection becomes of crucial importance. Development is a high-cost and high-risk process, and the promise of a guaranteed period of protection for any successful product must be important in creating an atmosphere conducive to its being undertaken. A surplus must be gained from the sale of any successful products, not only to earn a fair return on their development costs, but also to cover the losses incurred on the failures.

There seems then, even in the absence of an agreed economic theory on which to build, to be good reason to postulate that intellectual property differs substantially from normal 'economic goods' only in the static sense and that, in the real world, patents offer an incentive, not so much to invent as to undertake the high risks of development. Patents are, of course, only one of a multitude of factors in the delicate balance of incentives and disincentives, but all other things being equal, an innovation of given risk is more likely to be developed with strong patent protection than without it.

At this moment in time several countries are reconsidering their patent



position\* and so the remainder of this paper is devoted to investigating, by appeal to what in a legal context might be termed circumstantial evidence, what empirical support there is for arguing that patents stimulate and reflect growth, and, secondly, what effects upon market structure and prices might be expected to follow in their absence.

#### NUMBERS OF PATENTS FILED

Such attention as economists have paid to the question of patent protection has, in the main, taken the form of enquiries directed at establishing whether patent numbers are an accurate reflection of innovational activity and whether there is any general correlation between patent numbers and other economic variables such as sales. Mostly these studies have led to negative conclusions. Patents are not homogeneous entities. Any reasoning based upon the number of patents must neglect the qualitative aspects of the disparate inventions they represent. Straight addition assumes each patent represents a similar innovational step. Again only some 50 per cent (according to a George Washington University survey) of patent filings ever prove to be commercially viable.<sup>1</sup> Thus any attempts at correlation with other variables must inevitably be very crude. Melman has shown there to be little relation between patent numbers and sales in the United States,<sup>2</sup> whilst despite the constant economic advance of Western Germany her patent numbers have been declining since they reached a peak in 1953. Again the economic set-backs experienced by Britain in 1952, 1956-58, and in the early sixties have not been reflected in her slowly increasing stock of nationally held patent filings. Numbers of patents, however, appear to take on rather more meaning when analysed for one particular industry than for the whole economy. A comparison by J. Jamieson and the author, for example, between the cumulative number of pharmaceutical patents over the past ten years in the British market, and a four-year average sales ranking, gave a correlation coefficient of 0.75 for British-owned companies and 0.64 for all leading forty-five concerns in the industry.

On the international front remarkably consistent ranking persists whether nations are ordered by research, number of important discoveries, patents filed, exports, balance of trade gap or, simply, production volume. The United States is consistently first, Britain and Japan second or third, with Italy and India trailing the field. This, of course, does not take us very far towards the formulation of a causal hypothesis. Is, for example, a high ranking in terms of patent numbers a factor inducing research activity or merely a reflection of it? Such questions involve the analysis

\* See J. A. Kemp's paper pages 22-36.

1. Reported in J. SCHMOOKLER, *Invention and Economic Growth*, Harvard, 1966.
2. S. MELMAN, *The Impact of the Patent System on Research*, Washington, 1958.

of factors influencing human motivation and as such are open to the usual pitfalls.

Numbers of patents have been frequently used as an approximate indication of overseas interests in any particular market, although, apart from global figures for the entire economy, no such data are as yet provided by the Patent Office. Personal investigation revealed that only 6 per cent of the pharmaceutical patents filed per annum are held by British-owned firms as against some 14 per cent twelve years ago. These figures may be compared with the estimate of 47 per cent for the entire economy over the period from 1957 to 1961. The French, German and Dutch claim the most rapidly increasing share of our pharmaceutical patents, collectively increasing from only thirty patents per annum to nearly 300 per annum since the early 'fifties. The Swiss and American pharmaceutical interests both file some 350 patents per annum and head the field. Once more, however, the problem remains that there appears to be no obvious method of determining the exact nature of the chain of causation. Do, for example, the foreign interests in our market sell more pharmaceuticals because they file more patents or do they file more patents because they sell more? Again motivations are obscure. The overseas-owned companies could for example file patents in Britain, not so much to achieve additional sales, but rather to check possible world market competitors at source. Certainly there are no signs that relative shares in patent holdings are reflected in the sales market. The Swiss, for example, hold over 30 per cent of the patents but only 12 per cent of the market.

#### GROWTH RATES IN THE FIVE COUNTRIES

Turning to the growth performances of the five countries under review little or no support can be found for the view that in all circumstances patents are an adjunct to growth. The rate of advance experienced by each nation's pharmaceutical industry appears to be more dependent upon the relative demand conditions each faces and the presence or otherwise of a sound basic chemical industry, than upon the particular patent legislation in existence. Since 1960 Japanese pharmaceutical output has been growing at 22 per cent per annum, a growth rate, as it happens, exactly mirrored by the rise in her patent numbers. Indeed in terms of total filings she ranked fifth in the world in 1950, but is now second only to the United States. However, whilst there can be little doubt that some part of this post-war recovery is due to the importation of foreign technology, which was in turn facilitated by the existence of her patent system, the main impetus to growth was the latent demand for mass drugs, which rising real incomes rapidly made effective. This backlog of demand is now being largely satisfied and the Japanese domestic market is increasingly turning towards more advanced and sophisticated products—a tendency



reflected in the industry's rising royalty bill. It is the development of these advanced products which will really test the patent system.

In India pharmaceutical output has been growing only slightly less rapidly than Japan's at 16 per cent per annum. Here the latent demand for basic drugs such as penicillin has barely been touched so that it will probably be many years before patents become a significant growth factor. Again, Italy with no patent protection on medicines is nevertheless growing at 10 per cent per annum. The crucial factor here appears to be that she is greatly aided by the existence of a strong basic chemical industry, which both Japan and India lack. To provide the market with even the most basic pharmaceuticals in the absence of such an industry necessitates raw materials and often semi-finished drugs being imported, or else produced at home at very high unit cost.

The growth rates of Britain and the United States are noticeably lower at 8 and 6 per cent respectively, again a probable reflection of their stage in market development. The demand for mass pharmaceuticals having been completely met, their growth potential is now dependent upon the discovery and marketing of new products for sale in both the home and overseas markets, and therefore, in turn, upon the existence of a strong patent system. The dependence upon research expenditure and new products is shown by the fact that ten pharmaceutical companies in Britain account for nearly 90 per cent of the total research effort and all but two of them are ranked in the first twenty by sales. No British-owned company spending less than £200,000 per annum upon research managed a better sales ranking than twenty-fifth, and all but one such company came lower than thirty-third. The largest research spender amongst the British-owned companies spent only one-fifth of the leading American budget, and managed only twelfth place by sales. In fact only two British-owned firms are in our own top ten sales ranking based on purchases by the NHS pharmaceutical service. All of this probably reflects the fact that whilst the British-owned interests in our industry finance only £9 million of research effort between them, the foreign subsidiaries they compete with draw upon the discoveries accruing from over £160 million of world-wide research expenditure. It is interesting to note that the same three firms lead the British-owned companies sales and research ladders; had the most new products between 1960 and 1965; and have been the most profitable British companies in the industry.

If the link between research and sales is fairly readily demonstrated, then the link between patents and research remains elusive. What is clear is that failures to obtain patent protection for a product in this industry are very rare, and that this, combined with a high obsolescence rate, explains why over 70 per cent of current British pharmaceutical sales are of protected products. Clearly, however, even in the advanced countries,

the information necessary to establish a relationship between patent protection and growth is lacking.

In the case of the developing nations, although patents might well be a necessary precondition to research activity (certainly the risks to be covered will be no less than in the developed countries), other and far greater obstacles exist. The production of advanced pharmaceuticals with high research content is largely the preserve of some hundred international companies based in the western nations. In general only those firms commanding world-wide markets can today support adequate research programmes. The leading pharmaceutical research investor at present is the United States with an expenditure of over £140 million. Japan having acquired her know-how from abroad (in terms of formal agreements, 60 per cent from the United States and 20 per cent from Switzerland) is now spending the world's second largest research budget. Five years ago she spent only £6 million, but now spends over £23 million, which represents a higher proportion of her sales pound than that spent anywhere outside Switzerland. Britain and Western Germany are established in the middle of the world's research expenditure ladder with some £12 million worth of research carried out in each. In sharp contrast, only £3 million is spent in Italy, and this is confined to her seven leading firms.

#### RESEARCH AND THE STRUCTURE OF THE INDUSTRY

The importation of foreign techniques has made advanced medical treatment available in India and Japan in a very short span of time. Many have argued that a nation like an individual learns properly only by doing and that, therefore, such importations lead to dependence on others and to a lack of indigenous initiative. The evidence, however, is against this. Japan, having imported the basic pharmaceutical tools, is now improving the imported techniques and selling them back to the rest of the world. Vitamin B, under the brand name Alimanin, is one of several examples. This product forms 7 per cent of all prescription medicine sales in Japan (in Britain no one product exceeds 4 per cent), the techniques involved have been sold to thirty-one countries for valuable royalty income and they now form Japan's principal pharmaceutical export.

In India, Hindustan Antibiotics, an entirely state-owned company, was given free know-how by the World Health Organisation and UNICEF, and more recently know-how from Merck in exchange for a 2.5 per cent royalty. The result has been not only the successful manufacture of penicillin, but also, by applying the techniques gained, the discovery in India of Hamycin, Dermostatin, Aureofungin, Antiamoebin and streptocycline. Indeed, it was only recently announced that Sherman Laboratories, an American company, have taken a licence for Hamycin, whilst another American firm, Upjohn, are expected to pay some £150,000 a year in



royalties for Antiamoebin. Against this must be set the fact that the more advanced but non-patent awarding Italians have to date only produced one product of note (Rifocin).

The distribution of the world's research expenditure being very heavily skewed and concentrated in the western nations, a developing country can only gain access to the world's latest know-how by importing it in return for royalty payments as in Japan, or by encouraging foreign subsidiaries to set up and manufacture locally as in India, or, alternatively, by means of a gift from such a body as the World Health Organisation. All these courses hold out the hope that by building on the knowledge obtained, the developing country will itself eventually begin adding to the world's stock of medicines.

All, except the last, of these routes to the latest research discoveries, imply the existence of patent protection in the developing nation. There remains one other route which does not. Italy provides the classic example of a country attempting to build up a pharmaceutical industry in the absence of patent protection, by imitating the world's leading products whilst making no royalty payments to the originators. Such a course carries with it, however, great disadvantages both for the true innovator, whose market is correspondingly diminished, and for the imitating country itself in that the growth of indigenous research is inhibited, the market fragmented and each firm's output cut back to small high cost dimensions.

In Italy, for example, there are over 1000 companies, 300 of which employ less than nine persons, producing over 60,000 registered products. Almost as soon as a research based firm markets a new product about a quarter of its potential market is lost to imitating companies. As a result every chemical entity has up to twenty duplicate products.<sup>3</sup> Again in Japan the existence of only process, as against product, patents, has led to a very similar situation. Research is directed towards finding a non-patented method of producing known products rather than towards new chemical compounds and entities. As in India, demand is very responsive to increases in supply, so that there is every commercial incentive to pursue this kind of policy. Why search for the new at high risk, when the old is readily saleable at little or no risk? The Japanese antibiotics have proved a notable exception to this rule. As the Patent Office has been liberal in the coverage afforded by each filing in this therapeutic field, the Japanese firms have developed a wide range of products of their own including Leucomycin and Tricomycin.<sup>4</sup>

3. See MICHAEL H. COOPER, *Prices and Profits in the Pharmaceutical Industry*, Oxford, Pergamon Press, 1966, pp. 160-7.

4. Evidence of the Japanese Patents Association to the Indian Parliamentary Joint Select Committee on Patents, 1966. Minutes of evidence, p. 396.

Like the Italian, the Japanese market is typified by a great number of duplicate products together with small scale, high cost production units. The market is supplied by some 2390 firms employing 83,000 people. Only 136 firms employ more than 100 people. It requires sixty firms to account for 30 per cent of the industry's employees, in sharp contrast to only twenty-one firms in Britain, twenty-four in the United States and thirty-three in Italy. The situation is, however, improving. The number of companies is decreasing and the average firm getting larger. There are now eleven factories with a labour force exceeding 1000, whilst in 1960 there were none. Further in 1955 the leading twelve companies accounted for 43 per cent of sales, but the figure has now increased to 52 per cent. Clearly both Japan and Italy make a pointed contrast with Britain's two or three hundred firms producing some 5000 products, with only 1.1 brands per chemical formulation.

#### PATENTS AND PRICES

The lie to the assertion that in the absence of patents, prices would inevitably fall is readily made. Market fragmentation, plus the high promotional outlays necessary to convince the doctor that duplicated products are genuine equivalents of the original product, have led to higher, rather than lower, prices in Italy. A study by the author of 154 leading pharmaceuticals common to both the Italian and British markets showed that over 70 per cent of them were more expensive in Italy. The average price of the 154 drugs when weighted by British sales was 9s. 5d. in Britain and 11s. 9d. in Italy, and when weighted by Italian sales, 8s. 7d. in Britain and 10s. 6d. in Italy.\* Indeed the six leading Italian drugs in the sample cost on average 4s. 6d. more in Italy than in Britain.

The Swiss drug Librium is a classic example. In Italy nineteen different companies including the originator, Roche, manufacture it under nineteen different brand names. None of these imitating companies pay Roche any royalties, but nevertheless the patient enjoys no price advantage. Roche has managed to retain nearly 80 per cent of the market, whilst all but 3 per cent of the remainder is held by competitors charging approximately the same price. Seven companies charge 30 per cent less than Roche but have failed to make any headway in the market, whilst four companies actually charge more.

In India pharmaceutical prices appear very high despite the fact that only 12 per cent of her leading 800 products are subject to patent protection. An investigation of fifteen very commonly prescribed but unpatented medicines, all of which were manufactured locally (including

\* All prices are chemist buying price net of taxation. The sample amounted to approximately one third of the National Health Service pharmaceuticals purchases by value.



phenacetin, penicillin, and sodium PAS) revealed them to be ten times dearer on average than their imported equivalents. The chief cause of these high prices is undoubtedly the cost of indigenously manufactured raw materials. Eleven basic raw materials investigated (including benzene, hydrochloric and sulphuric acid) could all have been imported, in the absence of exchange controls, more cheaply from any one of at least five countries—a clear reflection of the weakness of the Indian chemical industry.

Indian prices have, however, been grossly exaggerated in the past both by accepting the Indian exchange rate as meaningful and, secondly, by making comparisons with international (usually Italian) dumping prices. A study by the author showed that prior to devaluation, the average manufacturer's realisation price for 217 drugs common to both the British and Indian markets was 21s. 2d. in Britain and 32s. 4d. in India. Since the devaluation of 36 per cent, however, India appears to have become slightly cheaper than Britain. Clearly neither picture represents the truth, which probably lies somewhere in between the two.

A recent Indian Commission set up to investigate fifteen cases of 'high prices', included in its list five non-patented products. In fact two of the most quoted instances of alleged high prices are not subject to patent protection at all. The first, cortisone, is a naturally occurring compound and as such has never been eligible for a product patent, whilst all process protection has expired. The second, penicillin, is made by the State-owned undertaking, Hindustan Antibiotics, and sold at ten times the average world price. There are only two other penicillin producers in India and both are forbidden to charge less than the State.\* Half the sales of the State concern are to other firms, who cannot turn elsewhere for their raw materials due to import and exchange controls; thus as consumer prices are frozen at 1963 levels, the State effectively controls industrial profitability.

There appears then to be little or no evidence that patents lead to, or are a significant factor in, high prices. It would in any case seem that any highly priced *patented* product the State could comfortably ignore. Most patented products, like Librium, are luxury items in a country such as India where 350 million people are totally unmedicated. If they are too expensive the answer is surely not to buy them.

#### FOREIGN DOMINATION AND THE BALANCE OF TRADE

In many developing countries patents are frequently dismissed with contempt as being merely a route to the foreign domination of indigenous

\* Given this protection, Hindustan Antibiotics make a return on capital employed of 30 per cent compared with an average of 23 per cent for the foreign subsidiaries, 15 per cent for the entire industry and 10 per cent for the Indian-owned companies. In effect the State is imposing a tax on the sick.

industry. Any truth in this picture is clearly the result of the unequal distribution of the world's pharmaceutical research rather than anything inherent in the patent system itself.

In Japan, whose research efforts are of comparatively recent origin, there are thirty-seven foreign investment interests, of which eighteen are wholly foreign-owned concerns. Far from these companies dominating the market, only one, Pfizer, manages a higher sales ranking than fourteenth, and then it is only ninth. In fact the two leading Japanese owned concerns supply over 20 per cent of the total turn-over of prescription medicines. Again, foreign know-how is only directly responsible for 10 per cent of the industry's output.

The basic chemical industry is totally inadequate however. Only £82 million worth of drugs out of the £400 million plus total were completely produced in Japan. This reliance on the world market for raw materials and semi-finished products results in an adverse pharmaceutical balance of trade of £9 million, with imports currently twice as large as exports. Of her 2500 firms only some 2 per cent are in any sense integrated, whilst of her forty-eight drugs achieving sales in excess of £1 million, twenty-one were either imported or manufactured using overseas techniques.

There are, however, signs that this dependence on other countries is likely to be short lived. Only 26 per cent of her patent filings are foreign held, her research is rising rapidly and the degree of capital intensiveness has grown in real terms from only £400 per worker in 1955 to £1500 today. This last figure compares with the £2000 per head of the United States leading fifteen pharmaceutical concerns. Productivity has increased 3.1 times, and labour has been liberated from the productive process and diverted to research and a growing sales force. The ratio of tertiary (or 'service') workers to those on production has increased from 1:2 to 4:5. Indeed, at the same time as production workers in the twelve leading firms increased by 70 per cent, the total labour force increased 130 per cent. For the whole industry, a growth of 250 per cent in output was accompanied by an increase of only 50 per cent in labour.

In the case of India, the foreign subsidiary has brought capital, technology and western standards of quality. They have established an industrial nucleus and employed and trained the indigenous population. Only forty-six of the industry's executives are alien personnel, whilst at least three major foreign-owned concerns have Indian managing directors. These companies provide 80 per cent of the total output and nearly 90 per cent of India's pharmaceutical exports.

Certainly these figures amount to foreign domination, but then they are not too dissimilar to those for the British market where foreign-owned companies provide 75 per cent of the National Health Service's needs.



Even in terms of the number of foreign held patents, India with 89 per cent in alien hands is better off than Canada with 95 or Eire with 99 per cent. In fact only the United States, Japan, Western Germany and Britain have a majority holding in their own patent filings, and if present trends continue, Britain will shortly be leaving their number. Nor is 'foreign domination' limited to the patent recognising nations. The companies in Italy attempting to undertake research have been running at a near loss for some time with the result that foreign inspired take-over bids have become rife, and have been the subject of a Parliamentary inquiry.

Indian opposition to patents has made much of the claim that patents protect the foreign subsidiary interests by preventing local manufacturers from competing. This argument seems to totally ignore the fact that 88 per cent of the market enjoys no such protection. Indeed, even the protected products are vulnerable under present Indian patent law to applications for compulsory licences. There are, however, few, if any, instances of such applications being made. Aspirin, phenacetin, insulin, riboflavine and pethidine could all be produced by Indian-owned firms without any patent infringement but none in fact are. It is clearly *want of know-how* rather than patent protection which forms the barrier to local manufacture and know-how can generally only be acquired by offering patent protection to the owners of research information as an inducement to share their discoveries.

In a world market situation in which research is heavily concentrated in five countries, it is not surprising that only these countries have positive balances of pharmaceutical trade. Japan is an exception, for, although she has the second largest research budget, she remains in deficit—probably due to her orientation towards process development. The export performances of Japan, Italy and India are all very poor. Expressed as a percentage of sales they amount to only 4, 11 and 2 per cent respectively, as against 79, 24 and 18 per cent in Switzerland, Britain and the United States.

In Japan and India the advanced products for which a ready world market exists are usually produced under licence and therefore carry export restrictions. The long term solution to this problem lies only in the development of indigenous research which, in turn, depends upon strong patent laws. Japan is clearly well on the way, whilst India appears to be standing at the cross-roads undecided whether to follow the Italian example or stay true to the British patent model.

#### CONCLUSION

This paper can do no more than offer some tentative thoughts on an extremely complex subject more befitting a substantial treatise. Patents are seen as establishing the legal right to intellectual property, whilst their

precise incentive value and 'side-effects' remain open to dispute. The empirical evidence presented suggests that the high growth rates experienced by the developing nations are much more a reflection of given stages in the development of their consumer markets than of the particular patent legislation in existence. The major obstacle to satisfying the backlog of demand for pharmaceuticals which exists in these countries is want of basic know-how. This want is being overcome by the importation of foreign technology which is, in turn, facilitated by the existence of patent laws. The knowledge that a company can freely disclose its discoveries without risk has tended to ensure that an international body of information is built up, often stimulating new thought and new starting points.

The zeal to reduce or abandon patent protection seems to spring from a mistaken idea that this will lead to lower prices. International experience has been that the absence of patents tends to fragment the market and raise costs. Further, process patents, instead of diverting research funds towards developing new and cheaper methods of production, have had the same result. All the signs are that the developing nations have a good bargain in the patent system, and one which should not be thrown away in the quest for short term and often imaginary, advantages.



# Prices, Profits and Innovations

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## PRICES, PROFITS AND INNOVATION

OVER THE PAST three or four years a clearer picture of the pharmaceutical industry's economic workings has emerged. In the ABPI Annual Reports, in the first series of OHE Winter Lectures, and most particularly in Cooper's recent study, the industry is characterised by a high level of industrial research expenditure and a fast rate of innovation leading to rapid obsolescence of existing products. The industry is therefore highly competitive but the competition is more in products than in prices. The history of virtually all the major advances in chemotherapy is one of the dramatic emergence of a single new product which dominates the scene for a while, but which is rapidly matched and often superseded by later developments. This competition within the industry is best described as substitute competition. It is clear that substitute competition is the direct result of research developments made by an initial innovating firm or its competitors, which in turn is a reflection of research expenditure. Research spending must in the long term be linked to the returns from sales and the profit margins in prices. Thus prices, profits and competitive innovation are intimately linked.

In this paper this relationship is explored to show how wide margins between the direct factory costs of production and selling prices promote competitive innovation and thereby the public interest. The competitive model, centred on substitute rather than on price competition, is relevant to the broad range of innovating industry, where the mechanism of competition differs markedly from the traditional concepts of price competition. Indeed, price competition so far as it reduces the revenue flow required to sustain expenditure necessary for research and marketing is inimical to substitute competition and to a high rate of industrial innovation.

The picture contrasts sharply with earlier appraisals of the industry's operations. Formerly, the industry was judged almost entirely in terms of

how effectively price competition operated. This to some extent was understandable since to many competition merely means price competition. Reports such as the Kefauver inquiry and other studies conditioned by this approach, led to recommendations and actions designed to pivot competition within the industry around prices.

It is not suggested that substitute competition is wholly devoid of price competition. It is primarily a question of emphasis and the degrees to which price or substitute competition operates. As will be shown later, the question of competitive prices appears to play an important part in the price determination of new pharmaceutical products. The existence of high price levels relative to production costs is nevertheless obvious to casual observation with new innovational products. Although the study of substitute competition apart from price competition oversimplifies, it characterises the extreme case where the important factors can most clearly be identified.

An appreciation of the way substitute competition works must start with a fuller examination of the internal working of the firms themselves. It is here, within the firm, that the sources of innovation are found; thus a better understanding is required of the ways that the flow of revenue coming from sales is used by the firm to generate innovation and how this in turn feeds back to complete the cycle as revenue from sales.

The problems here are relevant over the range of science-based industry. A far better understanding of the process of substitute competition, of what sustains innovational progress within industry, by politicians, administrators and the general public, as well as a greater awareness of the implications of this process in decisions made within firms are needed if Britain is to sustain or to increase the current rate of economic growth. The industrialists' attitudes to pricing is as critical as that of the Government and the general public. Anthony Bembridge writing in the *Observer*, put his finger on a critical difference in the management approach between British and American industry. 'No one would expect big business in Britain to beat the lush returns earned in America; it is not because the Americans necessarily make better managers. The fact is that in Britain more of the benefits accruing from size tend to be passed on as lower prices to the consumer rather than retained as extra profit. There is also a reluctance to take advantage of fluctuations in supply and demand. In periods of short supply, rationing is more often by long delivery dates than by price. There is a built-in resistance in Britain against charging what the market will bear.' The same observation applies with equal force to the products of science-based industry.

A change in the approach to prices, profits and innovation is critical to Britain's future economic health. Because of international product or substitute competition in world markets, Britain cannot opt out. It is a



choice between a low price, low cost and low wage and profit economy, and a high price, low cost, high wage and profit economy. Under the first choice, there is little future for Britain attempting to compete in low prices and low costs, a kind of western Hong Kong, unless the country works as hard for as little. As this role is clearly unacceptable, it is necessary to develop a fuller understanding of how to market and sell expensive goods in innovating fields to the advantage of the community and to the benefit of the British economy.

#### THE MODELS

This study concentrates on the central features of substitute competition, on how the flow of revenue a firm receives from sales is employed within an innovating firm. Only the salient features and interrelations are considered. There is, however, an important point of definition arising from these relationships. Here, innovation is considered as a single continuous process from the initial discovery through the laboratory and clinical testing of the product, through pilot plant production and product developments to reach the final stage of factory production and marketing. From the standpoint of the firm or the workings of substitute competition, an innovation has no current value until it has been successfully marketed. It has been long recognised that the division between research and development is largely artificial. Within science-based industry it is equally artificial to segment arbitrarily the interrelated processes of research, development and marketing.

To explore the relationship between prices, profits and innovation, it has been useful to construct some simplified models of firms showing different uses of their funds. These are given in Table A. Three models have been constructed which show the essential differences between firstly, a non-innovating firm, secondly an innovating firm and thirdly what can be termed the super-innovating firm. The first, non-innovating, firm is simply the trader in commodities and is characteristic of the type of firm existing mainly under discipline of price competition. The second, innovating, firm is representative of science-based industry in the long term. The third, super-innovating, firm represents what is probably a short-term condition during a period of rapid growth, following, say, a new major breakthrough into a virgin market.

It should be stressed that these models are theoretical. Although figures are based on actual experience, they are not meant to be typical of the pharmaceutical industry as a whole; rather they attempt to be representative of what an individual company in a given circumstance may do. The information on which the models are based comes primarily from unpublished UK data, from US-published accounts, and from FTC reports. The bias towards American sources is unavoidable because up to

**TABLE A**  
**Flow of Revenue: Innovating and Non-innovating Firms**

	<i>Firm A</i>		<i>Firm B</i>		<i>Firm C</i>	
	<i>Non-innovating</i>		<i>Innovating</i>		<i>Super-innovating</i>	
	£	%	£	%	£	%
Sales	100	100	143	100	200	100
Factory costs	50	50	50	35	50	25
Gross margin	50	50	93	65	150	75
Admin. and marketing.	35	35	49	34	60	30
Research and development	nil	nil	14	10	25	12.5
Pre-tax profit	15	15	30	21	65	32.5
Corporation tax (40%)	6	6	12	8.4	26	13
Dividends	6	6	11	7.5	22	11
Retained	3	3	7	5.1	17	8.5
Sales growth per annum	7.5%		15%		35%	
Risk rating	*		**		***	

*Sources:* 1. UK data.  
2. US Annual Reports.  
3. FDC Pink sheets.

the present far more information is available in American company accounts than in British.

The models are, of necessity, over-simplifications. They assume that the companies operate entirely in one given market, pharmaceuticals. The real world is not so tidy. Cases have occurred where funds for pharmaceutical research have come from sales of quite unrelated consumer products, while the results of research by pharmaceutical companies frequently find important commercial applications in many and diverse fields. The model is also restricted in that it considers only sales revenue as the major source of research and marketing funds and ignores the other conditions which might be found, such as government subventions in the USA or the introduction of new-risk capital. This, however, is not a severe limitation, as sales prospects govern the possibilities of raising and introducing new risk capital.

**THE MODELS DESCRIBED**

Table A shows the flow and the employment of sales revenue for each of these three firms. Figures are given both in absolute values and as a percentage of the total sales revenue. The difference in the volume of sales can be assumed to come entirely from different price levels ruling in the three markets. Price levels faced by firm A, the traditional commodity firm, are those which are set by the normal workings of price competition. The substantially higher price levels per unit for firms B and C reflect the



value of their products and the measure of protection they receive either through patent protection and, in the case of firm C, the virtual uniqueness of its important innovation in its field. The price levels are, of course, trade price levels. If retail and wholesale distribution costs are added, the price differentials to the consumer become proportionately greater.

The factory cost of goods is then deducted for each of the firms and the gross margins shown. The factory costs of production are taken as the same in each of the three firms, as would be appropriate to an industry with largely standardised production techniques and facilities. It may be noted that the residual gross margin of 150 for firm C is three times that in firm A although the sales by value are only twice as high (Model A 100; Model C 200) and the sales by volume are equal.

The deductions from gross profit margins to gain net profits are summarised under two main headings: first, general administration and marketing, and, second, research and development. The selling and administrative expenses are common to all three firms, but rising steeply in absolute terms for the innovating firms. The research and development expenditure is by definition characteristic of the innovating and the super-innovating firm. The figures for these items are the annual cost of a continuing programme of research and development and not the amortisation of previous expenditure.

These two deductions give the pre-tax profits; again because it is a residual calculation, the proportionate differences between the three firms increase. Net profits of the innovating firm are twice as great, and for the super-innovating firm four times as great as the non-innovating firm. The profit appropriation account follows, showing taxation, at Corporation Tax rates of 40 per cent, dividends and the amount retained within the company. Below these accounts are shown firstly the prospective growth rates of the firms per annum in terms of sales and finally some measure of the risk rating. Both these factors are important in appraising the proportion of net profits appropriate to the dividends, which affects prospects of raising new risk capital.

These are the bare bones of the model. They provide a basis on which it is possible to consider and to speculate about the factors affecting individual items of expenditure and the interrelations between them.

#### REVENUE

The sales revenue for each firm is the simple product of quantity sold and price. For the non-innovating firm, operating in a traditional price competitive market, these two factors are directly interrelated. For the innovating firms, it may be assumed that the major innovational products are sheltered from price competition by patent protection. The benefits conferred by modern sophisticated pharmaceuticals are out of proportion

TABLE B  
Pricing of New Prescription Medicines

<i>Product group</i>	<i>Number of new products</i>	<i>% of new products with prices</i>		
		<i>Above mean price of existing products</i>	<i>Below mean price of existing products</i>	<i>Number of new products priced outside price range of existing products</i>
Broad spectrum antibiotics	14	29	71	2
Analgesics	13	46	54	1
Cough preparations	13	37.5	62.5	0
Hormones, corticosteroids, anti-infectives—skin	13	54	46	0
Oral contraceptives*	11	9	81	1
Psychostimulants	9	89	11	0
Ataractics and tranquillisers	8	50	50	0
Haematinics	8	0	100	0
Bronchodilators	8	37.5	62.5	0
Diuretics	7	29	71	0
Anti-diarrhoeals and intestinal absorbents	7	14	86	0

\* Conovid with an exceptionally high price range of existing products.

to their cost and therefore the total volume sold is only tenuously linked to price charged. Thus the dominant and to some extent independent factors determining revenue are firstly the levels at which prices are pitched and secondly the share of the market obtained by the firm.

The scope for freedom of pricing (of charging what the market can bear), as well as the share of the market captured is, however, set by the degree of uniqueness of the product. The major innovational breakthrough into an entirely new therapeutic field has no competitors offering a reasonable substitute and thus can look to dominance of the whole market in that new therapeutic group. For less unique products, and this applies to the majority of new innovations coming from the pharmaceutical industry which have small but worth-while improvement over existing products, the situation is different. Table B shows that for products introduced between 1963 and 1966 the majority were priced to give a treatment cost below the average for others in the same therapeutic group. Practically none were pitched outside the prevailing range of prices. Also, given the existence of comparable substitutes in their therapeutic group, the share of the market a firm can hope to achieve is limited. This clearly is related to a later item of costs, marketing expenditure.



#### FACTORY COSTS

For the traditional non-innovating firm, the factory cost of sales is clearly of considerable importance, proportionate to their total revenue. A 10 per cent saving here makes a substantial difference to the gross profit margin. For the innovating firms it is of proportionately less significance. Reduction in the factory production costs are of importance and a major source of competitive growth for the traditional firm where competitive pressures exist through the price system. It is to be expected that the traditional firm would behave in the traditional fashion. On the other hand these pressures are less important in the innovating and super-innovating organisation.

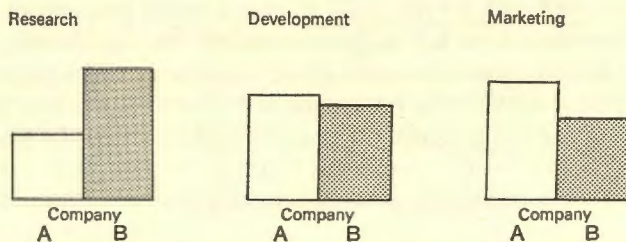
#### MARKETING AND RESEARCH EXPENDITURE

The most interesting relationship, and the one which distinguishes the innovating from the non-innovating firm, concerns the effects of marketing and research expenditure. The marketing budget is important to both the innovating and the super-innovating firm but in different respects. For the innovating firm operating in a therapeutic sub-group or market where close substitutes exist, the marketing effort has a considerable effect on the share of the market captured by the firm, and therefore its total sales revenue. For the super-innovating firm with a major breakthrough in a new therapeutic field, the marketing effort determines the speed at which the product is introduced and the potential market is dominated, and, therefore, the duration of time-lag between investment in research and recoument of returns. The two sets of expenditure, on marketing and on research, therefore, are closely related. Could expenditure, for example, be moved in the direction of research at the expense of marketing? The effect of this could be quite varied. Units sold would be fewer, however good the intrinsic qualities of the product are. Because the number of units sold is smaller, research costs per unit would rise, giving a higher proportion of research expenditure in relation to sales, while promotion costs on the whole would be lower in absolute terms, although in terms of units sold they might in fact be higher.

There are in consequence two general ways in which expenditure on research is encouraged at the expense of promotion. One is that the more original the product, the larger the number of units which can be sold for any given level of promotion, so giving a better return. Also, of course, the larger the number of units produced, the lower the average cost per unit of production and research and development overheads. These are the bonuses from major innovations.

It is possible to speculate further about the interrelationship as suggested in Figure 1. Levels of research, development and marketing expenditure per unit are shown for a major innovation which is unique in a

FIGURE 1  
Possible Alternative Allocation of Research and Marketing Efforts of Two Companies



therapeutic group compared with a new product introduced in competition with existing products. With the major innovation, initial research costs are relatively higher, but marketing costs are lower. With the new product which represents only a marginal advance over existing competing products, the research costs are lower but marketing costs higher. The difference between development costs is not great. The example is purely diagrammatic since it would be difficult to place a precise absolute or relative value on the items: the general orders of difference, however, accord with experience in the industry.

#### LIMITATIONS OF RESEARCH EXPENDITURE

If the pressures in the model encourage concentration on research, are there factors apart from finance limiting the expansion of research expenditure? It has been suggested that the supply of research-trained personnel is a major brake, but so far as pharmaceutical or any science-based industry is international the supply is not limited to one nation. In Britain, with a 'brain drain' to the USA, clearly the indigenous potential is not being fully used. British companies must, therefore, be yielding to competitive pressures from America for the attraction of these personnel, which in turn flows from the competitive ability of American firms generally, and perhaps the higher status of industrial research in the United States.

There are, of course, the general questions of the right size of an operation and how the size of the research effort relates to the size of the firm as a whole. The test of the right size of an operation is not the size of a company, but its ability to get a significant proportion of the world market for its particular special products. If the firm is dealing in a small field a small company is quite appropriate and can handle it, provided that it is something which can be efficiently sold on its own. If the costs of marketing are enormously high per unit because there is only one product, clearly this becomes a limiting factor, or one which tends towards aggregation



and large size units. In pharmaceuticals, where there is a substantial number of specialist markets, there is also obviously scope for a wide range in sizes. If one takes the largest markets used by the general practitioners and a large number of hospital doctors, these are usually served by the larger companies. If one takes relatively smaller specialised fields, such as the products used by the comparatively small number of radiologists, the market size is smaller and the logical or optimum size of the company needed can be correspondingly smaller. The size of the firm is related to the size of the market, increasingly on a world-wide basis. Pharmaceutical innovation is appropriate to a wide variation in the size of research organisations. It differs from some of the major research fields in other industries such as space research or aircraft. A pharmaceutical company can concentrate on a narrow therapeutic field and have reasonable chances of success.

Research expenditure, therefore, depends ultimately on the premium price which can be obtained on the innovated product, while the absolute size and flow of revenue depends on the share of the chosen international market which the firm attains.

#### PROFITABILITY AND SUPPLY OF CAPITAL

The three firms show strikingly different profit levels. As a proportion of sales, the super-innovating firms attain approximately twice the level of the non-innovating firms. The current convention of assessing profitability is to relate it to capital employed. Because of the difficulty of obtaining comparable data and wide variations in definition, it was not possible to include this in the build-up of the model. The difficulties are familiar; the non-innovating firm tends to be long established and the book value of its capital assets low as a consequence of both inflation and depreciation. The super-innovating firm by definition would tend to be recent with new capital equipment. Clearly in considering book values, one is not comparing like with like. However, one might assume that since their factory costs have been taken to be similar, the real capital employed in production would also be uniform. In this case, if it is taken to be equal to the sales of a non-innovating firm, profits in terms of capital employed would be 15 per cent for firm A, 21 per cent for firm B and 32.5 per cent for firm C. However, in practice debtors will be proportionate to the value of sales, and innovating companies have a great deal of capital tied up in their research facilities.

But even given that comparable figures could be obtained, what conclusions could be drawn from them? Real capital employed is an artificial measure when considering the performance of an innovating firm. Such a firm has a substantial capital asset in its research, know-how and in the goodwill attached to its branded products. These are excluded from the

TABLE C  
Taxation: Innovating and Non-innovating Firms

	<i>Firm A</i> <i>Non-innovating</i>		<i>Firm B</i> <i>Innovating</i>		<i>Firm C</i> <i>Super-innovating</i>	
	£	% revenue	£	% revenue	£	% revenue
Sales	100	100	143	100	200	100
Pre-tax profits	15	15	30	21	65	32.5
Corporation tax	6	6	12	8.4	26	13.0
Tax on dividends	2.4	2.4	4.4	3.1	9.1	4.5
Schedule E	1.5	1.5	2.4	1.7	4.0	2.0
Total taxation	9.9	9.9	18.8	13.2	39.1	19.5

Source: Table A.

calculation of real capital employed. Research expenditure is written off annually as a current cost of operation; it is, however, in reality the creation of a capital asset from which the firm eventually expects to benefit. It is therefore highly misleading to judge profitability of innovating firms in terms of real capital employed; the absence of this feature from the model is not of major importance. The current conventions are, in another sense also, inadequate for judging levels of profitability. They need to relate profits to risk borne by the firm. A firm which is devoting a major part of its effort to research is clearly a more risky enterprise than a firm content only to produce goods to satisfy existing and secure markets.

The problems of risk and the hopes for further growth for new discovery raise the question of the supply of risk capital and the relations with shareholders. Industrial innovation is a process which is largely geared to competitive growth and which, therefore, demands, particularly for the smaller firms moving up the innovational scale, a capital flow to support it. A good profit record is essential to obtain most advantageous terms for extra capital. If a firm is growing extremely rapidly, for all practical purposes it is impossible to finance this growth internally from sales revenue. The only way to avoid going to the market is by growing slowly.

#### TAXATION

Profits are inseparable from taxation. Table C abstracts the tax burden of each of the firms, showing not only the Corporation Tax but also the taxation generated by the firms' operations in its payments to employees and to shareholders. The substantially higher absolute and proportionate tax burden borne by the innovating firms is immediately apparent.

The discriminatory effects of this can be seen if the amounts of Schedule E taxation are considered. The super-innovating firms are attempting to attract research personnel in face of world-wide competition for their



services. Firms in Britain are clearly at a disadvantage in this competition because of the more steeply progressive rates of personal taxation in this country on top bracket incomes. In attempting to retain or to attract top class research staff, British firms need to offer comparable net emoluments after tax to those obtained overseas. This means, in effect, a massive contribution by the company directly to the Exchequer. It is strange to reflect that if the non-innovating firm sought to replace its capital equipment it would receive tax concessions and possibly even grants from the national exchequer. The innovating firm wishing to expand its research team and to compete in offering post-tax incomes comparable to those which could be obtained from its international competitors must in effect incur high gross salary costs, most of which are consumed by taxation.

The main point, however, is that given the greater proportionate tax burdens faced by the innovating and super-innovating firm, a disproportionately greater margin would have to be included in the revenues which these firms sought in pricing their new products. This, however, is not generally possible. An additional problem faced by innovating companies is their need to make substantial investments overseas to capture their share of the world market. To do this a premium has often to be paid for the funds.

#### CONCLUSION

Without firm figures and without detailed case studies, discussion of how the factors governing the operations of an innovating firm, and their interrelationships, must remain speculative. The lack of specific information is alarming, but this is slowly being made good. However, compilation of further data and a number of case studies will not provide guidance of what can happen over the full range of different situations and postulates. The general arguments of substitute competition are persuasive and go far towards explaining the characteristics and problems of innovating firms. It is a valuable analysis, particularly in contrast to the former examinations of the industry in terms of simple price competition. However, it is clear that we are far from understanding the ways in which all these factors interrelate and, therefore, far from being in a position where it is possible to stipulate the optimum combination of the various factors. The general problem is becoming clear and the objective, increasing the speed of innovation, is undeniable. The problem appears to be one which is suitable for investigation by a series of computer-based business studies when, using the types of models considered, all the variables may be changed and the results studied. Another factor of major importance, which it has not been possible to include in the models, is the effects of one or more innovation firms on another. Their inter-action clearly influences critical decisions about expenditure on marketing and on

research by individual firms. The effect of these possible interrelations could only be reviewed on a computer based model.

With the National Health Service acting in many ways as a single buyer for its products, the pharmaceutical industry in Britain stands in a special position. To many this may be seen as a severe disadvantage; but clearly, considering the past contribution of the industry to the health of the nation, there is a long term identity of views and interest on the future development of chemotherapy between the industry and the Ministry of Health. Given the growing significance of the industry's exports to the national economy, there is corresponding identity of views with other departments of government. It should be possible to evolve a realistic policy based upon the special needs of innovating firms operating under the discipline of substitute competition. The special position of the pharmaceutical industry in Britain and its principal customer provides the opportunity for the rapid implementation and development of such a policy. This should provide a climate conducive to the long-term growth of all research-based industry in Britain and to the increase in its stature in world markets.



# The Problems of Sales Promotion

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IN STUDYING THE economics of the research-based pharmaceutical industry it is useful to think of its business as being *centred* on the innovation of new medicines. In the traditional industries, such as steelmaking, research is to some extent incidental to the principal task of production. By contrast in a modern research-based industry, such as pharmaceuticals, production can be regarded as subsidiary to the primary task of innovation. This is an overstatement, but it is not all that far from the truth. The corollary is that sales promotion, which has been described as 'the lubricant of change', has a much greater significance for modern medicines than it has for traditional products. Two years ago, during our first series of OHE Winter Lectures, I expounded at some length on this special significance of marketing activities for prescription medicines. It is a measure of the progress which we have made since then that I feel it unnecessary to do so again tonight. I believe that the essential relationship between innovation and sales promotion is now generally accepted; the ghosts of Emerson, with his better mousetrap at the end of the beaten path to 'his house in the heart of the woods', have been largely laid to rest. We can, therefore, move forward to an examination of the very special and very real problems which arise in connection with the marketing of pharmaceuticals.

First, there is the question of whether the total level of sales promotion expenditures on prescription medicines is correct. This presents almost as intractable a problem as the corresponding question about the level of pharmaceutical prices, which Dr Fryers and Mr Lee have just been discussing. Looking at the broad overall pattern of sales promotion expenditure Table A suggests that, taking market costs to include both advertising and the use of representatives, the prescription medicine industry falls well within the range set by other types of manufacturer.\*

\* Industries vary in the extent to which representatives serve a distributive as opposed to a promotional role. However, their total cost has necessarily been included in all cases.

TABLE A  
Marketing Expenditure—Orders of Magnitude

	<i>No. of firms</i>	<i>Expenditure on all forms of promotion and salesforce: per cent of turnover</i>
Household medicines and toiletries	5	26-42
Office machinery and supplies	3	20
Food (1)	n.a.	14-19
PRESCRIPTION MEDICINES	54	13
Mixed group	7	10
Food (2)	14	10
Household supplies	8	9
Light engineering	16	7
Textiles	4	7
Engineering	4	7
Electrical and electronics	n.a.	3-8
Industrial goods	11	4

*Notes:* Prescription medicine figures relate to 1964; others to 1962-64. The 'Mixed Group' was based on returns from seven industries. The two figures given for food result from different surveys.

*Source:* R. Jones; ABPI.

However, in looking at promotion expenditure for prescription medicines it is wrong to regard the whole market as one, in the sense that detergents constitute a single market. Tranquillisers do not compete with cough mixtures, nor do antibiotics compete with diuretics. Each therapeutic sub-market is an entity on its own, and pharmaceutical competition can only be between products with similar therapeutic indications. Thus, when considering the inevitable waste which must occur in all competitive advertising, it cannot be related to the total of £12 million or so spent on pharmaceutical sales promotion. Competition, and hence competitive waste, applies only *within* the individual therapeutic groups. Taking the total expenditures on direct mail, journal advertising and medical representatives, for different types of therapy, it is only for antibiotics that the figure exceeds £1 million. For hormones, for cough and cold preparations and for psychotropics, sales promotion expenditures exceed £500,000. But for each of the other therapeutic groups the total expenditures on these forms of sales promotion account for less than £500,000. In some cases, for example, with special groups where only a small number of doctors are potential prescribers it accounts for only a few tens of thousands of pounds. Looked at in this way, the extent of areas in which potentially 'wasteful competitive advertising' could occur falls into a better perspective.



TABLE B  
Marketing Expenditure for Various Groups

<i>Product group</i>	<i>Total expenditure on medical representatives, direct mail and journal advertising as a percentage of sales to retail pharmacists</i>
Cardiovascular preparations	5.0
Antibiotics	5.1
Psychotropics	6.0
Hormones	6.8
Bronchodilators	7.9
Analgesics	8.9
Diuretics	9.5
Sedatives and hypnotics	9.6
Cough and cold preparations	10.4
Antacids	11.7
Haematinics	13.5
Dermatological preparations	15.7

*Note:* Gynaecological preparations (including oral contraceptives) are excluded because of the proportion sold outside the NHS.

Table B shows the estimated percentage of sales revenue spent on representatives, journal advertising and direct mail for those therapeutic groups where this promotion expenditure exceeds £250,000. In some cases the figures substantially overstate the true percentages of sales spent on promotion. This is because the sales figures are based on those to retail pharmacies only; those to hospitals, which make up a significant proportion of the total for some therapeutic groups, are excluded. Nevertheless, for the four largest groups in terms of sales value, the antibiotics, hormones, the psychotropics and cardiovascular preparations, the sales promotion expenditure never exceeds 7 per cent of the revenue from sales to the retail pharmacists. The higher figure of about 10 per cent for cough and cold preparations results from the fact that their sales promotion expenditure is of the same order as that for hormones, for psychotropics and for cardiovascular preparations, but that their sales value is only about half as great.

This point led me to look at this sales promotion expenditure from another point of view; that is, in terms of the average amount spent on medical representatives, direct mail and journal advertising per prescription written. Table C indicates the expenditures in pence per National Health Service prescription. Once again, the figures are approximations only, and will all tend to overstate the true expenditure per prescription because sales to hospitals are ignored.\* Returning to the cough and cold

\* Because of the data available, it was also necessary to relate 1965-66 promotion expenditures to numbers of prescriptions in 1965. This should have little significance.

## *The Problems of Sales Promotion*

TABLE C  
Cost and Marketing Expenditure

	<i>Average total cost per script in pence</i>	<i>Average promotion expenditure per script in pence*</i>
Sedatives and hypnotics	62	3
Cough and cold preparations	62	5
Antacids	78	8
Haematinics	89	9
Analgesics	104	4
Bronchodilators	140	10
Psychotropics	175	9
Cardiovascular preparations	198	8
Diuretics	205	19
Antibiotics	225	9

*Note:* Hormones and dermatological preparations are excluded because different grouping of products are used in calculating numbers of prescriptions and total promotion expenditures.

\* Promotion expenditure is total cost of representatives, direct mail and journal advertising: numbers of prescriptions are only for those dispensed outside hospital.

preparations, the table shows that fivepence per prescription was spent on sales promotion. Apart from the sedatives and hypnotics and the analgesics, at threepence and fourpence per prescription respectively, this was the lowest expenditure for any group. For the rest, eightpence or more is spent on sales promotion for each prescription written.

Table C also shows the average total cost of prescriptions in each of the groups. It would be expected that there would be some relationship between the cost of prescriptions and the expenditure on sales promotion per prescription: from the commercial point of view, sales promotion expenditure must be restricted for relatively low priced prescriptions. In fact, however, a comparison between the selling price and the marketing expenditure per prescription clearly suggests the influence of other factors as well. These must include the rate and degree of innovation within a therapeutic group, and the complexity of the new treatments. If there are relatively few new products, and their use is relatively straightforward, sales promotion expenditure can be correspondingly limited. This seems to have been the case for sedatives, analgesics and antibiotics. At the other extreme the diuretics have a promotion expenditure of 1s. 7d. per prescription; although proportionately this amounted to less than 10 per cent of the cost of the average prescription. This figure is inflated because hospital sales account for a considerable proportion of the total in their case. There were also substantial innovations involving relatively complex therapy, which in turn explain the high average cost of prescriptions in this group. There is certainly evidence in general that sales promotion expenditure is concentrated more on new than on established products.



**FIGURE 1**  
**Promotional Expenditure Per Product Promoted by Age of Product**

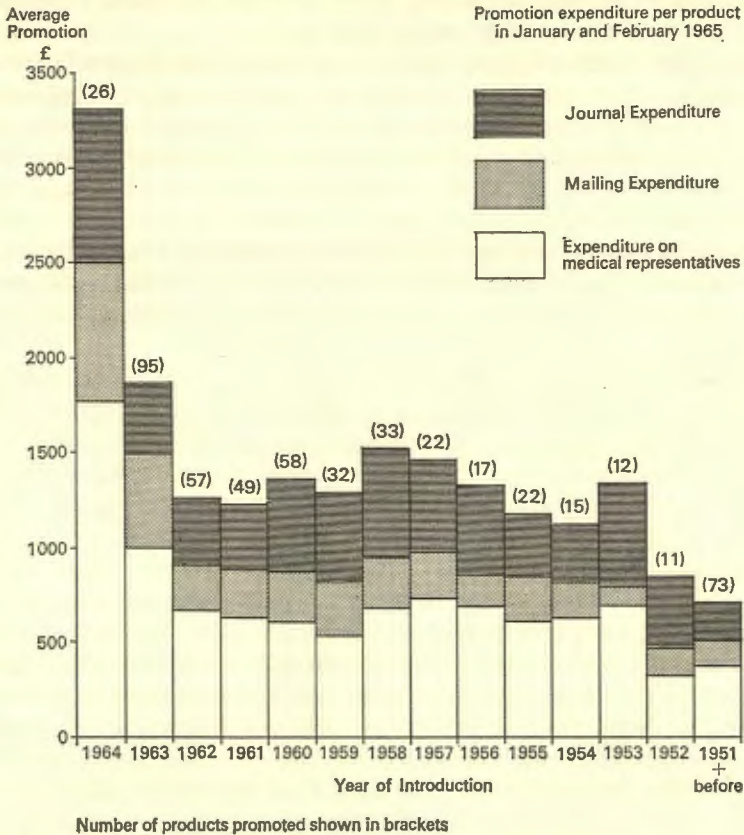


Figure 1 shows the extent of concentration on new products: it understates the position because it excludes the many old products which are not promoted at all. It should eventually be possible to study in more detail the way in which the rate of innovation in a therapeutic group affects the level of promotion expenditure.

However, these facts and figures in isolation do not answer the question of how an appropriate level of sales promotion expenditure should be decided for a particular product. This question often tends to be approached emotionally. The result is that sales managers frequently believe that too little is spent, while the over-burdened doctors and hostile politicians protest vigorously about excesses. A more logical approach is possible, which both has a sound commercial basis and is essentially in the public interest. Quite simply, sales promotion expenditure is only

justified for prescription medicines—as with other products—if it is a sound commercial investment. In other words, the cash spent on advertising must bring back a suitable return in terms of added profit and contribution to overheads including research.

This added profit and contribution must be computed in terms of what is earned by the product *as a result of the sales promotion*, disregarding what it would have earned anyway even if it had received no promotion. For a new product such a calculation is easy. Without sales promotion there will be virtually no sales and no contribution. In this case, all the eventual earnings of the product can be regarded as a consequence of the promotional expenditure. For an established medicine, the calculation is more difficult because some fairly sweeping assumption has to be made about the level of sales which would be maintained without reminder advertising.

This is difficult, but not impossible. However, a further discussion of the techniques of assessing the return from promotional expenditure on different medicines belongs to the field of management rather than economics. It is sufficient here to emphasise that, despite the difficulties, a realistic attempt can be made to assess the commercial return from expenditure on advertising, or the use of a costly medical representative force, to promote a particular product.

If this is the situation, is it really in the public interest? Does it not stimulate excessive and wasteful advertising? There are three further considerations which must be taken into account in answering these questions. First, if advertising for older products is assessed in this way it is often found to be commercially unsound. Even quite a modest expenditure on sales promotion may prove to be greater than is justified by a realistic appraisal of its effect on sales. Thus, this commercial approach militates against the promotion of older and less effective preparations. Second, this approach encourages the management to look also at the effectiveness of advertising expenditure. If a poor commercial return is being obtained, it may be simply because the advertising is bad. Ineffective sales promotion is wasteful and undesirable from every point of view, and anything which brings it under scrutiny is in the public interest.

The third consideration is the most crucial. Naturally for any product a higher price results in a greater profit and contribution to overheads per unit sold. Thus, on my commercial criterion, a higher unit price would automatically justify a greater promotion expenditure. This situation appears to support the critics who claim that unrestricted competition based on innovation (as opposed to price competition) militates in favour of a policy of pricing high in order to provide greater margins to finance sales promotion. In the absence of true price competition, new products might be expected to be introduced at premium prices to provide money



for heavy advertising campaigns; in turn the price of existing preparations would tend to escalate to allow their advertising to be increased correspondingly.

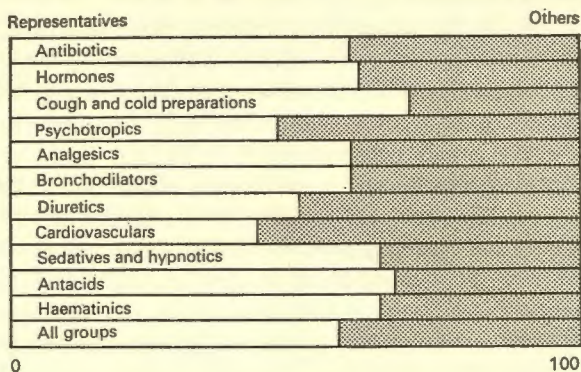
However, this prediction appears to be the reverse of the truth, probably because it confuses the absence of classical price competition with a complete freedom on initial price setting. The paper by Fryers and Lee has quoted evidence that new products in an existing therapeutic category are introduced more often below the average price for competing therapies than above it. Thus new products tend to be introduced at depressed rather than at premium prices. In addition, Cooper, in his book on the industry, showed that between December 1959 and October 1965 twenty-two of the thirty-four leading products fell in price, whereas only three increased in price. The introduction of new products at below average prices, as well as other political and commercial pressures, tend to bring down the price levels of existing products. This overall picture is, therefore, the opposite of that predicted. The factors underlying this pattern of pricing are at present being investigated by economists at the University of Exeter and elsewhere. Perhaps, in part, they result from fears that the opposite pricing policy would attract professional and political accusations of profiteering. Certainly, it appears that in practice the pricing policies in the industry do tend to impose limits on the margins available for sales promotion expenditure.

More important, these limits appear to operate in a direction which should be in the public interest. For a new product in an entirely new therapeutic field—that is, a new treatment for a previously untreatable disease—there is no framework of existing competitive prices. A company with such a product can, therefore, price its product with reference only to its own commercial objectives. It can allow margins which not only contribute substantially to the research overhead, but also provide for what the company considers to be the optimum sales promotion expenditure. This should result in the existence of the entirely new treatment being made widely known in the shortest possible time. To some extent the same might be true of a major therapeutic advance in any field, which will often be prescribed irrespective of its cost.

However, in general, the evidence has suggested that new products introduced to compete with existing treatments are marketed at lower than average prices. Possibly, apart from the political pressures, this also reflects a management decision that such a product should have a 'price advantage' as well as whatever therapeutic advantages it may have over its competitors. If this motive does enter into pricing decisions, it should particularly tend to limit the amount which could justifiably be spent on promoting minor therapeutic advances. In addition, the downward trend of prices for established products tends to reduce the amount which it is

FIGURE 2

Expenditure on Medical Representatives; Rank Order of Therapeutic Groups and Percentage of Total Promotion Expenditure (as defined)



commercially justifiable to spend on their continued promotion. None of these facts prove that prices or levels of expenditure on sales promotions are correct; but they do suggest that the patterns of pricing and the consequent pressures on the sales promotion expenditure should operate in a direction which is in the public interest. It is possible to spend heavily on promoting the sales of radically new treatments. However, a commercial approach to the subject coupled with the companies' pricing policies must make it more difficult to do so for products which compete with existing therapies.

So much for the general levels of sales promotion expenditure. The second question concerns how effectively the money is spent. This is an even more difficult question than the first; all I can do is to list some of the questions which should be asked, and describe some of the measures already taken to eliminate wasteful promotion practices.

Figure 2 sets out in rank order the eleven therapeutic groups accounting for the greatest use of representatives' time. Antibiotics take up most of their time, and haematinics least. It also shows the proportion of the *total* promotion expenditure (that is, on medical representatives, direct mail, and journal advertising) which is accounted for by the representatives. The proportions are surprisingly similar. From the figures, representatives do not appear to play a significantly larger part in promoting newer and more complex therapies than they do for simpler remedies. However, more than anything this probably reflects a weakness in the data. The representative costs are estimated from 'diaries' kept by a



sample of general practitioners. They record all products discussed, whether it is a cough mixture, which may be mentioned in passing, or a new antibiotic, which may be discussed at length. Thus on a more valid assessment of the use of representatives' time, the simpler products would probably get a much smaller share of representatives' effort. Only individual company records could give a more meaningful indication of the real pattern of their work.

As far as direct mail is concerned, it is often criticised for its volume and its consequent failure to attract the attention of its recipients. How could it be made more selective, and consequently more efficient? Will we come to see a time when the present 'broadcast mailings' are replaced by very much more selective approaches to small groups of doctors most likely to welcome information on the particular product?

Turning to the journals, how much are the advertisements themselves read? How do the new controlled circulation medical newspapers compare in effectiveness with the traditional journals? How does expenditure on the three media, representatives, mail and journal advertising compare in the return it brings? These are not new questions, but they have never been adequately answered. We accept the need for controlled experiments to evaluate the efficiency of new medicines. On a smaller scale, such experiments are also needed to find how proven therapeutic advances can best be promoted. As an aside, this is not a problem which applies only to pharmaceuticals. It would certainly be advantageous if some effective way could be found to promote efficiency in practice organisation, for example, in stimulating group practice and the adoption of appointing systems. The only difference is that all too often in these 'non-clinical' matters it is not even accepted that their efficacy must be proved before introduction.

Returning to pharmaceutical promotion, some progress has already been made. Carefully controlled readership surveys of the advertising in different journals has been carried out. This should help to eliminate waste. The Association of the British Pharmaceutical Industry publicise how easily doctors can receive only selective mailings or can have their names removed from mailing lists altogether. We hear talk at present about 'restricting the numbers of mailings' in the sense that all doctors would receive fewer. Perhaps what, in fact, should happen is that limitation in the total volume of mailing should come about by a proportion of doctors having their names removed from or placed on restricted mailing lists. They are always free to do this; and if in fact they are not opening mailings at present they obviously benefit everyone by stopping them from coming.

Last year the industry spent over £100 per medical representative on their training. This is an average covering the initial training of new

recruits and refresher training of their present staff. Some companies, probably because they cost their training programme more fully to include the salaries and overheads of all who participate in courses, estimate their expenditure on training to be nearer £500 per representative per year. This should presumably make them more competent and more effective in discussing complex therapies. The Association of the British Pharmaceutical Industry together with the recently founded British Medical Representatives' Association are taking active steps to ensure that the best standards of qualification and training of representatives are applied universally. On this last point, Britain is setting an example to the rest of the world in the measures it is proposing to establish minimum standards of representation.

However, one thing is certain. The problems of pharmaceutical sales promotion, whose proper conduct is essential to pharmaceutical progress, cannot be regarded on a purely national basis. It is an international problem applying to the whole of the technologically advanced world, and increasingly to the developing countries also. The results of research in one country has to be made known throughout the world. The British pharmaceutical industry spends the same proportion of sales on promotion overseas as it does in Britain. The problem is how to ensure as economically as possible that doctors are rapidly aware of pharmaceutical advances, can understand and appreciate their implications, and can be persuaded to use them in appropriate cases. British companies' success in this respect overseas is one of the keys to our pharmaceutical exports, and the contribution which our pharmaceutical innovations make to our balance of payments.

Just how difficult it can be to ensure that new products are properly understood and used has already been illustrated by the case of the anti-depressives. Depression as a clinical entity was something which few doctors had been taught to recognise because no therapy was previously available for it. Once a treatment became available, it almost became necessary to persuade doctors of the existence of the disease as well as the treatment. Long after the anti-depressives were available, doctors were still treating cases of depression with tranquillisers.

At the same time as powerful persuasion is needed to encourage the adoption of new therapies, care must be taken to avoid over-optimism about them. This is sometimes particularly difficult, for the medical profession, at least as much as the manufacturers, may be unjustifiably enthusiastic about the prospects for some new treatment. However, at any rate with pharmaceuticals, the principle of carefully controlled evaluation before general introduction is now well established. There is certainly no question of short-cuts over safety testing. In addition, despite the sceptical views sometimes expressed by pharmacologists, the practitioners must



surely be becoming more objective towards their own prescribing under the critical pressures which are continually being applied to them.

There is no doubt that we will see improvements in pharmaceutical promotion in the future. To a great extent the industry, up to the present, has borrowed marketing techniques from others and used them sometimes undiscerningly. Now the need for promotion in science-based industry has been accepted, in the same way as it was earlier recognised for consumer products. The challenge is to find particularly appropriate techniques for particular industries and to ensure that existing methods are used efficiently. It is towards this, rather than general restrictive methods of control, that both the pharmaceutical industry and those outside it should be looking.

As a tailpiece I cannot resist one fact. From April, the Ministry of Health is sending regular prescribing advice to all general practitioners in a colourful and glossy publication called *Proplist*. The entry of the Ministry into this field may not make glossy mailings any more popular or more effective, but at least they should become more respectable than they have been in the past!

# The International Pattern of Finance

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IN THIS PAPER I shall examine some of the reasons for the 'international' nature of the pharmaceutical industry, and the implications of this important characteristic, for the individual firm, for the national economy, and for the balance of payments. I shall be concerned primarily with the British industry including firms which operate in the United Kingdom, whether they are British or foreign-owned, and the overseas operations of British-owned companies, although this should not exclude some consideration of problems of the pharmaceutical industry in other countries. Very little has in fact been published on the international pattern of finance of the pharmaceutical industry; this paper is therefore largely the result of a gathering together of pieces of information, many of which have come from personal discussion with those in the pharmaceutical industry. A substantial amount of the basic data has been culled from semi-confidential sources. The result tends to be something of a patchwork of objective fact and subjective judgement—but a patchwork which it is hoped might form the basis for an informed discussion and perhaps provide a springboard for more intensive research by persons better qualified for this task than the present writer.\*

## WHY A SPECIAL PROBLEM?

The British pharmaceutical industry has for many years had a strong international flavour. As long ago as 1908 and 1919, the Swiss giants Roche and CIBA respectively, had established themselves in the United Kingdom. Sandoz followed in 1921. With exceptions such as Parke Davis, the American firms appeared somewhat later; but by 1940, Merck, Sharp and Dohme, Lilly and Warner had also become established. Most

\* It would be invidious to single out particular persons from the many who have helped me in the preparation of this paper. I should, however, like to express a debt of gratitude to Mr George Teeling-Smith of the Office of Health Economics and to Mr Robert H. Jones of the Association of the British Pharmaceutical Industry for the considerable help they have given me.



TABLE A

International Ownership in the UK Pharmaceutical Industry ABPI Division  
'B' Members, December 1966

<i>Nationality of Company</i>	<i>No. of firms</i>	<i>Per cent</i>	<i>Market share, 1964*</i>
UK	31	41	27
USA	25	33	53
Swiss	5	7	12
French	5	7	5
German	4	5	2
Netherlands	2	3	1
Swedish	1	1	
Danish	1	1	
Italian	1	1	
	75	100	100

\* Share of Prescription medicine sales. Exports are excluded.

Source: ABPI.

of these firms started as manufacturers of chemical products. Although they had been engaged in making pharmaceuticals for a number of years, the great surge forward in the pharmaceutical sector came during and after the Second World War. Today, of the sixty or so member firms of the Association of the British Pharmaceutical Industry Division B,\* which consists of firms manufacturing medical and dental speciality products, only thirty-one are British-owned. Table A also shows that United States-owned firms supply more than half the total of prescription medicine sales in the United Kingdom. Swiss firms are less numerous, but the five† firms which are members of the ABPI together account for 12 per cent of total prescription sales.

The international nature of the pharmaceutical industry has a two-way aspect—not only do many overseas-owned companies operate actively in the United Kingdom, but a very large number of British pharmaceutical firms have built up extensive interests overseas. In the case of some companies these overseas activities are almost as important as those they conduct in the home country. To take but one example, in the financial year 1965–66<sup>1</sup> the UK-owned Beecham Group attributed to overseas sales

\* It has been estimated that the members of the Association account for some 95 per cent of the total sales by the industry to the National Health Service. The only really large concern operating in the United Kingdom which is not a member of the Association of the British Pharmaceutical Industry is ICI Pharmaceuticals Division.

† These are CIBA Laboratories Ltd., Geigy (UK) Pharmaceuticals Division, Roche Products Ltd., Sandoz Products Ltd., and A. Wander Ltd.

1. Beecham Group, *Annual Report Year ended 31st March, 1966*.

no less than £11.9 million or 47 per cent total sales of pharmaceutical products. It has been estimated by the ABPI that overseas subsidiaries of British companies in 1963 remitted (after paying overseas taxes) to the UK no less than £6.1 million.\*

The reasons for the international nature of the industry are manifold. Historical accident played some part in the early establishment of the industry in Britain by Swiss and other companies. These firms, which originally engaged in chemical manufacture, found their domestic markets wholly inadequate for the size to which economic factors were forcing them to grow, even at this early stage in their development. CIBA, for example, entered the pharmaceutical field at the end of the nineteenth century with the introduction of the antiseptic *vioform*. It was to be expected that with the development of such products, wider markets should be sought, particularly in Britain where, at the turn of the century, medical science was relatively highly developed.

Even today the main justification for the extent of overseas expansion is to be found in the importance for the pharmaceutical industry of market size. The degree of concentration in the industry is relatively high. According to the 1958 Census of Production, one quarter of the total output of the British pharmaceutical preparation industry was produced by twelve firms, each with over 1500 employees. Firms employing between 100 and 1500 employees accounted for another 60 per cent of output. Thus over 85 per cent of the total output was concentrated in firms (of which there were altogether 112) employing at least 100 people. Although many small firms marketing rather specialised products continue to make satisfactory profits, the greater part of the industry requires a larger market for the reaping of adequate economies of scale, and this market cannot always be achieved within the United Kingdom alone. The United Kingdom accounts for less than one fifteenth of the world market for pharmaceuticals—as against one half accounted for by the United States.

In theory, economies of scale might be reaped equally well—perhaps better—by means of exporting rather than by the setting up abroad of subsidiaries and branches. In practice, however, not only do Governments of most countries encourage the establishment and growth of domestic pharmaceutical industries by means of tariffs and (more important) by direct trade controls; they frequently impose health control requirements of varying complexity which seriously increase the difficulties of exporting bread-and-butter products. This is particularly true of France where since the war registration of all drugs has been rigidly enforced, often in such a

\* Estimates based upon questionnaire issued to all members by the ABPI and the Proprietary Association of Great Britain. Satisfactory replies were received from nearly three quarters of the Associations' members. The results of the questionnaire have been embodied in a hitherto unpublished Paper *International Balance of Payments of the Pharmaceutical Industry*, by Michael Lee and Robert H. Jones.



way as to discourage imports. The Governments of developing countries have been particularly anxious to foster home production of pharmaceuticals, in many cases by the grant of a production licence to a foreign firm which was prepared to establish local manufacture behind a wall of almost prohibitive import restrictions.

In the pharmaceutical industry, research and development expenditure account for a high proportion of annual costs. It has been suggested that throughout the world research expenditure amounted in 1964 to over £150 million a year;<sup>2</sup> about £10.4 million of this took place within the United Kingdom, and about £100 million in the United States. Research in the United Kingdom accounts for about 11.5 per cent of the value of total sales of the industry to the National Health Service. It is estimated that in the United Kingdom about one fifth of research expenditure is devoted to fundamental research, as distinct from applied research.<sup>3</sup> About 10 per cent of all employees in the manufacture of prescription drugs are engaged on research, which in 1959 was estimated to be the highest proportion in any British industry.<sup>4</sup>

The relatively high expenditure on research is itself a justification for large scale production. Only if output is large—and this often necessitates a world market—can such expenditures be maintained without placing a heavy burden on unit costs. Thus the sheer size of the research effort required of the modern pharmaceutical industry is an important driving force in sales expansion. In a very real sense, the Research Director can only do his job properly if the Overseas Director and his staff provide him with a sufficiently large market to justify his calls upon the firm's financial and manpower resources.

Although research expenditures are regarded as a current expenditure item, once embarked upon they become a fixed charge on the firm's financial commitments and are not at all easy to curtail.\* Moreover, research tends to be cumulative and more expensive as the frontiers of knowledge advance. Only rapidly growing sales can enable the additional burden of such expenditures to be spread over a greater output.

The significance of research expenditure is relevant to the finance of firms as well as to the size of their sales. Research commitment adds a continuous and increasing financial burden on firms. This burden is in

2. Association of the British Pharmaceutical Industry, *Annual Report 1965-66*.

3. MICHAEL H. COOPER, *Prices and Profits in the Pharmaceutical Industry*, Pergamon Press, Oxford, 1966, p. 169.

4. Federation of British Industry (now the CBI), *Research in Manufacturing Industry*, 1959.

\* In his book, Michael Cooper tells the sad story of a nameless British firm which used to be among the leading British companies, but gave up work on glyceryl ethers, only to lose one of its research scientists to the United States, where a small company made use of his know-how to develop a famous anti-anxiety product! See p. 175.

TABLE B  
Sales of Domestic Output £ million

	<i>NHS</i>	<i>Exports</i>	<i>Household Medicines</i>	<i>Other</i>	<i>Total</i>
1963	79.2	54.0	36.1	29.9	199.2
1964	83.6	59.4	35.7	40.1	218.8
1965	97.6	66.6	42.0	44.5	250.7

Source: ABPI.

some ways more akin to a steady increase in debenture obligations than to an increase in current expenditure. The gestation period for research investment in the industry could well be as long as seven or eight years. During that period substantial sums are tied up in purchase of materials, equipment, salaries and training. There is also a considerable element of goodwill in most branded specialities; this goodwill may—like the research expenditure we have discussed—be regarded as a part of the firm's capital.\*

Now if research expenditure may be regarded as part of a firm's capital, a high level of financial plough-back is necessary in order to maintain momentum in development. Plough-back of this magnitude is more readily achieved if the firm is operating in the world market than if its activities are confined to one country. This is even more true of British-owned than American-owned firms. There can be little doubt that if British companies had not been operating on a world-wide scale, they would have been unable to finance out of profits the heavy research and development expenditure necessary for them to achieve maximum growth.

In the light of these considerations on the reasons for the international nature of the pharmaceutical industry we shall examine in a little more detail the implications of this fact, firstly for companies operating in the UK, and secondly for UK-owned firms operating overseas.

#### INVESTMENT IN BRITAIN

Table B shows the distribution of the British pharmaceutical industry's £250 million output among the National Health Service, Exports, and Household Medicines for recent years. In 1965, the National Health Service accounted for nearly two fifths of the sales of home-produced medicines. Imports of finished pharmaceutical preparations were about £10 million—less than one sixth of the value of exports.

\* Some idea of the importance of trade marks and goodwill in the pharmaceutical industry may be obtained by the fact that for the Aspro-Nicholas Group in 1965, trade marks and goodwill were valued at £5.9 million, while fixed assets were valued at £3.6 million. See Aspro-Nicholas Ltd., *Thirtieth Annual Report and Statement of Accounts* 1964-65. For the Beecham Group Ltd., fixed assets and trade investments were valued at £17.5 million while goodwill was valued at £18 million.



TABLE C

Foreign-owned Companies in the UK Growth in Value of Fixed Assets  
£000

	1955	1959	1963
Net fixed assets	7745	24,095	40,382
Depreciation	4310	7866	14,971
Gross fixed assets	12,055	31,961	55,353
Number of firms	25	31	34

Source: ABPI.

TABLE D

Size and Ownership of Foreign-owned Companies in the UK 1963

GF assets* £'000	US firms		Swiss firms		Other firms		Total	
	No.	Total	No.	Total	No.	Total	No.	Total
		GEA		GEA		GEA		GEA
0-50	4	35	0	—	3	85	7	120
51-100	1	84	0	—	2	155	3	239
101-500	3	766	0	—	3	864	6	1630
501-1000	4	3491	0	—	0	—	4	3491
1001-2000	3	4902	1	1107	0	—	4	6009
2001-3000	4	9487	1	2911	0	—	5	12,398
over 3000	2	13,035	3	18,431	0	—	5	31,466
Total	21	31,800	5	22,449	8	1104	34	55,353

\* Gross Fixed Assets.

Source: ABPI.

According to ABPI sources, the foreign-owned stake in the UK pharmaceutical industry in 1963 was over £55 million.\* Tables C and D show the growth of this stake, and its breakdown according to size and rationability of firm. Table D shows that nearly 60 per cent of the foreign-owned stake in the British pharmaceutical industry is in companies with gross fixed assets of over £3 million; this share is accounted for by only five companies, three of which are Swiss-owned, and two of which are US-owned. Less than 10 per cent of the total value of gross fixed assets is accounted for by foreign-owned firms with gross fixed assets of less than £1 million.†

\* This amount which is gross, is made up of a net value of fixed assets, in 1963 of £40,382,000 with a depreciation figure of £14,971,000.

† These estimates should be treated with reserve, in that many of the companies produce goods other than pharmaceuticals. But the firms concerned are primarily engaged in making pharmaceuticals.

What does the United Kingdom industry and economy gain from the presence of such foreign-owned and foreign-controlled giants in their midst?

So far as the pharmaceutical industry is concerned, there are undoubtedly external economies which arise from the operations of United States, Swiss and French Companies in the United Kingdom. As we have noted, the foreign firms are generally large ones; they are usually in the forefront of research and business methods. Almost certainly, too, there is an important 'overspill' effect which is advantageous to the British-owned sector of the industry. If there were no foreign-owned firms operating in Great Britain, the overall size of the pharmaceutical industry would undoubtedly be smaller, and a number of economies which are external to the individual firm would no longer exist. Let me say here that I am far from suggesting that British-owned firms in the industry are relatively inefficient, but there can be few who would deny that British firms learn much in regard to efficiency, organisation and, above all, research and development, from being in close proximity to American and Continental firms, whether operating in this country or elsewhere.

As regards research, the presence in Britain of foreign companies employing scientists with world-wide experience and contacts must have important consequences for the whole British industry. Since fruitful research depends essentially upon the regular meeting together of minds which are engaged upon solving interrelated problems, the pharmaceutical industry above all others simply cannot afford to be parochial in its outlook. Many of the gains from the international nature of the industry overflow from the industry to the British economy. It is an enormous advantage to the economy as a whole that an industry, which must inevitably be a growth-point in the years ahead, should be able to draw upon world-wide resources in the provision of skill, capital, and ideas. Neither should it be overlooked that many of the foreign-owned companies which have established themselves or expanded in recent years are in parts of the United Kingdom where there is relative under-employment. Abbotts, at Sheppey, Pfizer at Richborough and Winthrop on Tyneside are cases in point. Thus the influx of foreign-owned companies has an important influence upon the growth of the economy.

The establishment of American and Continental firms has had an effect upon the British balance of payments. There is no means of measuring the inflow of capital resulting from the operations of foreign companies in the United Kingdom—but Lee and Jones have estimated that in the year 1963, what they describe as 'subventions and financial transfers' from foreign parent companies to their subsidiaries in the United Kingdom amounted to about £2.3 million. Although such companies send abroad much more than this—Lee and Jones suggest a figure of £6 million—it would be a



TABLE E  
Remission of Profits by Foreign-owned Pharmaceutical Companies in  
the UK 1964

<i>Ownership</i>	<i>No. of firms in survey</i>	<i>No. paying dividends</i>	<i>Profits remitted as % of total*</i>	<i>Profits remitted excl. shares as % of total†</i>
USA	19	14	48.8	41.5
Swiss	5	5	38.2	(38.2)
Other	7	4	53.1	5.2
All firms	31	23	48.0	40.5

\* As total of unappropriated profit.

† This column excludes share transfers to the parent company which involve no case transmission.

Source: ABPI

mistake to overlook the 'inflow' element which is of course a credit item on the UK balance of payments. In general, however, the foreign-owned companies do not normally finance development in the UK by the transfer of funds from their home countries, so much as by the ploughing back of profits made in the United Kingdom. Indeed as regards United States companies in recent years, US Department of Commerce 'guidelines' have made it virtually impossible for them to raise additional funds in the United States for the finance of overseas development.

United States companies have recently tended to borrow locally in order to finance expansion in a particular country, rather than raise funds in the US or in third countries. Short-term positions are often covered by obtaining bank overdrafts, increasingly in the countries where development is to take place. A number of expansion schemes on the Continent have been financed on the Euro-dollar market, where borrowing rates have been slightly lower than the sterling rate in London. But there is no doubt that in general, expansion in Britain by US and other firms has been financed by the ploughing back of profits made in this country.

Table E shows the results of a recent ABPI survey on the treatment of profits by overseas-owned pharmaceutical companies operating in the United Kingdom. It is clear from that table that the greater part of the profits made by foreign-owned companies is left in the UK.

The practice of United States and Swiss companies is to remit to the US rather less than half the profits made in the UK. According to Lee and Jones the outflow of funds from the UK in respect of remittances to all foreign parent companies amounted in 1963 to about £5 million—a quarter of total profits. About half these profits were paid to the UK Government in taxes, leaving rather less than a quarter for retention by the companies in the United Kingdom.

A substantial part of the total retained in the UK is devoted to research and development expenditures. In 1964, the research expenditure of foreign-owned firms in the UK was estimated at £3.4 million—about a third of the total for all research expenditure by the industry in Great Britain. Thus so far from this part of the profits made by foreign companies being a strain on the UK balance of payments, it can be looked upon as one of the sinews of British economic growth.

Foreign-owned firms also contribute quite substantially to British exports—a figure of £21 million has been suggested for 1963. It cannot, of course, be argued that none of these exports would have taken place if the pharmaceutical industry were entirely British owned. But there can be little doubt that exports would have been smaller had it not been for the existence in the United Kingdom of the international companies.

Lee and Jones have estimated that taking into account imports, exports, royalty payments, and the remission of profits and capital transfers, the foreign-owned companies have had a virtually neutral effect on the UK balance of payments. Total outgoings are just about equal to total receipts. It is not possible here to examine the results of the researches of Lee and Jones, but if their estimates are reasonably reliable it seems that the balance of payments has neither gained nor lost as the result of the establishment of the international pharmaceutical companies within our shores. The real significance of the existence of these companies can only be appreciated by a consideration of the alternative position—suppose the British authorities had out-de-Gaulled the General and had forbidden the establishment of any foreign-owned company on British soil? The evidence we have is that the British pharmaceutical industry and economy would be worse off than is the case today; there is little to suggest that the balance of payments would be healthier than it is.

#### BRITISH COMPANIES ABROAD

What can be said about the finance of British companies abroad? How do their operations impinge upon the British economy and the balance of payments?

In the introductory section to this Paper we noted the importance of the overseas activities of British companies. By enlarging the market (and often the establishment of overseas manufacture is the only way of expanding or even maintaining a market), direct investment abroad enables the high costs of capital depreciation and of research and development to be spread over a wider output, thus substantially reducing unit costs and prices. In the past this expansion was financed either by the ploughing back of profits or by the remittance of funds from the United Kingdom. Even before the restrictions of 1964–66, the former seems to have been a more significant source of finance than the latter. Lee and



Jones put a net figure of just under £1 million for the outflow from the UK in respect of subventions and financial transfers between the UK companies and their overseas subsidiaries and branches.

Subsidiaries of British companies appear to remit to the United Kingdom a rather higher proportion of their total profits than do foreign-owned companies in Britain. With the general tightening of Treasury control, the British authorities now reinforce this tendency by insisting upon what they regard as a 'reasonable' rate of profit remission to the home country—a fact which sometimes leads to difficulties with foreign Governments who are equally insistent that remittances should be kept down to their particular concept of what is a 'reasonable' level.

In general, overseas subsidiaries of British firms are reluctant to accept local ownership of share capital; this applies also to foreign-owned companies operating in the United Kingdom. There is the difficulty of determining price and output policies if local interests are strongly represented in a subsidiary company. The starting of new processes or the discontinuance of old ones, would be likely to set up serious strains and stresses in local companies, some Directors of which would have a vested interest in the expansion in their own areas, perhaps to the detriment of the wider interest of the Group. In some countries, notably Pakistan and Ceylon, the authorities have insisted on a fixed proportion of share capital (usually of the order of 15 per cent) being held by local interests, but in general the ownership of share capital is kept firmly in British hands. On the other hand, overseas subsidiaries of British companies welcome local participation in the holding of loan capital. Indeed, the fact that once established in an overseas country, a British firm has access to local loan capital is one of the less frequently discussed favourable side-effects of the whole exercise. Thus the establishment overseas by British companies gives them wider access to capital and a broader field of activities than they would otherwise enjoy.

Now that British companies operating in most overseas countries have been virtually forbidden to transfer capital from their UK resources, they must have recourse either to the more intensive ploughing back of profits or to the raising of local loan capital. We have noted that a diminution of dividend remittances to the UK would be frowned upon by the British authorities, but there can be little doubt that if present restrictions persist, overseas companies will be under constant pressure to squeeze remittances to their parent companies, in order to finance local development. It is possible that an astute Finance Director might obtain additional local finance by the extension of more generous credit and payment terms by the parent company to the subsidiary in respect of goods and services supplied, but Her Majesty's officials at the Treasury can be relied upon to prevent too frequent a recourse to this technique!

In the recent past many British-owned companies have used the Euro-dollar market for the finance of their subsidiaries in Western Europe. Euro-dollars are simply dollar deposits in banks outside the United States. Since the later nineteen-fifties the market has provided a ready source of short-term finance, and it has been used increasingly by British companies requiring finance for local development.\*

What is the overall effect of direct investment overseas by British companies on the UK balance of payments?

The outflow of funds to finance development has clearly been a strain on the balance of payments, but there is evidence that the strain has been a short-term rather than a long-term one. We have noted that a relatively high proportion of overseas profits made by subsidiaries of UK companies are remitted to the UK.

As for effects upon exports, the existence of the UK-owned company often ensures the continuance of supply of exports of semi-processed goods from the UK, although in aggregate it almost certainly *reduces* the overall level of exports from the UK. But even in the absence of direct investment it is by no means certain that the export level would be any higher. Particularly in the developing countries, the refusal of the United Kingdom companies to set up branches and subsidiaries would simply open the way to American or Continental companies and the consequent fall in British exports might be even greater. Virtually all the evidence points to the fact that for British industry in general, the after-tax return on capital is higher in subsidiaries abroad than it is for the parent companies in the United Kingdom. In part, of course, this is because few British companies (with the notable exception of Burroughs Wellcome) conduct large-scale research activities in their overseas subsidiaries. But these overseas profits provide a valuable additional source of revenue to the companies—and it is from these revenues that home research and development are in part financed. Neither should it be overlooked that the British Government tax revenue benefits substantially from the inflow of these profits.

Suppose that no further expansion overseas were permitted to British companies. Would the domestic pharmaceutical industry and the economy as a whole benefit from this standstill? As regards the firms which make up the pharmaceutical industry, the answer must presumably be in the negative; otherwise the scale of overseas expansion would have been less than it has in fact been over the last few years. It is doubtful whether a ban on direct investment overseas would have encouraged the domestic growth of the industry. Few firms, if any, have limited their domestic growth rates in order to finance overseas expansion. Indeed, the situation in the very recent past has been that some firms have possessed substantial

\* The origins and development of the Euro-dollar market are described in the Bank of England *Quarterly Bulletin*, June 1964, p. 102 ff.



liquid funds in the UK but as the result of Government policy have been forced to raise finance abroad, often at disadvantageous rates, in order to carry out overseas investment projects.

I do not think that it would be fair-minded to suggest that one can draw too firm a conclusion from a paper of this nature, which has been based upon a very limited amount of research carried out over a relatively short period. Much work clearly needs to be done. But there seems at least a strong possibility that the pharmaceutical industry and the British economy have reaped substantial gains from the international nature of the industry. Indeed, if the British economy is to be driven forward with real dynamism into the last quarter of the twentieth century, spearhead industries like pharmaceuticals must play a leading part in the advance. These industries can only perform such a role if they break the narrow confines of national boundaries and become truly international. Government policy which restricts this expansion can result ultimately only in economic 'little-Englandism'. Let us hope that in this field as in others the authorities will not be allowed to kill geese that lay golden eggs.

# State Support for Research

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## INTRODUCTION

IT IS NECESSARY for me to remind you that although the subject of my contribution is State Support for Research the main title for the series is 'Innovation and the Balance of Payments: The Experience in the Pharmaceutical Industry'. We are therefore to consider Government support of research in the area of medicine in this particular context.

This clarification of the subject matter of my contribution will I hope indicate more clearly than might otherwise be the case, why I was asked to speak on this topic. I am talking to you this evening primarily against the experience I have acquired over the last few years as a member of the staff of the National Research Development Corporation. I will be saying more later on about the origins, responsibilities and interests of this Corporation, but put briefly it was set up to ensure the effective use of inventions arising primarily out of Government supported research. This was to be ensured wherever possible through the medium of the appropriate established industry. The Corporation was conceived, therefore, and in fact is a link between Government research on the one hand and industry on the other.

## FACTS AND FIGURES

What first is the scale of the investment by the Government in medical research? To answer this we must identify the main avenues by which the investment is made. While the Ministry of Health has power to conduct or assist by grants or in other ways, research into matters relating to the cause, prevention, diagnosis or treatment of illness, such research is confined generally to investigations which can best be carried out, at hospitals within the framework of the National Health Service. The wider and long term problems of medical research are the responsibility of the Medical Research Council (MRC) and the whole of its income is devoted to this end. It is, therefore, the main Governmental agency



specifically committed to promoting medical research. A second avenue, however, is through The University Grants Committee (UGC) via the money it provides for research workers in various University Departments. Finally there is a contribution, albeit a small one compared with the other two sources, by the Science Research Council (SRC) which also provides money for research in the Universities.

If we take the year 1964-65 the MRC spend is easy to determine and was approximately £9 million. The UGC have not in the past given a breakdown of their spend on research and development between different subject matters—although I think it is likely they will attempt to do so in the future. However, in 1961-62 it was estimated that its contribution to medical research was £8 million. At that time the total Government supported civil research and development in the universities was approximately £21 million (presumably mainly from UGC). In 1964-65 this total university civil research and development figure had risen to £38 million and, therefore, it can be assumed that the figure in this for medical research is not likely to be less than £10-11 million. This assumes, of course, that the earlier estimate of £8 million was reasonably accurate. Because of the wide spread of subject matter which is relevant to research in the medical field, it is also rather difficult to arrive at a SRC figure but it is relatively modest, say £500,000. Thus the MRC plus UGC plus SRC contribution make a total Government investment of approximately £20 million.\* This compares with a UK pharmaceutical industry investment of about £12 million in 1965. By comparison in the same 1964-65 period the total UK Government expenditure on all research and development was £427 million. Thus medical research expenditure was about 5 per cent of the total. Again for comparison the USA Government investment in medical research for the same period was \$1235 million (£440 million) or 6 per cent of the total USA research and development spend of about \$21,000 million (£7,330 million). The scale difference is enormous between the two Government's spend on medical research and there is similarly a large order of magnitude difference between the UK pharmaceutical industrial investment compared with that of its USA counterpart (£12 million compared with £160 million). It will be seen that in both countries the Government investment is substantially greater (2-3 times) than that by the respective pharmaceutical industries.

#### ORIENTATION OF RESEARCH

It is obviously incumbent on industry to spend its research and development monies generating the sort of information which will most likely lead

\* By 1966-67 the Department of Education and Science reported that total Government support for medical research had reached £31 million.

and as quickly as possible to new products or improved processes of manufacture.

These are the means whereby sales and profits are maintained or increased and business is based on doing just that. This has the consequence that inevitably most of its research must be of an applied and practically oriented character. In this context it is worth remembering that important leads in chemotherapy subsequently opening up areas of both basic and applied research have in the past and still will arise in the future through the selective or indiscriminate screening of chemical compounds for biological activity.

On the other hand, while it is obvious that in this country at least the State has a significant interest in both the availability of new drugs and their price, the responsibilities of the State in the field of medicine range much more widely than this across a very broad front. It has to take into its purview the general issue of the health and welfare of the community and has to cater for advances in the many branches of medicine which do not depend solely on the use of drugs; for example new techniques and equipment in surgery, in many areas of general medicine and in psychiatry. In addition, since medicine cannot yet be called an exact science it can only make progress and become more exact as a result of the accumulation of interrelated but quite separate disciplines. The living human organism still represents the most intricate science-based mechanism yet known.

The State's investment in research goes in, therefore, against an organisational set-up which allows for the maximum scientific freedom in the generation of the relevant basic information. The Medical Research Council from its earliest days has stood in a special relationship to Government, being in effect an autonomous scientific body, and not part of the departmental system, in the sense that the Ministry of Health is. Equally the UGC and the Universities have been and still are essentially free from any 'accountability' in the sense of being required to solve practical problems as the price for receiving continuing financial support. Indeed it may be said that in using two such instruments the State encourages or at least allows a significant element of competition in its supported research. Anyone who has had experience of carrying out research in this area will recognise the wisdom of maintaining this state of affairs.

To obtain a rapid impression of the extreme diversity of the work supported by Government in this field, one has only to thumb through the most recent MRC Annual Report (1965-66). The Council carries out its work via its own central establishment, the National Institute for Medical Research (NIMR), its separate seventy-nine research units and the thirty-nine research groups it is backing in the universities and the 1035 research grants it has awarded to institutions and to individual workers in the



universities. The same breadth can be seen in respect of the medical research carried out in the universities by studying the annual publication issued by the Department of Education and Science which details research interests in the universities. Life Sciences now occupy one complete volume of 290 pages.

There are, therefore, significant differences to be seen between the requirements against which the State on the one hand and industry on the other approach the question of which areas to research in and how to proceed in them. This is not intended to imply that industry does not do any basic research, but it must obviously contain it; in general the larger the size of the pharmaceutical company the more of such research is likely to be undertaken.

I would like to make one further point on this theme. If there is a well developed, highly research conscious and active indigenous pharmaceutical industry pursuing essentially practical research projects, it would seem eminently sensible for at least the majority of state supported research to be backing up this effort by breaking new ground and filling in the vast areas of unknown knowledge.

#### INDIRECT CONTRIBUTION TO INNOVATION

From what I have already said I suggest that while the large majority of State supported research cannot be expected to contribute directly to innovation, it will nevertheless be contributing indirectly on a continuing basis to innovation inside the industry. This arises simply as a result of the scale and character of the work. A study of the areas of work of the MRC's Research Units and Research Groups will quickly demonstrate the potential relevance of many of them to areas of innovation or potential innovation by industry. For example, to mention but a random selection, cardiovascular disease, mineral metabolism, blood coagulation, tuberculosis and chest diseases, trachoma, molecular biology, experimental virology, virology, neuropsychiatry, neuropharmacology, basic immunology, immunochemistry and many others. Also clinical research and trials carried out in the teaching hospitals are an essential part of the innovating process for industry, and here the State is proposing to make an increased contribution through the setting up by the MRC of their new Clinical Research Centre now in the building at Northwick Park outside London.

The extent to which all this type of activity makes an indirect contribution to innovation must depend primarily on the expertise of the industry in assimilating and using as rapidly and effectively as possible the information which is disseminated by publication in the scientific journals, at meetings or through the normal personal interchange channels which

exist between academic and industrial research workers, including the ill-defined but nevertheless effective grape-vine!

At this point I would refer to a remark made I think in discussion at one of the earlier meetings in this series. This was that 'Academic research does not contribute to the balance of payments because it is published; industrial research is kept under control and does contribute.' Academic research in the context of the remark obviously meant state supported research. This remark would need considerable refinement before it could be said to represent the true state of affairs. Conceivably such research might on occasions contribute more to industrial innovation if it could be released on a restricted basis to the local industry prior to publication, but the problems such as those of selection would be substantial. In any case basic research cannot flourish satisfactorily and progress apace without the stimulation and cross-fertilisation that stems from early interchange of information and ideas between research workers both on intra and international level.

#### DIRECT CONTRIBUTION TO INNOVATION

*Government Patent Policy:* Since all innovation is at least in part a function of the total research and development effort, it would be anticipated that from time to time State sponsored research could contribute directly as well as indirectly to innovation in the pharmaceutical industry. However, when and how it will do so is even more unpredictable than in the case of the industry's own research. Even in favourable cases the programmes of work are not likely to be as closely knit together as they would be in industry and there will not necessarily be immediately available at the source of an early lead the will and more particularly the resources to produce a concentrated effort which are a hall-mark and strength of industry. At the risk of appearing repetitive can I ask you to consider once again the remark about academic research not contributing to the balance of payments because it is published, and industrial research contributing because it is 'kept under control'. The key qualifying words used to distinguish between the two types of research as far as their value in this context is concerned, are 'kept under control'. By this was presumably meant that in industry useful results were protected primarily by the seeking of patent protection and probably also by delay in publication. This cannot be disputed and it is therefore a fundamental requirement that if a direct contribution to innovation is to be made by State supported research the Government must accept the responsibility of seeking patent protection wherever possible on any inventions which arise from its own research. In this country Government did adopt in 1948 such a policy across the whole field of its research activities. It had indeed approved of



and initiated the seeking of patent protection in some limited areas well before this date, but not specifically in medicine.

*NRDC:* In 1948 Parliament passed the first Development of Inventions Act which set up the National Research Development Corporation as an independent public Corporation with the responsibilities of, first, seeking patent protection wherever possible on significant inventions deriving particularly from public (namely Government supported) research followed by its subsequent exploitation through industry and, second, spending money on the 'development' of any significant invention whenever this appeared to the Corporation to be a necessary pre-requisite in order to achieve the object of getting the invention into use through industry. To finance it in its early days and also provide it with working capital for development it was entitled to borrow money from the Board of Trade provided it did not have outstanding as a debt at any time a sum in excess of £5 million. All this was to be achieved against essentially a commercial background in so far as the Corporation was obliged to attempt to pay its way. To do this would involve paying all its running expenses and overheads and interest on its borrowings which, in principle, the Act made obligatory.

There have been three amending Acts passed by Parliament since 1948. The Corporation's borrowing powers were raised first to £10 million and then in 1965 to £25 million; also it was enabled to undertake work at an earlier stage of development than the original Act envisaged. In principle it can now finance research work in certain circumstances but this is always most likely to be of an applied rather than a basic character.

*Government Department Inventions:* Soon after NRDC was set up, Government Departments were obliged by a Treasury Circular to assign to it outright rights in most inventions either held or subsequently acquired. These general obligations applied to the MRC which following discussions with the Corporation decided to proceed essentially on this same basis.

*Medical Ethics:* At about the same time the British Medical Association reviewed its policy in respect of patenting and took the view that with the creation of NRDC there was no longer any ethical objection to medically qualified inventors seeking patent protection, on the assumption that the rights would be offered to the Corporation.

*University Inventions:* The universities did not fall inside the scope of the Treasury Circular because of the intentional independent status of the universities and the Corporation has had, therefore, to deal separately with each of them. Over a period of time the concept of seeking patent protection came to be accepted at Vice-Chancellor and then at working level in the universities. No university, however, has insisted that staff assign inventive rights to NRDC, although most would encourage them

to do so. Our access to university inventions is based essentially on the establishment of direct personal liaison with all significant research departments and individuals. Many university Professors and others have consultancy or other direct links with industry to the extent that they may feel obliged to offer some inventive rights directly to industry. This means that we cannot have access to the total inventive capacity of the universities but nevertheless we have now handled inventions from every university in the UK, and have financially backed projects in many of them.

*The Work:* For the most part the Corporation is attempting to identify interesting leads in research or responding to leads brought to its notice. Depending on the state of the work, an invention may or may not already exist and it may or may not be possible to protect it adequately by an immediate patent filing. If adequate protection can be sought then an early disclosure of the invention to industry may be sensible and possible. If this is so it is ideal because it allows one immediately to expose the invention to the critical eyes of the people who will ultimately have to be convinced it has some commercial potential if the necessary further industrial development, production and sale are to take place. In many cases this is all that is justified because the invention may look marginal or a doubtful starter from the beginning. However, protection may need to be sought then or not at all, because the inventor will probably want to publish soon; sometimes tomorrow and if possible yesterday! In other cases this may also suffice because the lead is sufficient to encourage one or more firms to proceed on the basis of a licence agreement.

In other cases the inventor may intend to proceed further with his own programme of research and we can carry out a patenting holding operation. Where we and our advisors (we take expert advice wherever it can be found) are of the opinion that a real lead may exist, we can and do contribute development finance. Since this is normally for support of further work in the laboratory where the invention has been made, it is really more by way of being support for applied research rather than development in the industrial sense. The latter will always be undertaken by our ultimate licensee(s) as part of any commercial deal.

In some cases it may be necessary to attempt to obtain industry's active help and co-operation even in the relatively early stages of such applied research and it may even be necessary to set up a full collaboration involving detailed technical interchange.

*Results:* At the start it has to be said, as this audience will appreciate only too well, that anyone who is looking to make quick financial returns should not indulge in the business of seeking out, patenting and developing inventions in pharmaceuticals, or at least not when it is done as incidental to basic research. Success is more difficult for NRDC to achieve because



of the manner by which it must come upon invention, but the pharmaceutical industry's own experience world-wide is not dissimilar. As far as pharmaceutical inventions are concerned, many are called but few are chosen.

However, to quantify some of this. We have, since we were set up, handled well over 100 items in the pharmaceutical field alone (this does not include other biological chemicals such as veterinary medicals, insecticides, or herbicides). Out of these we have licensed about fifteen. That may seem to be quite a high success rate. It has to be qualified, however, by saying that so far only two of the licensed items can be represented as major ones, although there are several others which have been significant, and there are also a number which have been licensed relatively recently and which may yet yield substantial income. I would draw attention to the fact that many of these useful inventions have stemmed from the MRC's own laboratories or work in the Universities supported in part by MRC funds.

As far as financial benefit is concerned, while we do not disclose a detailed breakdown of our income since this would not be in keeping with the commercial nature of our work, I can tell you that our cumulative income from pharmaceutical inventions is well over £1 million and rising quite fast. Put another way, it represents innovations on the market worth substantially in excess of £20 million net sales value. All this contributes in some measure to the balance of payments, but not all stems from sales by UK companies. The Corporation licenses on an international basis, albeit always considering the interest of the UK industry. Licensing arrangements must take into account such things as the territories protected, the markets and the inherent and the long term strength or weakness of the patent protection.

Of the more than 100 items I have referred to, in nineteen we supported development work. Of the nine of these which have been completed two were commercially successful; ten are still current.

Against the above statistical summary, I would now like to give you some details of just a few of the items we have handled to illustrate their diversity and the different types of activity that they involve us in.

*Hecogenin*: This is a starting material for steroid synthesis and takes us back to 1951 soon after cortisone had emerged. Due to currency exchange problems at that time, if this drug were to become readily available in the UK a non-dollar source of a suitable starting material was required. MRC workers (Spensley, Callow and co-workers) found that such a suitable starting material existed in the juice of the sisal plant and we not only took out patent protection on the method of extracting it but also financed and organised the building of a pilot plant for its extraction in East Africa. We also arranged contracts for its purification by industry

in the UK. Subsequently we sold out the pilot plant and licensed the basic patents. Hecogenin is still in use in the UK.

*Tri-iodothyronine:* This was isolated and identified by Dr Rosalind Pitt-Rivers and Dr Gross at the MRC's National Institute for Medical Research at Mill Hill, and was found to have high thyroxine-like activity. This was a relatively simple item and mainly involved us in seeking patent protection for it and subsequently setting up licensing arrangements. This has turned out to be a substantial revenue earning invention and represents for us an unusually uncomplicated situation.

*Miroestrol:* Another item arose from work being done by Dr Pope and colleagues at the National Institute for Dairying at Shinfield, on the oestrogen-like activity contained in pasture and its effect on grazing animals. This led to an interest in a plant said according to folk-lore to possess 'rejuvenating' properties and later shown to contain a highly active oestrogen-like material. We financed two expeditions into the Siamese jungle to collect the tubers of this plant and also paid for and organised work to purify and then chemically characterise the very active principle. It turned out to have a novel but synthetically difficult chemical structure. Although biologically active orally it produced unacceptable side-effects in limited clinical trials. This was a technically successful project and a contribution to scientific knowledge but not commercially rewarding.

*Micro-organism Breeding:* Yet another project was concerned with attempts to harness the so called 'para-sexual' breeding cycle in *fungi imperfecti* discovered by Professors Pontecorvo, Roper, and colleagues at Glasgow University. Previously it had been assumed that these organisms reproduced by binary fission so that variation in the strain could only arise by random natural or artificially induced mutation, for example, using UV light. It turned out that given the right environmental conditions a sexual type of crossing could be made to take place and the hope was that one could breed preferred strains of organisms for producing antibiotics such as penicillin. We devoted a good deal of time and effort in addition to money to this project and following discussions with the industry at the appropriate stage, undertook a collaborative programme along with one company. Up to a point the project was a technical success but in our hands did not yield commercial success. The sophisticated manipulative and interpretative techniques were, however, passed on to industry and are still the subject of study.

*Collaborations with Industry:* Another class of project has involved the Corporation's skills rather than its money. These have been organised on behalf of the MRC on occasions when their workers have made significant advances which were not complete in themselves and required industrial collaborations to explore them further. In these cases in addition



to seeking patent protection we have set up the necessary agreements with the collaborating companies to define the basis on which the collaboration will proceed and on which any industrial property arising therefrom will be handled. Several of these have been mounted. As an example can be mentioned that on interferon. The discovery and isolation of this naturally occurring anti-viral agent by the late Dr Isaacs and Dr Lindemann at the MRC's NIMR at Mill Hill was very exciting and held out the possibility of a major break-through in this field. As is not unusual things have not worked out quite in this way, although the collaboration is still in being.

*Cephalosporins:* Finally I am glad to be able to match, at least in some respects, the very enthralling and exciting story unfolded by Mr Wilkins of Beecham in the second paper given in this series. This described the discovery of the nucleus, 6-amino-penicillanic acid (6-APA), of penicillin which is the key starting material for a vast range of new semi-synthetic penicillins, a number of which have been very successful both medically and commercially. We also have been concerned with a new group of semi-synthetic antibiotics in this case called the cephalosporins.

Strangely enough the two groups of compounds have a number of similar background circumstances. Firstly, early work in respect of both was done in Italy. In the case of the cephalosporins, Professor Brotzu working in Sardinia first isolated the cephalosporium mutant and showed that when grown the broth containing it displayed antibacterial activity. In the case of the semi-synthetic penicillins Professor Chain was working at the Institute in Rome while collaborating with Beecham. Secondly Professor Brotzu passed the cephalosporium mould through an intermediary to Lord Florey and his colleagues, headed by Professor Abraham at the Sir William Dunn School of Pathology at Oxford. This was one part of the original Oxford team which isolated penicillin at the outbreak of war. The other part of that team was Professor Chain, now working on the semi-synthetic penicillins. Finally the cephalosporins turned out to be chemically what might be described as first cousins of the penicillins possessing a nucleus—7-amino-cephalosporanic acid (7-ACA)—comparable to 6-APA and from which a vast range of new semi-synthetic cephalosporins could be made.

Our entry into the cephalosporin situation is almost lost in antiquity and highlights that often the path to a success in this field can be long and hard. We filed our first patent application on the work at Oxford as long ago as 1951 and continued to file a series of further applications because this cephalosporium mould proved to be prolific as a producer of new antibiotics, which were discovered seriatim.

First, at least five similar substances called the cephalosporin P's were found; second, cephalosporin N (now known to be a new penicillin);

then finally in trace amounts the most important cephalosporin C. The immediate commercial potential of cephalosporin C was not obvious. It had important biological properties but its potency was very low, its structure was unknown and it could only be obtained with extreme difficulty in trace amounts. At that time the fermentation was being undertaken by the MRC Antibiotics Research Station at Clevedon. It soon became clear that if adequate quantities were to be obtained to complete the chemistry and explore further the biological properties the fermentation must be scaled up and this required industry's help. This we obtained, although at the time only Glaxo were willing to come in with us. They found the fermentation a tough one to master and indeed not a lot of progress was made until a much improved mutant strain of the organism was obtained at Clevedon. Once significant quantities of pure material were made available at Oxford work could proceed more rapidly. The work was now at a stage when we could effectively start to provide financial support for the work at Oxford, including crystallographic studies by Professor Dorothy Hodgkin and colleagues. Eventually the structure of cephalosporin C was determined. Soon after followed the discovery that a nucleus could be obtained from it and that from this much more active derivatives could be produced. The whole project now gathered momentum especially in a commercial sense. We licensed a second British company and after due consideration we acceded to requests for options to licences from a number of American, European and Japanese companies. Three main reasons decided us to enter into agreements overseas. First, the field was now obviously a very large one comparable to the semi-synthetic penicillins and therefore on an international scale the markets would justify and indeed need more than one or two companies for its rapid exploitation. Secondly, there were still substantial development problems to be overcome before commercial products could emerge and we felt it would be advantageous if we could get access to development know-how from the activities of large overseas companies. Thirdly, although potentially strong basic patent protection had been sought on the key starting materials the scope of our final product protection was understandably limited. The second point particularly concerned us and as it happened our arrangements turned out to be vital as far as this was concerned. Fortunately we were successful in negotiating extremely effective agreements abroad under which, in addition to royalties, we received a flow back of information. We also secured access to this and to patented developments on advantageous terms for our British licensees. In the event one of the first major development hurdles was crossed by one of our USA optionees, Eli Lilly. However both Glaxo and Lilly have invested heavily to date in this project and both companies have during the past two years marketed their own



particular cephalosporin derivatives, Glaxo—Ceporin and Lilly—Kefflin. These are the first products to emerge and it can be expected that others will follow as has been the case with the Beecham semi-synthetic penicillins. Already the business is substantial and this situation looks as if it could be the first major winner to emerge in this field from the linking through NRDC of state-supported research to industry.

I could go on with more examples but the above are adequate by way of illustration.

#### ADDITIONAL STATE SUPPORT

It is debatable whether in view of the enormous investment being made by the USA Government our own is substantial enough to compete in so far as the quantity of commercially significant innovation that may derive either directly or indirectly. Equally it seems doubtful whether the UK industry's investment will enable it to compete in the long term with its large USA and other overseas competitors, especially bearing in mind the increasing cost and difficulty of finding useful new products. It would be easy to suggest a requirement for increased Government support of medical research of the present type but almost impossible to apply any cost effectiveness technique to it. Much detailed economic analysis would be needed before any significant change in scale were made. Government has to meet many calls upon its money and in the end can only allocate logically against some pattern which is related to overall economic considerations.

I personally feel optimistic that even with only modest increases in expenditure our State-supported research and development scientists and doctors will continue to find a reasonable number of important commercial leads. Much more, however, needs to be done to impress on non-industrial research workers the dependence of the economy of the country on industry obtaining the maximum benefit from the fruits of the Government's research investment. It is also vital that we continue to take all possible steps to ensure that advances are patent protected wherever possible at a very early stage and developed rapidly by whatever means, preferably at home and unaided. If this is not realistic then the best commercial bargains must be struck abroad. I would warn, however, that this is not easy to achieve as once again many in this audience will appreciate. The cards in one's hand have to be strong ones.

One final thought occurs to me. It is I think reasonably accepted that in general the innovation benefit from State spending on research and development is greatest where a significant part of the spend is made in the relevant industry. For one thing, if innovation is achieved in such circumstances it is then already secure in the nest which will harbour and sustain it until it is launched on to the market. Science-based industries

require few external stimuli to encourage them to innovate in normal circumstances. Nevertheless, it is conceivable that due to changing circumstances and financial pressures the possibility of some forms of innovation may not be explored because of the large expense and extended time-scales of the research and development programmes which are required. Possibly a typical example of this sort of situation (although it happens to be one that was in fact tackled by a commercial company) is represented by the field of peptide synthesis. Ten years ago it would have required an adventurous company to mount a substantial research and development programme in this field, as distinct from a very modest or intermittent effort. The judgement to be made for the moment is not whether the investment in this particular example has paid off to date or not, but rather whether the concept is right. If so, and I suggest it is, then maybe there is a case for Government supporting research and development on some scale in the British pharmaceutical industry. What basis it might be done on is a nice point which may be taken up in discussion. May I, however, end by calling attention to the fact that my own Corporation is increasingly investing 'jointly' with industrial companies in development projects in a wide variety of technological areas. These are based on ideas, inventions or innovations conceived by industry itself, but where the risk element is too high for some particular reason for an individual company to feel it possible to bear unaided the total speculative risk. NRDC's investment is fully at risk in the sense that it is recoverable only if there is technical and commercial success. We have also developed attitudes and policies in relation particularly to the ownership of patent property which are acceptable to industry and allow such projects to proceed.



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