

has generally proved successful, and high powered marketing has been equally successful in selling the products overseas. But the method of organising science federally has changed more than once, and according to President Nixon's recent State of the Union Message it is about to be changed again, so perhaps the Americans have not yet found the right answer any more than we have.

Two points in conclusion. First, the signature of the EEC treaties in Brussels last week reminds us that we have to think in future on European terms, and try to secure that our organisation of civil R and D can make the most of European contracts and mesh in with our Common Market partners. There is a long way to go to find an effective way of managing collaborative projects so as to avoid delays and cut costs.

Secondly, I will end by once more quoting in part the book by Sir Richard Clarke. "We have been" he says, "through a decade of great uncertainty about the future structure of Government research, and it must soon be resolved. The next period will call for considerable rationalisation, not necessarily to create more large units, but to clean up scientific enclaves where small numbers work in cosy conditions year after year. It will call for continuous adaptation to the demand for the research facilities (and in some sense the requirements of the *market* in government and outside). . . New demands should be met . . . by contracts placed in under-employed establishments, (if such there be) and outside."

I detect here some presage of the Rothschild recommendations, and I believe that in spite of all the agonising in the Times correspondence page, it is along this general road that stability in the organisation of such research will in practise be found.

I am sure the ensuing discussion here today will bring out some constructive criticism and proposals, to add to those which are flowing in to the Chief Scientific Adviser.

GOVERNMENT, R AND D AND INDUSTRY; THE NEEDS OF THE PHARMACEUTICAL INDUSTRY

by
George Teeling Smith

The pharmaceutical industry's concern with government policy in relation to research and development differs from that of most other industries. This is because the industry is almost unique in financing virtually all of its research out of its own profits, instead of relying on direct government subvention. Less than a half per cent of the British pharmaceutical industry's R and D is paid for directly by the government, and the proportion is almost as small in other countries including the United States. By contrast, the British aerospace industry has more than 70 per cent of its R and D paid for by government grant, and the electronics and communications and industrial plant and steelwork industries each receive about 40 per cent of their R and D budget as direct payments

from the government. Thus in these other industries government is to a large extent able to dictate their R and D programme through a direct customer/contractor relationship. As an aside, one can point to the difficulties which this has created, for example with the cancellation of TSR 2 and a variety of missile projects, as well as the present controversy surrounding the Concorde programme. The pharmaceutical industry at least avoids these problems, because firms can control their own R and D programmes, and plan them in response to market forces. The industry, therefore, has no misunderstanding that its objective is to find new medicines which it can expect doctors throughout the world to prescribe for their patients. This in turn means that the industry is trying to solve the major disease problems, because the commonest diseases are generally those which create the largest markets and the most serious diseases are those for which doctors are prepared to prescribe the most expensive preparations.

The exception to that general statement, of course, is that underprivileged groups such as the lowest social classes may often be those most in need of medical care but least able to pay for it. This still applies in many less developed countries, because their governments perhaps rightly consider that nutrition, housing and environment control represent greater social and economic priorities than medical care. However, practically all developed countries apart from the United States the problem of maldistribution of medical care has been tackled by society. These countries have introduced various schemes for accepting as a community responsibility either the finance or provision of medical care. This has reinforced and extended the situation under which the greatest medical needs represent the potentially most rewarding pharmaceutical markets. It has, however, also brought governments or national social security schemes into a direct relationship with the industry. It is largely as a result of that relationship that special issues have arisen in connection with the pharmaceutical industry and government. It is these issues which are discussed in this paper.

Industrial and academic relationships

However, before discussing the problems which are central to the government-industry relationship in the context of our National Health Service (or any similar health scheme) there are some other less troublesome aspects which should be mentioned. First, there is the general relationship between the industry and the Universities, the Medical Research Council and the National Research Development Corporation. It is naturally true that much of the new fundamental understanding of disease processes comes from the Universities and the Medical Research Council. The research workers in the industry, therefore, need to maintain close contact with these bodies. To some extent this can be done by following the published literature, but in addition personal contacts can often be even more fruitful. In some cases this is achieved by an interchange of personnel, with industry research workers being seconded to academic laboratories, either on a full-time or part-time basis. For example,

the Royal Postgraduate Medical School has lately made arrangements for five visiting professorships for industrial scientists. In other cases, university medical research is sponsored by industry. In these cases the firm providing the money would expect to be kept most closely in touch with the progress of the research, so that potential leads to new products can be followed up by them. Finally, the Medical Research Council has itself recently become more aware of the importance for Britain of maintaining good liaison with firms in the pharmaceutical industry. The only problem which can arise from such interchange and liaison concerns commercial secrecy; but this should usually be overcome by good faith on the part of academic partners. All this, of course, is very much the field of the Licensing Executive, and this Conference is concerned with discussing the underlying policy as well as the detailed problems which arise when formal agreements have to be drawn up at the interface between government and industry.

In addition to their own formal and informal links with research in the industry, University laboratories and the MRC can pass on leads to industry through licenses from the National Research Development Corporation. An outstanding example of this was in connection with the group of antibiotics known as the cephalosporins. These have made an important contribution to health; they have been commercially very successful for the two firms to whom they were licensed by NRDC; and they provide by far the greatest part of the Corporation's annual revenue. We are fortunate in Britain that industry's exploitation of government-funded basic research appears to work much more smoothly than the corresponding arrangements in the United States. There the government has been so excessively concerned to "protect the taxpayers interests" that they have made collaboration between government and industry in medico-pharmaceutical research commercially quite unattractive. In this country, by contrast, one of the main difficulties in respect of the NRDC is that firms in the industry do not always seem to be aware of the help they could advantageously obtain from the Corporation, for example in funding very large or particularly risky research projects in their own laboratories.

Safety of medicines

The second main aspect of government industry relationships is also one in which Britain has so far avoided the pitfalls found in the United States. This is in connection with the safety of medicines. In practically all countries, it has been accepted by industry that government should have powers to exercise surveillance over the measures taken by industry itself to ensure, so far as practicable, the safety of medicines in relation to their efficacy. In the United States, this function has been performed for many years by the Food and Drug Administration. However, recently its ineptness and excessive bureaucracy have become notorious. Simply because of its cumbersome procedures and lack of balanced scientific judgment the Americans are prevented by the FDA from having important and even lifesaving new medicines until sometimes as long as three or four years after they

have been allowed on the market in Britain and elsewhere. Again by contrast, Britain has been held up as the model of good practice in this field. From 1963 onwards, manufacturers agreed voluntarily to submit details of their safety tests on new medicines to the government-sponsored Committee on Safety of Drugs, initially under the Chairmanship of Sir Derrick Dunlop. This Committee and its small permanent staff usually either gave clearance for marketing or else rejected the submission within two or three months — and sometimes within a few weeks. Since the latter part of 1971, however, these voluntary arrangements have given way to new statutory procedures, established under the Medicines Act, 1968. There have been high hopes that this new statutory machinery would work just as smoothly as the previous voluntary scheme. However, already there are signs that this may be hard to achieve. Indeed the delay of almost three years between the enactment of our Medicines Act and its first implementation illustrates the inevitably cumbersome nature of official bureaucracy. When everything has to be set down on paper, and made legally watertight, long detailed wrangles tend to ensue, often on quite insignificant points. Also, when it comes to implementation of even the most carefully worded regulations, difficulties of interpretation or practice can arise. If the new statutory Committee on Safety of Medicines, which has replaced the previous voluntary committee, gets bogged down in this sort of way it may quickly drift towards the situation of the US FDA. Everyone concerned is anxious to avoid this happening, but it will need constant vigilance to prevent it.

Patent protection

The third aspect of the pharmaceutical industry's relationship with government brings us closer to the central problems of prices, profitability and R and D. It is also of particular interest to this Society; namely the subject of patent protection. Going back ten years or so it was possible for witnesses before the Kefauver hearings in the US Senate, for example, as well as for many other critics of the pharmaceutical industry, seriously to argue that patents were unnecessary for pharmaceuticals. It was claimed, using the most inaccurate and misleading arguments and statistics, that pharmaceutical innovation could be successfully supported and fostered even in the absence of patents. Fortunately, that sort of irrational polemic is now confined to a minority of political extremists. Rational discussion on the pharmaceutical industry now takes it for granted that, in this industry in particular, new innovations — which are so costly and which can often be very easily copied — need to be sheltered from the chill winds of unfettered competition. However, before the importance of patent protection in pharmaceutical innovation was as clearly understood as it is today, an important anomaly had already crept in the British patent law. Regrettably it has also been copied abroad, particularly in many of the traditional commonwealth countries. This is Section 41 of the present Act, the Patents Act 1949, which singles out food and drugs as deserving less strong patent protection than any other class of goods.

This anomaly dates back to the 1914-18 war, when Britain had already lagged behind Germany and the United States in many technologies. She thus found herself deprived by the hostilities of the fruits of the recent advances in the German chemical industry, including the first newly emerging pharmaceutical chemicals. Emotionally, in the light of this experience, the British government wrote into the new patent law of 1919 provisions for more or less automatic and immediate compulsory licencing of pharmaceutical patents. Whereas to obtain a compulsory licence for other classes of goods it was necessary to allow a period of years to elapse and then to show abuse by the patent-holders, for pharmaceuticals this was made unnecessary. Although opinion was already swinging away from this discrimination against pharmaceuticals when the Patent law was again revised in 1949, Section 41 of the new Act nevertheless retained these special compulsory licensing provisions. The result is that unlike other innovators, the pharmaceutical manufacturers are under constant threat in Britain that if their product becomes commercially successful a copyist may obtain a license to introduce a competitive brand. Having borne none of the cost of innovation, these copyists can greatly undercut the originator's price and with little effort can take a large slice of the market built up by the original innovator.

In numbers, there have in fact been comparatively few successful applications for compulsory licenses under Section 41. However, when they have been applied they have obviously been used against the largest and commercially most important medicines. Also, Section 41 has so far been used mainly by very small entrepreneurs. This is probably because the larger companies have themselves been engaged in substantial research. They would not wish to invite retaliation by using Section 41 to obtain a competitor's innovations by force of law. The real threat to the industry would come if a large fine chemical manufacturer, or a large pharmaceutical firm which had opted out of trying to seek its own innovations, were to obtain a wide range of Section 41 licenses. Such companies would be in a position to indulge in large marketing expenditures which could make very large inroads into the original innovators' markets and profitability. This could make pharmaceutical R and D virtually impossible in Britain. Fortunately, this threat was foreseen by the Banks Committee which recently reviewed the British patent law. The Committee recommended that Section 41 should be repealed, and it is understood that the present government intends to implement this recommendation. Meanwhile, however, the threat remains and the industry is anxious for government to find Parliamentary time for this reform as a matter of considerable urgency.

The Banks Committee also made a general recommendation that the life of a patent should be increased from sixteen years to twenty years. This would, incidentally, bring Britain into line with the proposals for the EEC patent and will, therefore, no doubt also commend itself to our government. For pharmaceuticals, the extra years of patent protection will be especially welcome because so much of the original sixteen years has now been eroded by the time taken

to complete premarketing trials, safety tests and other preliminary procedures. Many medicines are now still in their prime of life when their patent expires.

The other area of difficulty in relation to patents is Section 46 of the present Act. As you will know, this allows the government to authorise Crown User of all classes of patented goods to obtain supplies from unlicensed sources if they feel it appropriate to do so. This is, however, best referred to in the context of the next section on prices and profits under the National Health Service. Although that forms the last section of this paper it deals with what is undoubtedly the central issue in relation to the government, research and development and the pharmaceutical industry.

The industry and the National Health Service

From the earliest days of the National Health Service both Parliament and the Committee on Public Accounts started to express concern about the possibility that too much was being spent on pharmaceuticals, either because doctors were prescribing too lavishly or because the prices of medicines were too high. Over the years, successive governments have taken steps to tackle both these aspects of what they see to be a "problem" area of expenditure. They have done this despite two facts. The first is that the pharmaceutical service has remained fairly steadily at only ten per cent of the total cost of the health service. The second is that there is increasingly hard evidence both that Britain spends less than other countries on medicines and that the prices in this country are lower than elsewhere. Nevertheless, following the pattern of its predecessors, the present government continues to promote low cost prescribing and to maintain strict surveillance on pharmaceutical prices.

Although the government measures to encourage low cost prescribing obviously affect the industry, they are peripheral to the main issue and are, therefore, not discussed here. Turning to the subject of surveillance on prices, the first Voluntary Price Regulation Scheme between the then Ministry of Health and the Association of the British Pharmaceutical Industry came into effect in 1958. This was based mainly on the principle that prices would be accepted under the Health Service in Britain if they were no higher than the average prices charged for the same medicines in markets overseas. As British prices were already generally below the world average, this first Scheme, to the intense disappointment of the politicians, produced little or no reduction in NHS prices. At the same time, however, the Kefauver hearings in the United States were calling into question the effectiveness of price competition for prescription medicines even when they were paid for privately by the patient. Because of this, the revised price regulation scheme in Britain in 1961 introduced an additional method of price negotiation. For the largest selling products manufacturers were asked to negotiate directly on the basis of the overall profitability of their business.

This new method of negotiation has two inherent difficulties, which so far from being resolved in the intervening years have instead become more clearly apparent. The first is that it is totally impossible, in

a typically multi-national and diversified pharmaceutical firm, to identify the actual profit earned on sales to the National Health Service. With the best will in the world, it is impossible to isolate all the costs and particularly the capital employed in relation to one narrow national sector of a complex and integrated international operation. Accountants now accept this; politicians have not yet done so. Second, even if hypothetically one could isolate the profitability of sales to the NHS, there are no criteria under existing economic theory to determine whether the profitability is reasonable or not. The essential question is whether a reduction in profitability would reduce R and D investment and hence stunt the future growth of the industry in this country. Industry believes it would. Government, on the other hand, challenges this claim and is tempted to squeeze profit margins and see what happens. Industry believes that would be altogether too dangerous an experiment! It also points to the undesirable side effects of lower prices in Britain which are discussed later.

These problems in assessing profitability were, however, not well understood in 1961 when the second Voluntary Price Regulation Scheme was agreed. The consequent difficulties which arose in the subsequent individual price negotiations led up to the incident in which the then Minister of Health, Enoch Powell, used Section 46 of the Patents Act to authorize the purchase by hospitals of some patented antibiotics and other medicines at low prices from unlicensed sources. At the time, the patent holders believed that they were acting in good faith, trying to obtain from abroad additional financial information being requested by government and trying to explain the reasons for their apparently high profitability. The Ministry of Health, however, believed the companies were dragging their feet in the negotiations. The Minister was also under considerable political pressure to authorise hospitals to buy from cheaper sources, which they were in fact already doing illegally. At least in political terms, it was probably inevitable that Powell should have chosen to use Section 46 in the circumstances. This was, in fact, the only occasion on which government has resorted to using Section 46, although the last Labour government extended its scope so that it could now be used for the general pharmaceutical service as well as hospital supplies.

Despite this early warning of the difficulties in direct negotiation on the basis of profitability the principle was extended to cover a wider range of medicines when the VPRS was next re-negotiated in 1964. Finally, in line with a recommendation of the Sainsbury Committee, which reported on the industry's relations with the NHS in 1967, the 4th VPRS moved away almost completely from the basis of international price comparisons. The present 4th VPRS relies instead predominantly on direct negotiations on profitability. Each company now files an Annual Financial Return, giving in great detail the sales and costs of its business. On the basis of these figures, the Department of Health and Social Security (which now incorporates the former Ministry) is entitled to discuss with each firm not only their profits but also individual costs (such as advertising) in cases where the Department

considers them too high.

Many firms in the industry always believed that this Scheme was impractical, for the reasons already described, although the majority agreed to go along with it voluntarily. However, having now had two years' experience of its operation many regret having agreed to it. The negotiations have proved much more elaborate and extensive than companies ever anticipated. Often the government accountants and those of the firm's own auditors are simply unable to agree what the correct figures on the Annual Financial Return should be. These disagreements arise mainly from the difficulties in apportionments of costs and capital between home and overseas business and between NHS medicines and other products. The result is that discussions with Department of Health officials may start off with two often very different sets of figures on the table — itself an unpromising basis for reaching agreement.

One of the most serious difficulties of all with the Scheme, however, is that it introduces a direct motivation for firms to reduce their profitability by inefficiency. If a ceiling is put on profitability, as it implicitly is under the VPRS, firms are much safer to keep below this ceiling by increasing costs than by reducing prices. By doing this, when sales fall as their best products are overtaken by competitive innovations the firms can restore profitability by trimming back costs. By contrast, under the Scheme, they would be unable to restore profitability — at least to the levels they felt reasonable — by putting their prices back up again if they had reduced them in happier days. That description, of course, is a gross oversimplification of the actual very complex pricing and costing decisions a firm will take in practice. Many prices are reduced quite outside the Scheme for good commercial reasons. However, it does characterise one of the most undesirable aspects of the present VPRS.

Looking abroad, other countries have been no more successful than Britain in finding ways of demonstrating that the prices paid for medicines are "reasonable". They usually fall back on general downward pressure on prices by the health schemes of the various countries, under various bargaining arrangements which are much less elaborate but probably no less satisfactory than the VPRS in Britain. In addition, increasingly, other countries have introduced the principle of international price comparisons much along the lines of the first British VPRS.

The spreading international practice of looking at prices of the same medicines in other countries has an important implication for the pharmaceutical industry and the economy of Britain. Insofar as Britain is a relatively low-priced country for medicines and insofar as the present VPRS tends to force prices down further this country becomes a relatively unattractive base for pharmaceutical exporting. The commonest practice in overseas countries is to look at the price in the country of origin of exports. Firms can, therefore, expect to get a higher local price if their exports have come from a higher-priced overseas base. Furthermore, in an essentially international industry, such as pharmaceuticals, companies have great flexibility in shifting production and R and D from one

country to another. The fear is that if undue pressure is put on prices in Britain it would, therefore, jeopardise the industry's present UK export performance. This was about £165 million in 1971 and its rate of increase has been more than 20 per cent a year since 1967. Any reversal of this upward trend would not only mean a slowing down in the growth of investment and employment by the pharmaceutical industry in Britain, but would obviously also have a direct adverse effect on the balance of trade — and incidentally a reduction in the taxes collected in Britain on export earnings. In addition, under an unfavourable political and economic climate in Britain both British and overseas-owned firms could decrease their local R and D investment. This would reduce scientific employment opportunities and probably encourage skilled manpower to move abroad.

Conclusion

The title of this paper is the "needs of the pharmaceutical industry". Let me briefly summarise what I have asked for on behalf of the pharmaceutical manufacturers. First, a continued good relationship with the Universities, the Research Councils and NRDC, and perhaps a better understanding on both sides of the benefits which can flow from co-operation. Second, as little bureaucracy as possible in the implementation of the new Medicines Act. Third, the early implementation of the Banks Committee recommendations in respect of the patent law. Finally, a better understanding by government of the dangers for the industry and the economy from the present very cumbersome Voluntary Price Regulation Scheme.

Despite past criticisms, the pharmaceutical industry is proud of its contribution to medicine and science and to the economy of Britain. It asks for government to help it in further improving this contribution.

GOVERNMENT RESEARCH AND DEVELOPMENT AND INDUSTRY

by
*Handel Davies, C.B.**
*Read for him by Roy Orford***

Introduction

The total expenditure on R & D in the United Kingdom is now running at around £1,000 million per year. Of this total the Government contributes about £600 million; considerably less than either France or Germany, less than 1/10 of the American expenditure, but substantially more than Japan.

Our future as an advanced industrial nation and consequently our future prosperity is clearly dependent to a considerable extent on the wisdom with which this expenditure is planned and the skill with which the resulting research R & D programmes are executed. The organisation for planning and executing our R & D programmes is, therefore, a matter of great public concern.

The reaction to the Rothschild/Dainton Green Paper, and in fact the conflicts within the Green Paper

itself, has brought into the open the very wide-spread controversy which exists on this subject. The scientific community have reacted strongly against the Rothschild proposals, particularly the recommendation that some of the work at present controlled by the Research Councils under the overall direction of the Department of Education and Science should become the responsibility of other "User" Ministries under a customer/contractor relationship. Correspondence columns of *The Times* have been inundated with protests. But it must be remembered that this controversy, important as it undoubtedly is, affects only a very small proportion of the total national R & D activity. It affects less than half the area of responsibility of the Research Councils, i.e. less than £50 million or 5% of the total national expenditure. By contrast R & D work carried out in industry accounts for well over £500 million of expenditure per annum; £200 million of this being funded by the Government and most of the rest by the industry itself.

I therefore make no excuse for concentrating most of what I have to say on areas outside those covered by the Research Councils. In any case my own personal experience lies entirely in the fields of Defence R & D and in Aerospace, and it may be useful if I discuss the relationship which has developed between Government and Industry in these fields. It is a relationship which has evolved over a period of more than half a century. I believe that on the whole it is a good relationship, but I must hasten to say right at the outset that the type of organisation which is ideal in one area might be quite wrong in another. It is not a question of whether the work is pure or applied research. The distinction between pure and applied research is in any case very arbitrary. The optimum organisation depends on the nature of the work which has to be done and particularly on the extent to which success is dependent on original ideas on the one hand or upon systematic hard work on the other.

Relationship between Government and Industry in Defence and Aerospace R & D.

Government expenditure in "Defence R & D" amounts to over £200 million per annum. This is, however, a misleading figure when compared with R & D expenditure in other fields, since most of it represents the cost of designing and making prototype and development batch aircraft, weapons and equipment.

A more realistic figure in the present context is the part of the total spend which is usually referred to as the Defence Research Programme. It represents all R & D work other than that which can be associated with particular approved projects. This amounts to about £40 million per year; about 60% of this total is spent in the Government's own R & D Establishments. There are 28 of these varying in size from very small establishments like the Stores and Clothing Research Establishment, to the Royal Aircraft Establishment which employs some 7,000 people including well over 1,000 Scientists. The ratio of the work in the Government's own Establishments to that in industry varies widely between different areas. In the Aero Engine field about one-quarter of the total expenditure