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the case for growth in Britain

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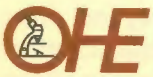

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Cover illustration by courtesy of the Wellcome Historical Medical Library.

The laboratory of the manufacturing chemist Ambrose Godfrey Hanckwitz built in 1706

Hanckwitz was previously a laboratory assistant to Robert Boyle. The firm passed to a son of Hanckwitz, who was generally known as Ambrose Godfrey. Later the firm became known as Godfrey and Cooke and survived until quite recent times.

Foreword

by the Chairman of the Editorial Board

ONE of the problems in Britain today is that too little of its academic research is associated with successful innovation in industry. The result is that we have contributed generously to the world stock of fundamental knowledge, but we have failed to benefit commensurately in terms of earnings from the sale of innovations in world markets.

This paper is concerned only with research relating to medicine. However, the picture which emerges and the lessons which can be learnt from it may apply in the many other cases, particularly where the government acts as an indirect sponsor of industrial research through its role as a customer. First class fundamental research has been undertaken by the Medical Research Council and the medical schools in this country. Medicine throughout the world is indebted to Britain's contribution. The major applied research in this field, which is undertaken by the pharmaceutical industry in their development of new medicines, also has a good record, in terms both of innovation and of its earnings from world trade. But an inbalance appears to be emerging between the support for academic research and for that of the industry.

Government expenditure on medical research has increased rapidly over the past decade. Yet the pharmaceutical industry, which could benefit from such fundamental work and develop new medicines based on it, appears to have expanded its own research effort at a slower rate. The emphasis seems to have been more on government financed academic research than on industrial applied research. To some extent this may result from public policy. There has perhaps been a greater willingness to provide direct support for research undertaken by the Medical Research Council and the universities, than there has been to provide economic encouragement for the pharmaceutical in-

dustry to expand its research. This, in turn, may have arisen from a failure to understand the economics of innovation in research-based companies.

Seen in the narrow context of the National Health Service, the pharmaceutical industry may have been judged primarily on its ability to manufacture and supply good quality medicines at the lowest possible prices. In the broader context of the national economy, the industry must be considered instead as an exemplar of the research-based industries, on the success and growth of which Britain's future depends. As such, its performance must be judged by different criteria. Competitive success in world markets will depend more on successful innovation than on price. We need an economic climate which is conducive to innovation.

If indeed the experience of the pharmaceutical industry is relevant to the problems of other research-based industries, this paper presents a case which is of the greatest significance for Britain. There have been criticisms of industry generally for its failure in innovation. At the same time there have been criticisms of the industry's high prices, profits and costs of sales promotion, which we believe to be concomitants of successful innovation. If we continue to criticise the profitability and marketing activities of the research-based industries in this country, we can never achieve the technological success of countries such as Germany, Japan and the United States. Before this argument is dismissed as special pleading on behalf of a much criticised industry, we would ask that those who determine public policy should at least consider Britain's pharmaceutical industry in a worldwide setting, rather than in terms of the National Health Service alone.

Colin A. Cooke
Magdalen College
Oxford

Pharmaceutical Research: the case for growth in Britain

THE great progress of medical science in recent decades, embodied in the development of new medical techniques and modern health products, has changed substantially the picture of sickness, disability and premature death in the community. This progress to a great extent explains the real increases of expenditure on the National Health Service[1]. The benefits which it has brought to the community at large need little reiteration. The declining mortality for tuberculosis, pneumonia and the infective diseases, the prevention of crippling illnesses such as poliomyelitis and the effective control of long-term organic disorders such as diabetes, tell their own eloquent stories[2]. For the future, the prospects of further progress are great; for example, 'it is possible that new drugs may make mental asylums as obsolete as tuberculosis sanatoria'[3].

The standard of medical care depends on the development of effective medical procedures and on the extent of their availability. Thus one key factor determining the progress of medical care is the financial support for medical and allied research. The last comprehensive estimate for medical research expenditure in the United Kingdom was for the year 1961/62, when it amounted to approximately £24 million current expenditure and a further £3 million capital expenditure on the provision of new buildings and equipment for research. Over half of this finance came from government funds, one third represented expenditure by the pharmaceutical industry in Britain, while the balance was made up by medical research charities and trusts[4]. Expenditure on medical research has been growing rapidly since this estimate was compiled. For example, the expenditure of the Medical Research Council rose from approximately £5·5 million in 1961/62 to £11·9 million in 1966/67, an increase of 116 per cent. Estimated total govern-

ment expenditure on medical research rose at about the same rate, from £14·5 million to £31 million, over the same period*. The research expenditure by the pharmaceutical industry in Britain grew from £7·8 million in 1961 to £11·6 million in 1965, a rise over this shorter period of 49 per cent. In 1965, all expenditure on medical research accounted for roughly £42 million, or 0·13 per cent of total national income.

The growth of medical research expenditure poses many questions. One of these is whether the current volume is adequate; which by implication also asks what the right level of expenditure should be. Associated with these problems are the more detailed issues of whether the direction of the research and the allocation of finance between various problems is satisfactory. For example, would some of the funds at present spent on cancer or poliomyelitis research being greater benefit if directed to the field of mental health or geriatric care? Perhaps most of all, however, it poses the question of whether it is desirable that in Britain, with its persistent economic problems, the growth rate of government financed medical research should have been double that of industry financed pharmaceutical research.

This paper considers some of the issues involved. It also examines the possibilities of answering these questions through using recently developed techniques, particularly cost benefit analysis, but concludes that the application of such techniques is unlikely to provide a clear and definite answer to these questions, except to underline the general presumption that there are good reasons to encourage the growth of research at least in the industrial sector. Also, even if a clear answer were provided, the question of implementation of any policy would remain. The problems of implementation, of stimulating growth are basic in any approach to the questions raised by the adequacy of expenditure and the opportunities open in medical research.

It, therefore, examines the potential for and the barriers to growth in research by the industry. Consideration of the adequacy of levels of research effort is purely academic without

*The MRC figures are based on Parliamentary grants in aid. (They do not include small sums received from other government departments or by private donation). Those for total government expenditure are based on two Parliamentary written answers, on 30 April 1963 (Hansard Written Answers Col 91) and 17 April 1967 (Hansard Written Answers Col 35) respectively.

examination of the restraints or of any existing barriers to growth. Indeed, considering the risks of research being unsuccessful and its already proven benefits for the community when it does succeed, there is little danger that its growth in this field will become overburdensome in terms of calls upon overall national resources. It should be recognised that for the present and for many years to come, there exist limiting factors on the growth of industrial research expenditure. A central feature of any policy should be the systematic reduction of the impediments to further financing of research by industry.

PRODUCTS OF RESEARCH

An important distinction exists in the products of the two types of research, which underlines the significance of this issue. Most Research Council expenditure results in new knowledge which is embodied in people and their abilities, such as in the development of a new surgical technique, or in understanding the causes or pattern of disease. By contrast, industrial research generally results in the innovation of material goods such as new pharmaceuticals or medical equipment. In practice, the two groups of products of research are frequently used jointly in medical procedures. However, the financial structure supporting research in the two fields differ, and they have different economic consequences for the nation. Finance for research into new techniques generally comes from direct or indirect government subvention. The benefits tend to become enmeshed in the general operations of the National Health Service, and thus cannot easily be separately identified or measured in financial terms. On the other hand, finance for research leading to the development of new products tends to come from sales either to the public or the State. The discovery of new medical goods is an integral part of the industrial process of research, development, production and marketing. As research is linked to industry, previous successes form the financial basis for future discoveries. Since this mechanism exists, a framework is provided for the analysis of problems concerning the levels of medical research in this field, and the nature of the problems involved are more clearly definable. Further, new knowledge by itself cannot generally be sold abroad. It is freely available, and overseas countries may often make use of it or even attract the individuals who have acquired it. New products on the other

hand are protected by patent and may be sold overseas to earn foreign currency.

COST BENEFIT ANALYSIS

The research effort of the pharmaceutical industry is part both of the total medical research effort of the country and of the total effort by UK research-based industry. For British-owned companies sales to the National Health Service are a major source of finance for research. The volume of research and the expenditure on the pharmaceutical service are thus closely related in more than one way: receipts from sales may finance research, leading to further new products, which in turn lead to higher public expenditure on the Service. In terms purely of industrial research, the industry is making call on the qualified manpower resources of the nation. In so far as sales to the National Health Service could be considered indirectly as government support, the industry's effort may be looked at as one part of the whole programme of government support for industrial research. Given these relationships, the question may be posed whether the volume of pharmaceutical industry research is, at present, optimal, relative to the competing demands for research resources and the opportunities open and whether a change in balance in the future is required.

It is now commonly suggested that cost benefit analysis technique could be used to determine the optimum balance in the distribution of research expenditure and effort among competing fields. Such an approach would include a consideration of the technologically trained manpower available in industry and the public service to make full use of research results because such trained manpower is drawn from the same limited pool. Implicitly this approach is closely related to economic planning across the broad field of public and private sectors of the economy. The 1965 National Plan showed a five year projection in broad categories such as public spending, private investment and consumer expenditure. The plan was in effect a mathematical projection of the economy's development assuming current policies and current attitudes on the part of consumers, management and manpower. Technological change is by definition generally excluded from such a plan, but it may be introduced through study of the various options open which might create deviations from the projection of current

trends. In this way it is possible to assess courses of action which would make the best contribution to the achievement of defined objectives. From this, by use of cost benefit analysis, an evaluation can be made of the amount of research effort required in different sectors. In essence cost benefit analysis represents an evaluation of the likely return on research expenditure in relation to its cost. Evaluation covers not only the immediate and measurable market returns but also the more intangible effects of new developments, by tracing the ripples of scientific advance and technological change through the community[8].

Such an approach thus presupposes the existence of defined objectives relative to the total research effort in all scientific fields of the public and private sectors of the economy. It removes the question beyond the confines of the immediate considerations of medical research expenditure and progress in the Nation's health. However, some general features of problems which arise in this approach when applied to the field of medical research expenditure in general, or the pharmaceutical industry's effort in particular, may be considered.

The principal difficulty is the problem of evaluating returns for any given piece of research. The difficulty is two-fold. First it is not always possible to relate particular research to a specific result. This may be done retrospectively, but rarely prospectively. The results of research cannot be guaranteed; chlorpromazine, a tranquilliser, resulted from research study of antihistamines, while the sulphonylureas for the treatment for diabetes were developed as a result of research on anti-bacterial sulphonamides. Secondly, and more important, it is questionable how far reliable estimates can be made of the general benefits resulting from new therapeutic advances. It is possible to make calculations of the life value of earnings of persons who might otherwise have died but for a specific therapeutic advance. However, such calculations involve many methodological problems. They may be of help in indicating the order of magnitude of the benefits which accrue from medical progress; but it is difficult to see how they could be used as a basis of comparison in deciding the direction of effort between different competing sectors of medical progress, or in choosing between increasing expenditure in medicine as against other sectors of scientific effort[5]. It is difficult, for example to envisage

on what basis a decision could be taken in weighing the relative merits of a reduction in mortality from cardiovascular disease against a reduction in the transatlantic flight time.

The problems are further complicated by the fact that currently an increasing proportion of research effort, particularly in the field of pharmaceuticals, is directed towards safety. All powerful medicinal chemicals carry the risk of side-effects. Therefore, research is increasingly undertaken to devise better methods of establishing the safety of both new and established medicines. It is particularly difficult to envisage how returns from such research can be measured. If it has been successful, the risks which it has forestalled may never be realised or even imagined. It is only against the background of unforeseen disasters as occurred with thalidomide and the early Comets that the value of such 'defensive' research can be appreciated. This problem illustrates the particular difficulties which emerge when one applies cost benefit analysis principles to the practical problems and situations of research in an industrial setting. It is the study of these problems which should provide, eventually, the guide lines for future policy. In the meantime only a pragmatic assessment can be made of the value of research by the pharmaceutical industry.

IN attempting to decide the right level of research expenditure by the pharmaceutical industry in Britain it might appear tempting to restrict the consideration of its operations entirely within the context of the National Health Service. The National Health Service is its principal customer, accounting for £98 million or 39 per cent of total sales in 1965, compared with export sales in the same year of £67 million or 27 per cent of the total*. However, an analysis of research within the industry purely in terms of the National Health Service ignores a major aspect of pharmaceutical innovation—its international character. In this connection, British-owned companies in the industry can be considered only in an international context: their sales to the National Health Service become relatively speaking incidental. Because of the high initial costs of research and development, new products must be sold for the benefit of at least 500 million people rather than 55 million people—that is throughout Western Europe, North America, parts of South America and the developed Commonwealth nations. Eventually, as other parts of the world raise their living standards, they too will increasingly represent a market for the latest and most sophisticated products of the industry, and a major source for future research growth. Already, in the case of antibiotics, it has been estimated that Britain represents, at most, only one fifteenth of the total world market, while the share in the United States is nearer one third[7]. For all medicines, consumption in Britain again amounts to about one fifteenth of total the value of world production, while the United States accounts for nearer one half. Under these circumstances, it is important that the whole problem of the future of research in

*The remaining 34 per cent included household medicines and veterinary products sold in Britain.

pharmaceutical companies in Britain should be considered in an international rather than a purely national setting.

This situation has thrown into sharp relief a distinction between different sectors of the pharmaceutical industry. Two main though overlapping groups of firms have emerged. There are first the traditional production-oriented pharmaceutical manufacturers making common or well-established products and secondly the research-based sectors of the industry, which operate under entirely different economic circumstances. The production-oriented manufacturers can, and increasingly must, rely primarily on a domestic market. Future prospects for international trade in well-established products are limited; primitive countries scarcely use established Western medicines, developing countries prefer local manufacture to conserve foreign currency, and advanced nations can usually manufacture such products more cheaply than they can import them. Thus international trade in traditional pharmaceutical products, which was typical of Britain's exports before the Second World War, is expected to dwindle rather than to grow. For the future, international trade in pharmaceuticals is likely to depend mainly on the products of the research-based sector of the industry. The international market is itself in turn necessary for the expansion of sales required to support a major research effort.

Considerations both of the international character of the industry and the nature of operations of research-based firms are central to the case for expansion of the industry's research effort. The case may, therefore, be reviewed independently of the broad social benefits flowing from medical research. The economic and social facets are nevertheless closely related: the specific economic problems require solution for implementation of a socially oriented scientific research policy, while the prospects of achieving goals in improved social benefits depend upon economic growth and an improved performance in international trade. Without very cheap labour it is necessary to compete internationally through the development of innovations which sell abroad on their design and quality, rather than on low costs or prices. The case for expansion of pharmaceutical industry research can, therefore, be posed in terms of impact on international earnings. The prima facie case must be based on establishing the relation between research investment and overseas earnings, and upon the evidence that among the

different research-based industries competing for research resources, the pharmaceutical industry is an appropriate investment for Britain.

THE PRIMA FACIE CASE: INTERNATIONAL EARNINGS

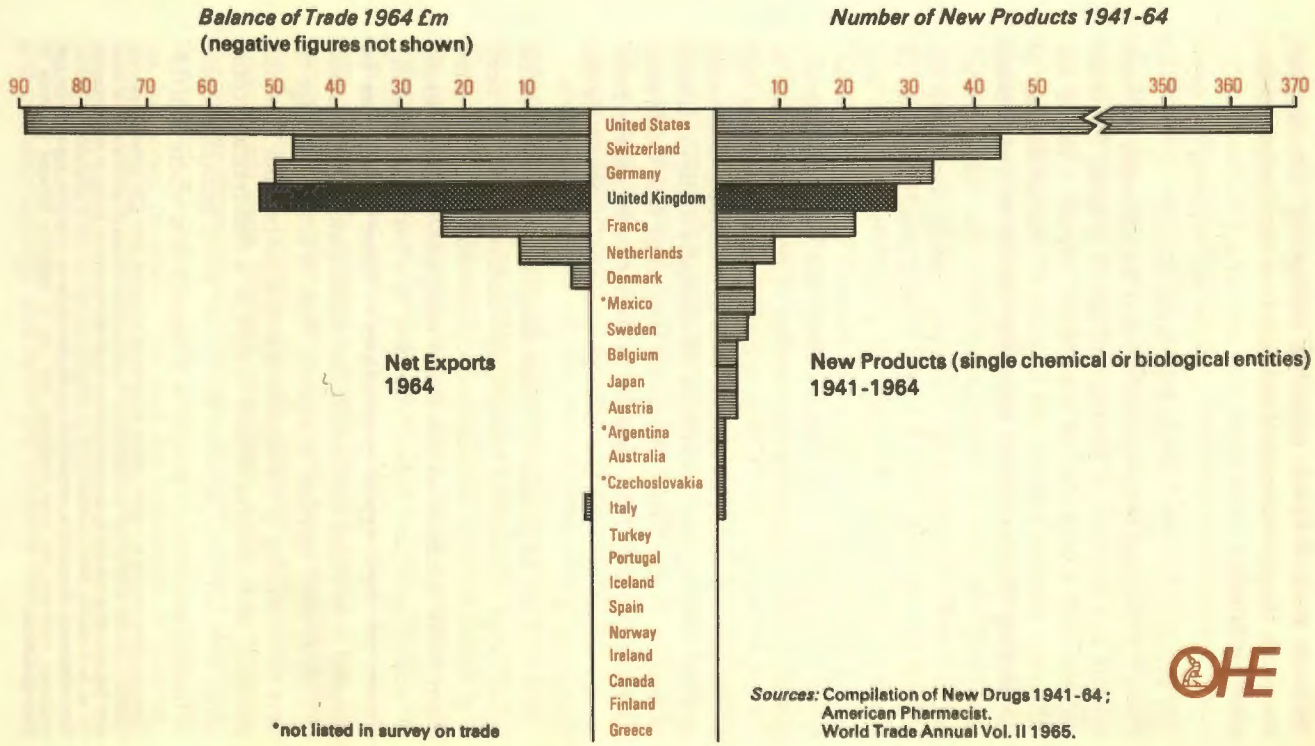
There is substantial evidence to show that the difference between exports and imports of pharmaceuticals is greatest for those nations with a high rate of innovation. Figure 1 shows the difference between exports and imports of pharmaceuticals of the leading pharmaceutical exporting nations in 1964, compared to the number of new pharmaceutical discoveries attributed to each for the period 1941 to 1964. Clearly, those with the highest rate of innovation have the largest positive balance in pharmaceutical trade. Although only the United States and Britain publish annual figures of research by their pharmaceutical industries, it also seems likely that research expenditure is closely correlated to the number of new products and to the net export figures*. There is, indeed, general agreement that British research-based industries, such as chemicals, electronics and instruments, must contribute substantially to the expansion of exports in the future. To do so, they must face worldwide competition, and their research in their chosen sphere must stand comparison with that of other countries, particularly the United States.

It would not be possible to meet this competition across the broad range of scientific research and development. 'The need now forced on us by international competition is to have some sharp peaks mounted on this broad base, some concentrations of technological and industrial power in a few fields carefully chosen for their export possibilities'[7]. Three criteria can be adopted to establish empirically the research most likely to lead to a short-term increase in exports. First, it is an advantage to have some existing or traditional expertise in the field. Thus, for example, with cameras Britain is now at a disadvantage compared with Germany, Japan or the United States. Second, because of limited resources, it should be a research field where individ-

*The exception to this is Japan, which is reported to spend over £20 million a year on research, second only to the United States. However, their research on this level is new. Also because they have only process patents for pharmaceuticals much of their research has so far probably been concentrated on developing new chemical processes to manufacture overseas innovations, rather than on developing new products. Japan so far has produced relatively few new products, and has a negative balance of trade in pharmaceuticals.

Figure 1

Pharmaceutical Discoveries and Net Exports.



ual projects are not prohibitively expensive. This has become a major criticism of Britain's participation in the development of supersonic aircraft. One single failure represents the loss of a substantial proportion of total research effort. The adoption of smaller projects which are not excessively expensive individually spreads the risks and increases the likelihood that at least some major successes will result from the same expenditure. Third, a given research effort should produce as great as possible a return in terms of balance of trade.

Judged against these three criteria, there is a strong prima facie case for promoting pharmaceutical research in Britain. First, there is an already existing and flourishing research-based pharmaceutical industry. Figures are available for research expenditure by the pharmaceutical industry in Britain since 1953. In that year, expenditure amounted to £2·8 million, or equivalent to approximately one twelfth of manufacturers' sales to the National Health Service. By 1965, the latest year for which figures are available, the total research expenditure had risen to £11·6 million, or approximately one ninth of the industry's total sales to the National Health Service. Compared with research effort in other industries, the pharmaceutical industry is outstanding. Though small in relation to the total research expenditure by British industry, its effort is, proportionately to size, among the highest*. One study suggested that the industry employed the highest ratio of scientific qualified manpower in Britain; 2·6 per cent as against an average of 0·6 per cent for all manufacturing industry[8]. Ten per cent of employees in specialist pharmaceutical firms are engaged in research[9]. Equally important, Britain is a leading nation for academic medical research in the universities research centres and the hospitals. It is often on this academic work that new pharmaceutical developments by the industry are based. The University Grants Committee and the Medical Research Council each spend at least as much as the industry on medical research. Expenditure by both has been rising more rapidly than research spending by the industry or by Britain as a whole which in turn have been rising faster than national income. (Fig. 2 and 3).

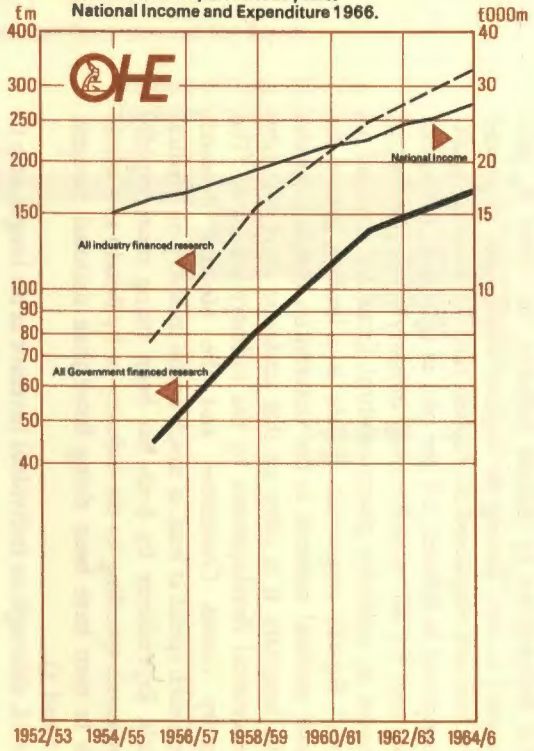
Second, although an individual inventor is no longer able to

*This is true whether the size of the pharmaceutical industry is measured by manpower, capital employed or output.

Figure 2

Civil Research Expenditure, UK 1955-56 to 1964-65.

Source: Report on Science Policy Cmnd 3007, HMSO 1966.
ABPI Annual Report 1965-66.
MRC Annual Report various years.
National Income and Expenditure 1966.

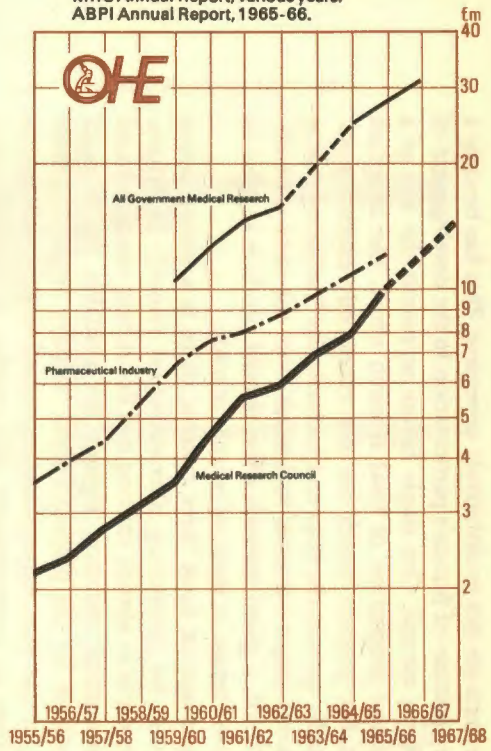


Note: All industry and all Government Research 1964-65 figures are provisional.

Figure 3

Medical Research UK 1955-56 to 1966-67.

Source: Department of Education and Science, Hansard and Per. Comm.
MRC Annual Report, various years.
ABPI Annual Report, 1965-66.



Note: Pharmaceutical Industry Research 1965-66 figure estimated.
MRC 1966-67 and 1967-68 figures estimated.

carry through single handed the development of a new medicine, an individual pharmaceutical research project can still be modest compared, for example, with the development of an aircraft or even an aircraft engine. The cost of synthesising and testing a range of potentially useful medicinal chemicals may be about £300 000: not all such projects will be successful, but with a probable success rate of around one in six, a new marketable product would represent an investment of £2 million worth of research. This compares with a sum of about £15 million budgeted by Rolls-Royce to develop a single aircraft engine, while the TSR 2 aircraft project was abandoned when its estimated research and development costs had reached £750 million.

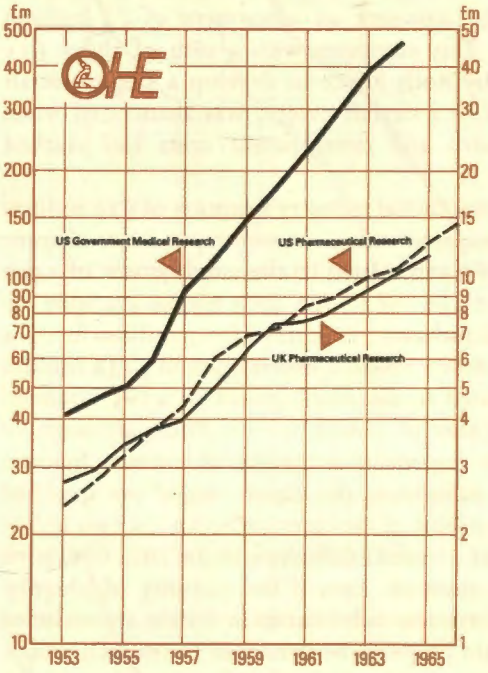
Finally, the pharmaceutical industry's exports of £75 million in 1966 may be compared with a research expenditure of some £12 million in 1965 and related to the employment of 1500 graduates on research in 1962—the latest figures available. By contrast, the aircraft industry's exports of £107 million in 1964 may be compared with a research expenditure of £138 million in 1964/5 and related to the employment of 4365 qualified research workers (also in 1962) [10 11 12]. Thus, although in terms of manpower (especially as the aircraft industry figure is based on a wider definition) the export record per qualified research worker is at least of the same order for the two industries, there is almost a tenfold difference in the ratio of exports to expenditure on research. Even if the majority of pharmaceutical exports of overseas subsidiaries in Britain are excluded (because they should properly be attributed to research undertaken in other countries) the ratios still differ very substantially.

In addition to these three criteria, there are two further secondary grounds upon which Britain's pharmaceutical research effort should be expanded. First, whereas British industry as a whole in 1964/65 depended on direct government assistance for 38 per cent of its research and development expenditure, the pharmaceutical industry financed its research expenditure wholly from its own sales revenue both from the National Health Service and from other sales at home and overseas. Second, the pharmaceutical industry has a long tradition of co-operation with academic research workers. The Chairman of the Science Research Council has said that 'much has been said about fostering closer relationships between industry and the

Figure 4

Total Federal Medical Research Expenditure, USA and Pharmaceutical Industry Research Expenditure, UK and USA, 1953 to 1965.

Source: ABPI Annual Report 1965-66 (UK).
PMA Annual Report various years (USA).
Resources for Medical Research No. 4 1963.



universities, but both sides are extremely slow and over cautious. In this country we simply cannot afford to do research on a large scale in the universities without having regard to its impact on the country's economy'[13]. The pharmaceutical industry, however, has an established long tradition of interdependence with the universities and academic research workers[14]*.

INTERNATIONAL INVESTMENT

The prime economic case for increasing pharmaceutical research in Britain, based on its export potentialities, requires modification to take account of the impact of international investment both by overseas firms establishing themselves in Britain and the converse of British-based companies establishing subsidiaries abroad.

Three-quarters of the sales of medicines to the National Health Service are by British subsidiaries or branches of overseas parent companies: two-thirds of this overseas total is American. Although the majority of their shareholding and their ultimate control is abroad these companies are an important part of the British industry. They normally manufacture in Britain, undertake some research here and contribute substantially to the industry's exports. In 1963 half the exports of pharmaceutical preparations and just over a quarter of the exports of pharmaceutical chemicals were made by subsidiaries in Britain of overseas companies. The American owned Winthrop Products Company is among the holders of the Queen's Award to Industry for its export achievement.

The international nature of the pharmaceutical industry in Britain is a logical consequence of the international nature of the scientific progress which has underpinned its development. Figure 4 shows how research spending has grown in both the United States and in Britain since 1953†. The lines of growth for the industry are parallel, but the scale of the two countries

*Collaboration between industry and universities usually takes the form of the exchange of ideas rather than financial payments. Nevertheless the contrast between the pharmaceutical industry and the rest is also reflected in the proportion of research budgets devoted to work undertaken in universities; in 1964/65 the pharmaceutical industry devoted 1.3 per cent of its research spending to work in universities, more than twice the average for the rest of British industry, 0.6 per cent.

†The figures for the two countries are defined slightly differently. That for Britain is the total pharmaceutical research carried out in this country, including a small proportion which is carried out by overseas-owned companies in Britain. That for the US includes all research carried out in that country (again with a small percentage by overseas companies) and in addition that carried out by USA-owned companies abroad.

differs by a factor of ten*. For Switzerland, Germany and France, it seems likely that pharmaceutical research expenditures have at least matched if not exceeded those in Britain. The pattern of innovation (Fig. 1) has followed the pattern of research expenditure. The United States is credited with the development of about ten times as many new medicines as Britain. Unless the American, Swiss, French, German and Scandinavian companies arrange for local manufacture in Britain, Britain would need to pay foreign currency for the import of these new pharmaceutical innovations. In the six years from 1959 to 1964 overseas pharmaceutical companies invested £24 million in Britain on major capital projects. Between 1955 and 1963, the total fixed assets of these companies reported at the Board of Trade increased from £12·1 million to £55·4 million. Throughout this period, this investment represented a substantial positive addition to our balance of payments; to offset this and the companies' export earnings, however, royalties or profits are transferred to the parent companies. Nevertheless in 1964 companies made a very slight net contribution to the overall balance of payments[15]. Thus, Britain was able to benefit from the products of overseas pharmaceutical research at no cost in terms of balance of payments, and to benefit from the employment provided and the taxes paid by the subsidiaries in Britain.

Further, the investment and activities by overseas pharmaceutical companies in Britain is paralleled by a corresponding overseas development by British-owned companies. For instance, the Wellcome Foundation has subsidiaries in more than 20 overseas countries, factories in 14, and a research unit in the United States. Three-quarters of their sales in 1966 were in overseas countries. The Glaxo group reported that for 1965/66 their total sales to external customers abroad amounted to nearly two-thirds of the total turnover. Other British companies have similar records. Beecham, BDH, Glaxo and ICI, all hold Queen's Awards to Industry for their export achievements.

Thus the case for expansion of the research effort of the pharmaceutical industry in Britain is strong when considered in terms of its contribution to exports and the potential for their growth

*The graph also shows total US government medical research expenditure. As in Britain, it has been rising more steeply than industry expenditure.

and in relation to the international pattern of investment and finance. This strictly economic appraisal of the importance of pharmaceutical research ignores the arguments which may be put forward in terms of improvements in the nation's health made possible with the development of new medicines. However, the possibility of obtaining substantial increases in the benefits to the community of new medicines through sales to the National Health Service depends largely upon the extent to which the finance of the Service can be expanded. As with the broad range of the social services, the possibility of increasing real expenditure on the National Health Service, depends to a great extent upon the growth of the economy, which in turn depends upon the long-term improvement in the balance of payments position. Thus, the social case for increasing pharmaceutical research in Britain would be closely related to and at many points is dependent upon considerations arising in the economic case for increasing pharmaceutical industry research.

RESEARCH AND STRUCTURE OF THE INDUSTRY IN BRITAIN

In general the results from pharmaceutical research are predictably correlated with the size of the research effort. However, it is suggested that very small pharmaceutical research units or very large units are relatively less productive than medium-sized ones[16]. The very large units may suffer from undue centralisation, so that decisions are too far removed from the actual work being undertaken. The very small units may lack finance to provide costly items of equipment and central services which are possible within a large organisation. At the smallest end of the scale, it has been estimated that a single research programme concentrating on a narrow field, becomes viable at an expenditure of £200 000 a year. A company spending ten times that amount will typically have about ten separate research projects in progress at any one time. In terms of results, a single limited research project, or a series of such projects each started when the last is abandoned, may take as long as ten years to produce a single marketable product based on a new chemical entity. It is unlikely ever to produce a really major new medicine, and will indeed probably have been specifically directed towards areas of specialist and limited scope which are particularly appropriate for a smaller research unit. A larger unit, for example with a £2 million a year pro-

gramme based on ten such projects, might yield an average of one new product every year or two.

Between 1950 and 1960, 432 new pharmaceutical products based on new chemical entities were placed on the market in the United States. Over the same decade, the US pharmaceutical industry's expenditure on research totalled about £410 million*. The rest of the industry's worldwide research during this decade cost of the order of a further £100 million, and the great majority of the new products resulting from this will be included in the total introduced into the American market. These figures, therefore, confirm that during this period on average rather less than one new product, based on a new medicinal chemical or biological, resulted from each million pounds of expenditure on research. Since then the figure has probably risen to the present estimate of nearer £2 million. Costs of research have tended to rise, and the demand for greater assurances of safety have reduced the productivity of research. The latter point has applied particularly in the United States. It has set up more rigid and bureaucratic safety procedures than Britain, which has preferred a more flexible system. Britain has thus been able to give more rapid approval for the introduction of new medicines, and in the long-term this should improve the British industry's internationally competitive position.

However, the fairly clear pattern of the relationship of research expenditure and results reveals some problems of scale in the present situation in Britain. The pharmaceutical industry's total expenditure on research of £11·6 million during 1965 included some £3 million by overseas companies: on the other hand, some British companies (notably the Wellcome Foundation which spends about three-quarters of a million pounds on research in the United States) finance research overseas, which is not included in this total. However, on balance, Beecham, Boots, Glaxo, ICI and Wellcome, each with a substantial research effort, shared a total research expenditure which in 1965 did not greatly exceed £8 million. Additionally, the smaller research efforts of Aspro-Nicholas, BDH, Guinness (on behalf of its subsidiary Crookes Laboratories), Smith & Nephew and others account for a further £1 million or so.

*For the years 1953 to 1960, the PMA report total research expenditures of £374 million. Extrapolating the trend backwards, from the expenditure of £24 million in 1953, the two previous years are estimated to account for a further £37 million.

Products such as synthetic penicillins, fluothane, betnasone, griseofulvin and many of the latest vaccines testify to the success which has resulted from pharmaceutical research in Britain; but the fact remains that with an expenditure of some £140 million in 1966, the Americans are very much more likely to discover and develop successful new medicines. At least one United States company spends more by itself than the total sum of all British research expenditure.

Table A shows the sales and research efforts of the five British, five American and five Swiss companies with the largest sales of prescription medicines in this country. Despite the fact that they are operating in, for them, an overseas market, the Americans substantially exceed the British sales. Their research expenditure is more than five times as great. The Swiss companies appear to have a proportionately less favourable ratio of sales in Britain to their total reputed research expenditure than the Americans. The significant fact from this table, perhaps, is that the leading British companies' research expenditure is equivalent to almost 40 per cent of their sales of prescription medicines through pharmacies in this country. This ratio underlines the necessity of these companies thinking primarily in terms of their overseas markets.

THE INDUSTRY AND THE NHS

Although the pharmaceutical industry finances its entire research effort out of its own sales revenue, the government does indirectly provide part of these funds in the price it pays for medicines supplied under the National Health Service. This applies, of course, not only to the research carried out in this country, but also to that carried out abroad.

In other cases, such as the computer industry in this country and the aircraft industry in America, where the government is a major customer buying the products of research, the price they pay sometimes contains a definite element of subsidy to support the early stages of a company's research programme and thus its future international trade. In the case of the pharmaceutical industry in Britain, there is understandably a difference in attitude. The National Health Service will never pay unreasonably high prices for its medicines simply to finance new research. Such expenditures, if they are fruitful, will be recovered in the price of future sales to the Service.

Table A

International Research expenditures and sales of prescription medicine to retail pharmacies in Britain for the five leading British, Swiss and American Companies.

Source: Sales : Intercontinental Medical Statistics Ltd.
Research : Company reports and personal communications.

	Sales 1964/65† £m	Research 1963/64 £m
Britain	19·2	7·5
Swiss	12·2	20*
USA	27·5	39·5

*Reputed expenditures : no figures are published
†June/May

Even accepting this government attitude, the problem has been to determine such prices. When research and associated costs have such significance, it is not easy to formulate an equitable pricing policy. The government recognise, on the one hand, that if they put too much pressure on prices it will exercise restraint on the companies' willingness and ability to expand research. On the other hand, the government is not willing to allow unduly large profits. The problem is further aggravated because in an industry with a high rate of innovation and obsolescence not only research but also marketing costs must be substantial.

For any customer, only a small element of the price of a recently introduced medicine is attributable to production costs. A greater part finances research and sales promotion. Strong resentments have arisen as a result[17]. Traditionally, it was considered easy to establish whether production was efficient, and whether a price related to production costs was fair. In the new situation it is much harder to establish whether research or marketing activities are efficient. There is, in any case, an emotional hostility to paying for advertising rather than for production, even though it is becoming increasingly recognised that much of modern industry operates on relatively low manufacturing costs and relatively high selling costs.

A Policy for the Future

A BROAD range of issues are involved in establishing a policy for the future. Pharmaceutical industry research in Britain in 1961/62 represented approximately one third of the total medical research programme, although under current policies this proportion appears to be diminishing. Its special characteristic is that since the results of research are embodied in saleable physical products, there exists a self-sustaining mechanism for financial support and the opportunity for direct benefits to the balance of payments. The question arises, however, to what extent the research effort should grow. The attempt to answer this in terms of broad cost benefit analysis techniques is fraught with difficulties. Consideration of the empirical case, centred on the impact of such new innovation on overseas earnings, points in favour of expansion, regardless of whatever case may emerge from the broad social arguments implicit in cost benefit analysis. However, probably more important, the possibility of expanding social benefit itself depends on improvement in overseas earnings, to which successful innovation by the pharmaceutical industry can contribute substantially.

It follows that there is much in favour of adopting empirical objectives in a policy for the future for the removal of obstacles to growth. This involves consideration of the appropriate structure of the industry in Britain to undertake a large-scale research programme, as well as the appropriate prices for the products of research sold to the National Health Service.

It must be recognised that expenditure on pharmaceutical research is a long-term investment. A compound synthesised for the first time in 1967 is unlikely to complete the necessary process of development and testing in order to reach the market before 1974. An entirely new research programme initiated in 1967 is unlikely to lead to any significant new product for

marketing before 1977. Even then, marketing costs may absorb all its earnings for another year or two. It may not be until 1980 that a research programme initiated in 1967 will begin to yield profits. The total cumulative investment in research may not be re-couped until many years later. In this situation the industry needs long-term stability if it is to expand research; companies may not risk investing in further research now unless they can forsee reasonable market conditions ten years hence. If the British-owned research-based pharmaceutical companies are not provided with an economic environment in which they can expand and compete internationally, Britain will become increasingly dependent on local manufacture of overseas innovations. The industry in Britain, instead of having its present international balance, will become wholly subsidiary, dependent on research carried out by overseas companies in their home countries, above all the USA.

If the British companies are to invest in more research they need the prospect of security in the maintenance of the market structure through effective patent protection and the prospect of adequate returns. At the same time, the government must ensure that the Health Service obtains its medicines at reasonable cost both from British and from overseas companies. The problem in the past has been the difficulty of establishing a basis on which the conflicting interests of the industry and the Ministry of Health could be balanced. As a result, too often, the debate has shifted to comparative irrelevancies such as the use manufacturers make of brand names or sales promotion. Insofar as these activities are associated with the total process of innovation, they should be accepted or indeed welcomed. In past criticisms, too little regard may have been paid to the long-term interests of the nation.

The problem of fair returns and ensuring adequate incentives does not apply solely to the pharmaceutical industry. These problems are common to all research-based industries where direct production costs may account for only a small proportion of total costs. A greater understanding is needed of the economic functioning of such research-based industries: even such questions as the relationship between innovation and the sales promotion necessary for its adoption are debated in emotive rather than economic terms. It has only recently been realised that any research budget—if it is to be productive in terms of

innovation—must be backed by the availability of very much larger resources for development, commercial application and marketing. A policy for the future must be based on economic thinking appropriate to research-based industry, rather than on traditional concepts. If wrong policies are adopted, the costs to the community in terms of opportunities lost will be substantial.

As far as the industry in Britain itself is concerned, it must adapt its research and marketing policies to the total international situation. It must find specialist fields of study, in which it can expect to stand on equal terms with its international competitors. The very wide range of pharmaceutical products in different fields makes it easy to find specialist areas in which British companies can achieve worldwide success. Beecham, for example, have already done this in the field of synthetic penicillins. Wellcome have done it in the case of immunological products. It would be wrong for these companies, small as they are by international standards, to attempt to cover the whole broad range of pharmaceutical endeavour. It seems likely, however, that the very steady and rapid process of amalgamation and rationalisation of individual British companies into larger groups which has been taking place over recent years may continue in the future. Past analysis suggests that this might increase the productivity of their research.

Medical Research Council expenditure, and that of the Universities, has been rising faster than that of pharmaceutical industry research*. On empirical economic grounds it would appear desirable that a greater proportion of this government research expenditure should be devoted to work which would encourage pharmaceutical innovation in Britain and hence benefit our balance of payments as well as our health. There is need for expanded facilities for properly controlled clinical trials of new products both in hospitals generally and perhaps especially in a few 'centres of excellence'. More fundamental work on pharmacology and toxicology would be of direct benefit to the industry's research programme, and hence to its success in world markets. The possibility must also be considered as to the desirability of some government research funds being used

*A similar, but smaller, imbalance between growth rates of government and industrial medical research expenditures has occurred in the United States. However, their greater overall wealth may justify this in their case.

to support directly the British industry's research programme. In the United States, the government provides about 4 per cent of the total finance for research undertaken by the pharmaceutical industry.

The general question of how much should be spent in the future on medical research and development is perhaps unanswerable. The problem is posed in terms of conflicting calls on scarce resources which is the essential question of all economic study. However, the benefits accuring from past efforts in research by the pharmaceutical industry have been substantial, and both socially and economically argue strongly for the general presumption that such effort should be increased. Thus, rather than speculate on defining appropriate levels of research, it is better to adopt a policy for the immediate future directed to stimulating growth. The specific benefits cannot be forecast precisely but this is scarcely surprising in the necessarily uncertain field of scientific research. For various reasons, not all the research-based industries in Britain have enjoyed such a notable record of innovation as the pharmaceutical industry. The costs of continuing to support the growth of pharmaceutical research in this country must be set against the risk of the pharmaceutical industry sharing the fate of others which have been less fortunate.

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