Pharmaceuticals Among the Sunrise Industries

Proceedings of an Office of Health Economics Symposium

Edited by

Nicholas Wells

The social and economic strength of the Western World in the 1980s and beyond will depend on a new pattern of industrial activity. The 'twilight' industries, such as ship-building and textiles, will survive only as a remnant of their former splendour. The 'noonday' industries, such as engineering and aerospace, will only keep ahead of their competitors in less developed countries by virtue of constant infusions of new technology. However, it is the 'sunrise' industries, such as electronics, nuclear energy and pharmaceuticals, which provide the greatest prospect of economic growth.

This book addresses issues and problems of the sunrise industries, using the pharmaceutical industry as an exemplar. It is based on a symposium held by the Office of Health Economics in October 1984. One issue in the book is that traditional economic theories do not explain pricing policies or factors necessary for growth in this industry. Another is that it is technology-intensive rather than manpower-intensive. As a result it faces a certain amount of hostility despite its potential for creating wealth. The book is thus likely to be of great interest to economists, including health economists and policy-makers in industry, science, health care and technology.

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PHARMACEUTICALS AMONG THE SUNRISE INDUSTRIES

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Edited by
NICHOLAS WELLS
Office of Health Economics

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To investigate other health and social problems.
To collect data from other countries.
To publish results, data and conclusions relevant to the above.

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SPEECH TO THE SYMPOSIUM DINNER

David Owen

What is going to happen to the UK economy once North Sea oil revenues peak in 1986 and then start to fall? Admittedly there will be a continuing return from the greater investments made overseas during our oil-rich period, but this will not cover the loss of oil revenues. This year alone without oil our visible trade deficit would be £11.4 billion. The degree to which oil masks the basic weakness of the British economy is frightening. The best hope that we will be able to reverse our long-term relative decline and replace the loss in oil revenues is if we rapidly apply the new technologies.

Yet research into and development of these technologies is still too slow and anyhow not enough to secure the future. Even though they provide our industry with a scientific and engineering foundation, the product has to be marketed. The lack of success overall in UK marketing, although there have been some brilliant results, has meant that we have failed in the past to get much of our basic research turned into products which our own consumers, let alone overseas consumers, will buy. The sequence of R and D is too often not viewed as a continuum, including the marketing process. We need to think more in terms of Research, Development and Marketing (R, D & M). Since development and marketing take considerable time, it is all the more urgent that the UK organises itself to capitalise on the new technologies now, well before the cushion of oil revenues fades away.

It is to the interface between higher educational institutions, industry and the market place that we must look to improve performance. The university/polytechnic companies now being established to exploit their research – and the other research and commercial organisations associated with the University Directors of Industrial Liaison (UDIL) – are starting to develop this new R, D & M continuum. They range from the established, such as Sinclair Research at Cambridge, to the latest, such as Newtech at Bangor, Clwyd. These companies, among others, are trying to catalogue technology development in universities and polytech-

nics at such a speed and in such a way as can best serve the national interest. Following UDIL's successful feasibility study, the Universities' Technology Index (UTEX) could be up and running by the autumn of 1985 as a valuable national data base.

There are already strong indications that much of UK industry is keen to use this data base. But the gap between higher education institutions and companies is still too large in the UK and more urgent action is required to bridge it. For the 'technology push' to succeed there has to be 'market pull'.

In the last five years several reports have examined the transfer of technological innovation across the university/industry interface. They all confirm that our universities and polytechnics are active in applied R and D and successful at it, but it is the transfer to industry where there are still gaps. Even the great corporate laboratories, which formerly devoted substantial resources to long-term projects, have been forced by financial stringency in the recession to limit much of their efforts to improving current products and processes and to the development of new technology for perceived markets two or three years away.

It has been argued that inward licensing – whereby we buy licences from overseas – could solve the immediate problems of some UK firms. The growing deficit of Britain's balance of trade in high-technology licence fees over the past few years is evidence of the popularity of this method.[1] There is a great risk that, as licensees, UK companies will end up buying the serviceable, second-hand technology while the licensor nations will be marketing new technologies. In the longer term, therefore, this solution can be good neither for individual firms nor for the UK as a whole.

Britain has a long history of being prolific in invention and innovation, but we have also allowed some of our best ideas to be developed overseas. There are worrying signs that this is being exacerbated at present through the early export of raw ideas followed by reimportation of technology based upon them from entrepreneurial foreign companies who make us pay a heavy price for the development value they have added.

If the processes of innovation are to reach a successful conclusion here in the UK, they must run in parallel with a deeper and consistent study of the target of the innovative concept or product or service – the customer. A comparative study[2] of the UK and West German machine tool industries,

while not conclusive, indicates how attitudinal factors influence performance. We once dominated world markets for machine tools, but we have lost heavily in the last thirty years to Germany, the USA, Japan and, most recently, to Korea.

The UK companies appeared to have more of the trappings and less of the substance of marketing than the Germans. According to this research, customers of the German firms tended to value technical attributes and were more likely to suggest ideas for product developments or new products than the customers of the UK companies. Given that the customers of the German firms have a more positive attitude to new technology, it is clear that their role may be crucial in new product development. An active user creates an active supplier. This is the maxim our industry needs to learn.

A report on the development of university-based enterprises in the USA[3] shows that, far from being innovative and daring, the UK is only now casting a first line into waters that the Americans have been fishing profitably for years. New types of business which work well in the USA will not necessarily adapt to the less entrepreneurial UK scene, but attitudes are changing and there is evidence that industries based on advanced technologies can thrive in the UK. New companies based on electronics, software, infomatics and biotechnology have been formed. One example, in the public sector, is Celltech, which was set up in 1982 with an advantageous technical position through its former agreement with the Medical Research Council (MRC) to exploit research of the Cambridge Molecular Science Laboratory. Although there has been criticism of the commercial advantage given by this flying start, this criticism is difficult to sustain in view of the scant interest of other UK companies in the MRC research programmes prior to Celltech's formation.

Besides an 'inside track' with the universities and colleges, the Americans have identified other ingredients which are needed to grow advanced-technology enterprises. In the UK there are three key requirements for the successful transfer of technologies from universities to companies. First, the selection of inventions from higher education institutions for development on the basis of feasibility studies which would be best carried out, in close collaboration with the inventors, by the UK university companies. Second, the development of these selected frontrunners to the point at which there is a product, not just an idea, so that there is

more profit to the initial investor because the risk, as perceived by the industry, is low enough to gain support. Third, the marketing skills needed to moderate raw 'technology push' with a knowledge of what the market is likely to want when the R and D period is successfully completed.

These three requirements, according to the 1984 *Annual Report* of the UDIL,[4] could be satisfied by, first, the rapid generation of an on-line data base of industrial technology in the higher education institutions, the British Technology Group (BTG), the Science and Engineering Research Council (SERC) and elsewhere, which could be screened for industrial feasibility and so provide a short list of candidate projects. This is being started already as part of the UTEX service. The second measure prepared by the UDIL would involve the formation of technology, development and marketing companies (TDM companies) and other higher education institutional liaison units. Following American experience TDM companies in the UK would work closely with those bodies that fund the upstream R and D in universities which generate suitable possible projects. They would also form downstream links with venture capital firms specialising in the finance of innovative projects. In addition, they might assist established bodies such as the SERC, which could receive a royalty on the results of publicly funded research that are used to generate profitable new technology and also the British Technology Group by possibly providing development facilities in exchange for the services of BTG's competent and experienced patents and licensing people.

We need an industrial credit scheme operated by and through the banks, with improved tax breaks designed to favour precisely this type of investment. In the USA both federal and state governments provide a range of tax and soft-loan incentives for data bases used by TDM companies.

There is money and prestige to be made from supporting the right research at the right time. If the UK misses this opportunity to turn its research results and findings into marketable products, there may not be many others to come. Action must be taken now if it is to be effective. It will be too late once the oil revenues have gone.

It is appropriate against such a general background to look at the pharmaceutical industry as an example of a successful research-based industry. Traditionally some 90 per cent of new

drugs (new chemical entities, NCEs) are discovered and developed by the industry itself. But the industry has also had very strong informal as well as formal links between academic and hospital-based research units. On the Medical Unit at St Thomas's in 1965 I worked very closely with ICI on a research project before propranolol was marketed and I have no doubt that these links are vital. Many companies are now turning to the biological route in the expectation that a deeper understanding of the biological and biochemical causes of illness will lead to a number of new discoveries. Hence the growing links between the companies and university departments of biochemistry and molecular biology.

Despite the innovative success hitherto of the British industry, substantial problems lie ahead and we should not necessarily believe that the former pattern should remain inviolate.

As a result of demographic changes and technological advance, health care costs will increase in the OECD countries at twice the rate of GNP over the next ten years. There will therefore increasingly be immense pressure on all OECD governments to attempt to introduce economies and the drug industry cannot expect to be exempt. In the developing world the financial pressures from the impending debt crisis are considerable and the medical needs even greater. The demand for low-cost drugs and vaccines is being accompanied by a perfectly understandable determination to break pricing policies from the predominantly OECD manufacturers which they feel exploit their position. The concentration on marketing brand names and not supplying the cheaper generic drugs will not last and does not deserve to last. I particularly applaud the initiative that the World Bank and the Wellcome Foundation have taken in establishing a discovery programme for developing an effective treatment for onchocerciasis.[5] Other pharmaceutical companies will hopefully take up similar opportunities to focus on developing countries' needs since in the long run with demand and numbers so large, even without exploitative pricing, it will bring substantial rewards.

Advances in medical science, particularly in the fields of immunology, genetics, virology, neurobiology and molecular biology, have been spectacular over the past few years. Yet pharmaceutical innovation, as judged by new chemicals marketed, has fallen to around 20 per annum over the past ten years – both in North America and in the UK – in contrast to around 50 per

annum two and three decades ago. The number of new chemical entities has not only decreased, but those that have been introduced have concentrated to a large extent on just a few heavily oversubscribed therapeutic fields.

New pharmacological knowledge, especially the discovery of regulatory peptides, novel transmitter mechanisms and the characterisation of receptors, offers numerous therapeutic applications. Novel pharmaceutical delivery systems such as transdermal devices and methods of targeting drugs to their sites of action offer considerable scope for real progress. The 'knowledge depletion' hypothesis that the industry has largely exploited medical science is therefore untenable. There are therapeutic needs and there are new worthwhile discoveries there to be made. The justification for a new drug must be, however, that it meets a therapeutic need in a way that offers advantages which are more than marginal – a view strongly endorsed by John Griffin, the new director of the Association of the British Pharmaceutical Industry (ABPI), writing in 1981 in the *British Journal of Clinical Pharmacology*.[6]

Some argue that the decline in innovation has been due to overburdensome data requirements by national drug regulatory agencies. But in the UK the operation of the Medicines Act has been largely successful, and the Committee on Safety of Medicines has succeeded in balancing the interests of the industry with the needs of the community. Consequently, the delays in introducing new drugs – the so-called 'drug lag'[7] – which have been such a feature of the operation of the FDA in the USA, have been less in this country. The Clinical Trials Exemption Scheme introduced in 1981 has also helped. As a result of the top ten overseas companies operating in Britain, seven have established major research laboratories here and launched their new products first in the UK.

An inevitable inhibitory factor in innovating drug research is its cost. In 1960 UK pharmaceutical firms, including overseas firms, spent 5 per cent of turnover on R and D (£2.8 million at current prices); in 1982 they spent 15 per cent on R and D (£295 million at current prices). At constant prices, the research and development costs of a new chemical entity increased from £15 million in the late 1960s to £60 million in 1982 – or £90 million if you take into account the cost of failures. With the possible exception of drugs for rare diseases, I see little prospect for this

to be substantially reduced when over half these costs are accounted for by the initial synthesis of the compound, its biological screening and its early preclinical evaluation.

According to a 1984 NEDO study on the industry,[8] a further inhibition on innovation is the reduction in government research funding threatening the quality of research in universities and hospitals. If less research is done, the flow of new ideas for development by the industry will be reduced. There is already a shortage of good researchers in biochemistry, biology and pharmacology, and increasing competition for them. Government policies which affect the volume of research and the attractiveness of research as a career should be urgently reviewed.

Although it will not be popular with some sections of the industry, I believe that the marketing climate for pharmaceuticals has also hindered innovative research. Over the last ten to fifteen years it has been too easy for companies to make handsome profits from the synthesis and development of 'me-too' drugs concentrated in narrow areas. In addition, the reliance of some companies on the sales of their older drugs, protected by brand-name prescribing but long out of patent, has provided them with a spurious form of protection against competition which has not been in the long-term interests of either the industry or the community. Brand-name protection of out-of-patent products, and the reimbursement of expensive 'me-too' drugs, will be amongst the first casualties. This trend has already started in the USA, and the industry must understand and accept that it will continue inexorably throughout the developed and developing world.

But the loss of brand-name protection for out-of-patent products should not mean that pharmaceutical innovation goes unrewarded. On the contrary, in my view the industry has a good case when it argues that the time taken to develop a drug from the laboratory to the clinic has eroded patent lives and tended to reduce incentives. The complexities of modern science, coupled with the time taken for regulatory review, have resulted in effective UK patent lives of only 5 years in 1982 compared with 14 years in 1960 and there has been a similar trend in the USA.[9] I strongly believe that companies which produce truly innovative new medicines must be able to expect a healthy return on their investment from society – both to act as a reward and incentive, and to finance further innovative research.

I therefore believe that in order to encourage innovation, the patent lives of novel pharmaceutical products should be determined from the date of first marketing, rather than the date of filing. Such a move is compatible with existing international agreements on patents, and is a measure the government should enact with speed and would certainly be the logical and fair offset to curbing brand-name prescribing by GPs and putting the emphasis on generics.

What about the Pharmaceutical Price Regulation Scheme (PPRS) – which I remember in my time as Minister of Health as the VPRS? It is of course a profit control system and only indirectly a price restraint system. It is a secretive, corporatist device which probably now inhibits innovation since it cocoons the industry from competition. As sadly one would expect, the House of Commons and Ministers concentrate on the immediate price aspect of the system, important though that is, but of far more long-term importance is the system's impact on innovation.

On price there is little doubt that the Public Accounts Committee argument will be accepted: that since 17 per cent is the target rate for a return on capital for defence contractors on projects which are deemed as commercially risky, 17 per cent should apply to the pharmaceutical industry as a whole. The NEDO study on the industry recommends that the civil servants who fix the permitted rate of return should encourage greater innovative research. This is already attempted but is very hard to achieve when the system allows prices to rise to offset lost profit, whether from generic prescribing or parallel importing.

The challenge to the pharmaceutical industry which constantly invokes the spirit of enterprise, competition and market economics is whether it really wishes to go into the next century living under government profit control. There is a strong case for believing that the real interests of innovation and research in pharmaceuticals would be better served by a system of price competition with reasonable patent protection so that profits go to those who make the real breakthroughs in therapeutics. This would mean the NHS and its suppliers, the companies, negotiating price drug by drug just as buyers and sellers do for different products in other public industries.

Notes

1. *Management Today* (February 1984).
2. *The Business Graduate* (July 1984).
3. *The Economist* (May 1984).
4. University Directors of Industrial Liaison, *Annual Report, 1984*.
5. Wellcome Foundation, *Annual Report, 1983*.
6. *British Journal of Clinical Pharmacology*, vol. 12, (1981), pp. 453-63.
7. *British Medical Journal*, vol. 281 (November 1980).
8 *Chemicals – The Pharmaceutical Industry* (NEDO, London, April 1984).
9. *Pharmacy International*, vol. 3, no. 7 (1982), pp. 230-6.

INTRODUCTION

Nicholas Wells

The performance of the United Kingdom economy has been the subject of much critical comment in recent years. Of course, economic achievement can be viewed from many different perspectives, giving rise to conflicting interpretations of national progress. Furthermore, it is axiomatic that global indicators camouflage a spectrum of experience spanning all degrees of success and failure. Yet, on balance, the censures would appear to be justified. Focusing on gross domestic product (at constant factor cost), for example, the data show that the average increase of 3.23 per cent per annum achieved during the 1960s fell to 2.25 per cent in the 1970s and that in the 1980s to date annual growth has averaged only 0.53 per cent. The figures reveal a yet more disturbing state of affairs if the revenues flowing from the nation's North Sea oil reserves are discounted. Thus between 1976 and 1983 growth in gross domestic product averaged 1.5 per cent per annum. Without the benefit of oil an annual improvement of just 0.7 per cent would have been experienced.

Oil has also become an increasingly important prop of the United Kingdom's external trading account. In 1983 exports of oil and related products stood at £12.5 billion or 20.6 per cent of the total value of goods purchased from the nation by her trading partners. (In 1975, by contrast, the corresponding figures were £0.7 billion and 3.6 per cent.) Without the contribution from oil exports, the United Kingdom's trade deficit in 1983 would have been almost three and a half times the recorded loss (£17.9 billion instead of £5.4 billion).

It is against this background of oil dependency that economists and others view with alarm the imminent peaking of North Sea oil revenues and their subsequent decline. No successor to oil, at least on a scale capable of generating levels of benefit akin to those noted above, is apparent on the immediate horizon. Yet hopes of escaping from this slough of economic despondency have not been abandoned entirely. Economic salvation, it is argued, may be achieved, in part at least, if full advantage is

taken of the opportunities currently offered by the 'sunrise' industries.

The term 'sunrise' is an appropriately optimistic adjective used to describe a range of industries displaying several common attributes. In general terms, those belonging to this group are relatively new, technologically progressive concerns investing heavily in research and development in order to foster not only growth but, more fundamentally, survival given the heightened vulnerability of their products to rapid technical obsolescence. Manufacturing companies operating in the fields of electronic data processing, electrical and electronic engineering, aerospace and pharmaceuticals – together these four accounted for almost two-thirds of the £3.8 billion spent on research and development in industry in 1981 (*British Business*, 1983) – thus exemplify the constituents of the sunrise industries.

It would, however, be misleading to imply that precise criteria exist for defining a sunrise industry. The boundaries of the concept are not rigidly circumscribed. For example, incremental developments antecedent to a specific technological advance or innovation tend to obscure the beginning of the sun's ascent. In addition, the points along the transition from sunrise through midday to sunset are equally as difficult to locate as those differentiating high-, medium- and low-technology medicine. Furthermore, as Sir Bruce Williams suggests in his paper, it is probably more accurate to think in terms of sunrise technologies rather than sunrise industries. Thus the new technologies founded on biological mechanisms and semiconductors, for example, are proving valuable in a wide range of long-established as well as relatively young industries. Focusing on the former, the entire September 1981 issue of *Scientific American* was devoted to the development of industrial microbiology and revealed a remarkable breadth of application for the techniques from food and drink production through pharmaceutical manufacture to their use in the detoxification and degradation of sewage and industrial waste.

Setting these conceptual niceties to one side, the essential point remains that future economic prosperity seems likely to be dependent in no small measure upon the success of the nation's innovation-based industries. Consequently, efforts must be channelled into promoting an environment that is propitious to their progress. And this need would appear to have gained wide

recognition. In September 1983, for example, the Prime Minister chaired a seminar on science, technology and industry at Lancaster House in London to explore potential ways forward. There is, in addition, no shortage of advice. Most recently, a report from the Conservative Bow Group has argued that financial support for the new technologies of the 1980s, such as information technology and robots, should be withdrawn and redirected into developments as yet untapped by the nation's industrial competitors. Thus resources should be allocated to 'ceramics, carbons, engineering plastics and nuclear fusion which are likely to be the industrial leaders of the 1990s' (*The Times*, 1984a).

Clearly, the sunrise industries embrace a multiplicity of issues worthy of detailed discussion, not the least important of which are the prerequisites necessary for their take-off and subsequent progress. Focusing on the latter, three major factors emerged during the course of the OHE Symposium and consideration will be given to each of these before attention is turned to the specific case of the pharmaceutical industry.

First, attitudes which welcome and encourage change are a key requirement. In this respect, Japanese thinking typifies the approach that is necessary. It has been argued that the Japanese are especially persuaded followers of the Schumpeterian concept of 'creative destruction' and that there seems to be 'an unusual appreciation of the fact that movement to higher standards of living requires that some industries are losers in the process while others become the next generation of winners' (Abegglen and Etori, 1983). This underlying philosophy has paved the way for the processes of industrial restructuring that have helped to more than treble Japan's share of the world economy since 1960 and that are now prompting increasing reference to 'Shinsangyo Kakumei' – a new industrial revolution.

At the same time, however, Japan has sought to ensure that those industries displaced during the course of industrial transition are not allowed, through neglect, to fade into economic obscurity. Instead their roles are being adapted to meet new needs. Thus as the sun rises on the electronics industry and steel manufacturers move into the shadows, the latter will increasingly focus on the development of sophisticated products that are beyond the technical capability of the new low-cost suppliers of standard grades of steel, countries such as Brazil and South

Korea. The critical point is that, as both Sir Bruce Williams and Erich Kaufer emphasise in their papers, 'declining' industries have an important role to play – as sources of economic stimulus and material supply – in the evolution of the sunrise industries. Adaptation rather than demise is thus the objective.

The second prerequisite is concerned with research and development, the foundation of innovative industry. In this context it is encouraging to note from David Owen's text that valuable links continue to be developed between industry and academia. This trend should facilitate more rapid and effective commercial exploitation of basic science discoveries. At the same time, however, there is considerable disquiet about the allocation of resources to research endeavours in this country. Thus the Chairman of the University Grants Committee has warned that 'Britain's scientific research is falling dramatically behind that of other advanced countries because of inadequate funding' (*The Times*, 1984b). And in a leading article entitled 'Dead-end for British Research', the internationally respected science journal *Nature* (1984) has recently argued that 'by parsimony, indolence and indifference, the British Government is killing off imaginative research'.

Latest complete expenditure data indicate that the United Kingdom spent around £6.3 billion on research in 1981. This sum was equivalent to 2.9 per cent of the gross domestic product and represented an investment in research valued at £113 per head of population. The significance of this level of spending, from an international perspective, is not immediately apparent. Irvine (1984) has suggested that as a proportion of gross national product British funding is in line with that of the United States, Japan and the rest of Europe. But given the vast disparities in national wealth, this of course implies substantial discrepancies in research finance in absolute terms. And the meaning of such sums is then further distorted by variations in currencies' domestic purchasing power and fluctuations in their exchange rates, leaving aside all questions relating to the strict comparability of different nations' basic data on research spending.

Focusing specifically on the funds available for research in the United Kingdom, there appear to be two major issues. First, there is concern at the level funding approach applied by the government to its support for the research councils (valued at £500 million in 1983/4 of which half went to the Science and

Engineering Research Council). This policy, the effects of which are exacerbated by the decline in the financial assistance available from universities and the reduction in the volume of research commissioned by government departments, is argued to be particularly harmful because of the special nature of costs in research (Humphreys, 1984). The expenditures necessary to purchase modern scientific instruments, without which a position at the forefront of progress cannot be retained, increase with each new advance at a rate which is substantially greater than that reflected by the mundane items comprising the retail price index. The problem is, therefore, that level funding fails to accommodate this 'sophistication factor'.

The second issue relates to the appropriate allocation of research funds. Humphreys (1984) has argued that the Japanese have been successful in choosing areas for research which have had a substantial economic pay-off. In contrast, 'Britain has backed the research equivalents of Concorde and has chosen to give priority to areas which are elegant, costly and of little economic benefit.' He contends, therefore, that the Science and Engineering Research Council's expenditure in 1983 of £50 million on nuclear physics but only £4 million on materials science (a broad field embracing, *inter alia*, semiconductor materials, ceramics, plastics and alloys) was misguided in the context of the long-term economic interests of the nation. Clearly, these views would not gain universal assent within the research community (Colley, 1985) and the debate to which they are relevant seems destined to intensify given the outlook for research funding.

The last of the three prerequisites for the successful development of the sunrise industries to emerge during the OHE Symposium concerns the socio-economic ramifications of the new phase of industrial evolution. At the present time, many economically advanced nations are experiencing high levels of unemployment – the latest official figures for the United Kingdom indicate that 13.4 per cent of the workforce are out of work. The new innovation-based industries of the future are not generally seen, however, as the panacea for this problem. Indeed, in sharp contrast to the substantial numbers of new jobs generated by previous waves of technological innovation, it is feared by some that the forecast patterns of industrial reorientation will swell still further the numbers of unemployed.

Generalisations in this respect are largely meaningless as some sectors of the economy will clearly gain while others lose. Predictions are especially hazardous because of the rapid changes in fortune – at company, industry and national levels – that may follow in the wake of innovative breakthroughs. Instead, it is perhaps more valuable to highlight two issues which, it seems certain, will have a critical bearing on the successful adjustment to the future. Given a continuing shift in employment opportunities away from manufacturing industries towards those supplying services, careful consideration has to be given to the skills that will be required of the generations set to enter the workforce in the years to come and thus to the nature of appropriate education and training programmes.

The other issue that has to be tackled concerns the distribution of future labour-based tasks among the population of working age. This question presages a fundamental reassessment of present concepts of working lifetimes, working weeks and even working days. Failure to achieve greater flexibility in this area may result in a further stratification of society, comprising a 'working elite' and those facing permanent unemployment. Deleterious developments along these lines would put at risk the social fabric of the community, diminish the purchasing power that ultimately underpins wealth creation, and breed attitudes yet more inimical to industrial and economic progress.

Following these general considerations for the sunrise industries, the OHE Symposium focused on the specific example of the pharmaceutical industry. Many of the papers contained in this volume explore in some depth the special circumstances of the industry but, in common with reviews of the sunrise industries as a whole, the need to provide an environment conducive to development emerged as the central theme.

The UK research-based pharmaceutical industry – currently about £500 million is allocated to the search for and development of new medicines each year – makes a major contribution to the nation's economy. It employs approximately 70,000 individuals in its own operations and perhaps a similar number indirectly in those industries with which it is vertically linked. In 1983 it exported products valued in excess of £1,000 million, yielding a positive trade balance of £600 million. Yet it may be argued that the industry's principal, albeit unquantifiable, contribution lies in the relief of suffering it has made possible for mankind.

The achievements of the industry in this context have been extensively documented by the Office of Health Economics in its series of publications on health care issues. It is manifestly clear, however, as Sir John Butterfield's contribution to this volume demonstrates, that much remains to be done. Contemporary treatments for diseases such as senile dementia, multiple sclerosis, schizophrenia, rheumatoid arthritis and many others are frequently inadequate or, in some cases, simply non-existent. But the development of novel drug innovations presents a formidable challenge. Major new chemical entities now take between ten and twelve years to progress from the laboratory bench to the medicines market and involve costs ranging from £50 million to £100 million.

Pharmaceutical investment is thus an expensive, long-term commitment. It is also fraught with risk. New product candidates may fail at relatively advanced stages of the development process; unexpected side-effects may emerge during widespread clinical usage, causing the drug to be withdrawn from the market; and innovative competition in the industry poses a constant threat of potentially rapid technological obsolescence to all products. Against this background, realisation of the pharmaceutical industry's essential contribution to therapeutic progress requires that the rewards to investment in research sufficiently outweigh the disincentives to allocating resources to this activity. Failure to meet this condition carries substantial penalties: patients may be denied effective treatments for their diseases, the economic benefits conferred by the industry may be forgone, and, of course, there is the loss of potential government revenue – asked by Gladstone the use of his research, Faraday replied, 'Sir, one day you will be able to tax it.'

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SESSION I:

THE SUNRISE INDUSTRIES BEYOND THE 1980s

CHAIRMAN'S INTRODUCTION

Michael Swann

Welcome to this first session of the OHE International Symposium, 'Pharmaceuticals among the Sunrise Industries'. I must say that, in my modest experience of industrial conferences, there is a tendency sometimes for industries to restrict their field of vision and to talk rather strictly about their own problems, neglecting the wider context. This conference is very much the reverse of that. This first session is concerned with other sunrise industries. It is followed in the afternoon by what I suppose one might call the macro-political element. And tomorrow it goes on to what undoubtedly is the micro-economic element.

I also rather like the title of sunrise industries, because it is a metaphor, and metaphors are good or bad depending on how far you can stretch them. I think I can stretch this one quite a long way. In the first instance, you cannot see very distinctly at sunrise because there is not enough light, and quite clearly this is an area where it is difficult to foresee the future. One is not altogether certain of the identity of the problems and even less certain where the solutions to them lie.

I was also puzzled, when I first saw the title, that pharmaceuticals could regard themselves as a sunrise industry because the sun really rose rather a long time ago. It was millennia, perhaps tens of millennia, ago that somebody somewhere in the world ate an opium poppy or chewed the bark of a willow and discovered that it eased their aches and pains and it is from that point, I suppose, that the science of pharmacology and the industry of pharmaceuticals must be reckoned to have begun. It has gone on in fits and starts ever since. The major developments – and I cast my mind back here to when I used to lecture to first-year medical students some thirty years or more ago in Edinburgh – and the biggest phase of increasing expectation of life really date from the nineteenth century. If you go much further back that than, you find a life expectancy of perhaps 20 or 25 years at the most, but by the end of the nineteenth century it was way up in the fifties. That particular phase of medical

advance did not have a great deal to do with pharmaceuticals unless, I suppose, you include antiseptics and anaesthetics. It was mainly a question of increasing prosperity leading to improved nutrition and better sanitation.

I suppose the second sunrise really began towards the end of the nineteenth century. It has extended on and off ever since into the twentieth century and has been much more closely related to the understanding that has grown up in physiology. Much more recently it has extended yet further with the new science of molecular biology. That, I have no doubt, is the sunrise with which this Symposium is primarily concerned.

Nevertheless it has, I think, been a long sunrise, and, stretching the metaphor a little further, it does not surprise me greatly because the length of sunrise depends where you are in the world. There are tropical sunrises which are very brisk. On the other hand, at the right latitude at the right time of year sunrise can last all the day round. The only trouble with the latter, of course, is that you do not actually know if it is sunrise or sunset, and when one looks at sunrise industries one is liable to get mixed up between sunrise and sunset which, if you are an industry, must be very confusing. I suspect that in every advancing industry the sunrises grow conceptually out of the sunsets and in large measure must depend, financially and economically, on the sunset industries. This I suspect is just as true and perhaps truer of the pharmaceutical industry than of many others. We are going to hear different facets of this particular problem in this first session.

As to the afternoon session, which I have called macro-political, I think you all know the various political troubles that surround the pharmaceutical industry, and on a world-wide basis. Governments want to nationalise them or screw down their profits. There are troubles with the Third World and how best to give them the benefit of the advances in pharmaceutical expertise. I think it is wise that the Symposium should be thinking about this because it is undoubtedly an increasing problem.

Then there is the micro-political session on risks and benefits. This topic has always seemed a fascinating one because it is full of irrationalities and ambivalences. I shall never forget when I was a relatively new Chairman of the BBC and was assailed on all sides, partly by the pharmaceutical industry, which kept

thinking, rightly I dare say, that many of the BBC programmes were not fair to it. It goes without saying how much the media love investigative journalism. At the same time we were assailed by Mrs Whitehouse and others who said that the BBC was responsible for the great wave of sexual permissiveness and violence in society. On one occasion I asked, a little incautiously perhaps, a bunch of young producers why they did not feel that they had the same obligation to prove the safety of their wares as the pharmaceutical industry had and this shook them rigid. I was told I had struck at the whole basis of freedom of speech. But the fact remains that there are some things people think have to be proved to be safe, and other things that do not have to be proved to be safe, and there is every sort of confusion in between. I am sure that Sir Douglas Black, who is attending this Symposium, knows this better than most, having had to chair an inquiry into one of the most troublesome areas of risk/benefit assessment.

One can see similar things in every walk of life. We take it for granted that enormous amounts of money are spent putting up central barriers on motorways, whereas all the cost-benefit analyses that have been done suggest that in terms of preventing accidents we would do much better to reduce the number of dangerous crossroads. Now why people think that meeting a car extremely infrequently coming in the opposite direction when they are on a motorway is more horrifying and more deserving of spending money than improving crossroads I do not know, but the fact remains that they do. There are many interesting problems in this area and I think we are going to hear about quite a lot of them.

Then, finally, the economic session. I am wholly incompetent to say anything about that, except that it is undoubtedly something that causes much concern to the pharmaceutical industry. It does have very major costs imposed upon it by the need to prove the safety of its products, and at the same time when it does make profits it gets into trouble.

The whole gamut of problems is coming up before us and I need only once again welcome you to what I am sure will be an extremely interesting meeting.

PROSPECTS FROM THE SUNRISE

Bruce Williams

'Prospects from the Sunrise' is an intriguing title. I wondered whether I should cast myself as a messenger from the East to warn as in Clough's poem:

> In front the sun climbs slow, how slowly

– a message that investors in many chips and biotechnology projects would say was not news to them – or as the bringer of good tidings with the next line:

> But westward, look, the land is bright.

Perhaps from the absence of careful definition, the concept of 'sunrise industries' has proved very popular. What I think writers have in mind is an industry that is new and has a technology based on research and development, that is at an early stage of development and will be considerably improved over time, that has a market which will respond to lower prices and new products, and that is exciting for investors, politicians and the press. Electronics is a splendid example, but I doubt if there are others. Information technology and biotechnology may be considered in this respect, but they are more accurately technologies and not industries. It therefore makes more sense to consider technologies rather than industries.

Biotechnology has a wide range of applications in agriculture, in the processing of human and animal food, in the mining industry and in the chemical and pharmaceutical industries. Biotechnology is, of course, not new, but once the genetic code was unravelled and the technique of gene-splicing invented it took on a new lease of life – it had a new sunrise. Nor is information technology new. It was transformed by computers, chips, television, fibre optics and satellites. The materials industry has a very long history but there, too, new composite materials and shape memory alloys – with promise of important

applications in precision engineering, microsurgery and space research – have created new growth opportunities.

Competitive strength in international trade and the rate of economic growth depend on innovations in products and processes. As new technologies mature and markets saturate, their contributions to growth rates and profits fall. And as a consequence of this maturing of technologies, the developing countries, with their lower wage rates, are able to build up their activity in industries pioneered in the developed countries and promote their share in the growth of world trade. In the sixties and seventies, for example, the share of the developing countries in world trade in manufactures rose from 7 to 9 per cent. The interest in sunrise technologies, as in the sixties and seventies in advanced technology or high technology, is therefore right and proper – so long as it is kept in perspective.

Britain once led the industrial countries in innovation, in rates of growth and in levels of productivity. But that lead was lost to the USA by 1900. Between 1870 and 1913 Britain's growth rate in output per head of population was only half the American rate and substantially less than the rates achieved in France and Germany. The main reason was that Britain had failed to make a sufficient adjustment to the change from mechanical engineering as the key skill in technology to the much more science-based skills required by chemical and electrical engineering. Britain's education system did not equip mental and manual workers to exploit very effectively the opportunities for productive industrial research and development in the new electrical industry. It also failed to provide the number of electrical and chemical engineers required for efficiency in production.

In the inter-war period Britain's export trade suffered badly as a consequence of industrialisation in developing countries. The textile, iron and steel and shipbuilding industries were badly hit and this produced heavy unemployment, though the problem was greater than it need have been because British producers did not modernise their equipment or management processes. The League of Nations study *Industrialisation and Foreign Trade* (Hilgerdt, 1945) analysed the nature of the problem and pointed out the need for the mature industrial countries to increase their involvement in research-based activities which required more advanced technological and design skills than were available in developing countries.

After the Second World War, the government gave considerable support to what was called advanced technology in aircraft, atomic energy and, later, computers. Indeed the first task given to the Ministry of Technology was to save the British computer industry. By historical standards, Britain's growth rate between 1950 and 1973 was high, but it was considerably less than the average for OECD countries and growth was frequently impeded by weakness in international trade. Britain's share of world trade in manufactures has fallen in the last twenty years from 14 to 7 per cent.

In fact we did not make a success of atomic power, where the research, development and design work was too detached from economic considerations. Many of the key people involved did not accept that the rate of interest was a relevant factor in the design of reactors. And when decisions had to be made about the rate of interest for calculating the cost of atomic power (from excessively capital-intensive reactor designs) an absurdly low rate was chosen. As in many other high-technology ventures financed from taxation, the approach was too technocratic. In aircraft and computers, and later on in chips, there was only limited success.

Governments have tended to over-emphasise the role of technology-driven innovations, and in both business and government there has been a failure to integrate research and development, production, marketing and financial plans. The Finniston Committee (1980) on 'Engineering our Future' commented that the companies they visited in Germany, Japan and the USA 'systematised, formalised and wrote down' working procedures far more than British companies which traditionally had emphasised personal freedom and initiative at all levels. That is not generally true of British industry, but I wonder how far the absence of systematised working procedures and the existence of a rather uncoordinated division of labour is explained by the small proportion of senior managers who comprehend technology. For this and other reasons, the continuing failure to produce an adequate supply of the craftsmen and technicians, the scientists and engineers, needed for the effective use of modern technologies has exercised a strong brake on the British economy.

It is instructive to compare the British performance with that in 'the land of the rising sun'. Japan has a remarkable record of strength in international trade and growth. It is strong in information technology, and it has also moved resources out of

industries such as shipbuilding, where it judged that the new developing countries would have an increasingly competitive advantage, and aluminium and steel, when the sharp rise in the cost of power left it with a competitive disadvantage. But it has also succeeded with mature industries like motor vehicles and machine tools by applying and further developing the 'sunrise technologies'.

Situations change. Microprocessors, robots and flexible manufacturing systems now provide opportunities for mature countries to compete in industries which twenty years ago seemed destined to be taken over by the developing countries. Great opportunities will be lost if government support and the recruitment of the ablest young people are concentrated on what are thought to be sunrise industries or firms. In the USA, which is currently setting an example in job creation, total employment has risen by 35 million in the last twenty years. 'High-tech' has provided only one-sixth of those jobs – which is about equal to the loss of jobs in 'smoke-stack' industries and government agencies. Five-sixths of the new jobs have been provided by what Drucker (1984) described in the *Wall Street Journal* as 'middle-tech', 'low-tech' and 'no-tech' entrepreneurs. Drucker exaggerates, for some of the entrepreneurs in growth activities like home equipment, surgical instruments, footwear, toys and package air tours have made very good use of sunrise technologies and provided a market for sunrise products. But Drucker's main point – that high-tech entrepreneurs cannot flourish alone without the support of a larger entrepreneurial economy – is perfectly sound and important.

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SOURCES OF ENERGY FOR THE TWENTY FIRST CENTURY

Aubrey Jones

I was a little puzzled at first why, in opening what is essentially a medical-pharmaceutical congress, I was invited to talk about energy over the next hundred years. Gradually the puzzle fell into place. Electrical power, as a form of energy, is a pre-condition for the appearance of 'sunrise' industries; without electrical power there is no sunrise industry. And without cheaper electrical power than other countries we shall find many of our industries migrating elsewhere. There is already talk in some British industries of migration to France. Energy therefore is very relevant to your preoccupations.

I was also intrigued by the connection between energy and medicine. A certain degree of warmth is essential to good health, particularly in a country like the UK with a high proportion of elderly people. The form of energy we decide upon could affect climate, making it warmer or colder; climate affects foodstuffs; foodstuffs have something or other to do with medicine. I hope that what I have to say therefore will be of some interest.

I am not going to bother you with any precise dates – who could over a hundred years? I am rather going to describe patterns as I now see them, though I accept that they can be changed. And I wish in particular to convey two messages, the full meaning of which will become clearer later.

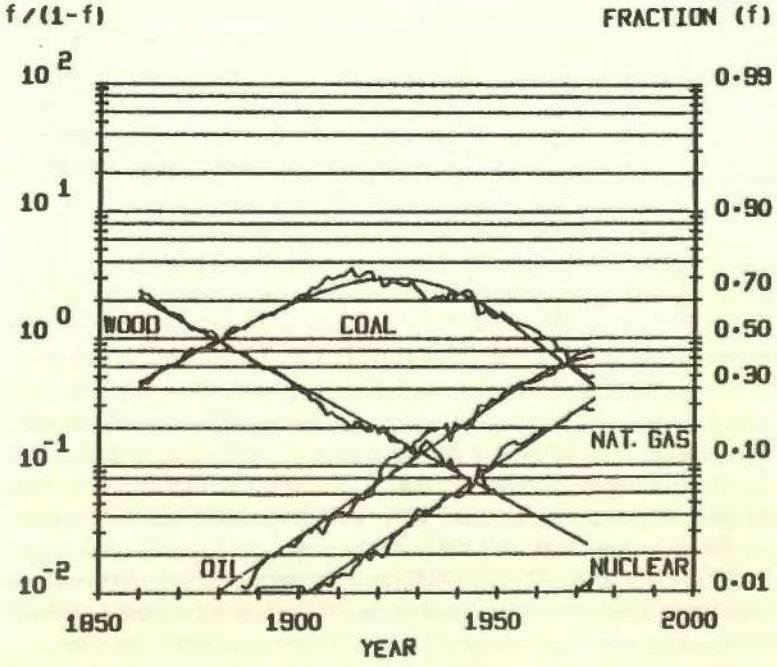
The first message is this. When I was young I was taught that economics was concerned with the allocation of scarce resources. I am not sure now that resources are scarce, at any rate over the long term. One resource can be substituted for another, and in this sense resources are limitless; the limitation is in man's mind, in his incapacity to adapt himself from one resource to another and in particular in his inability to accept the international accommodation which the exploitation of certain resources may require.

My second message is concerned with pollution. There is no form of energy which does not pollute or entail risk in one way or

another. The choice is therefore not between a source which does not pollute and one which does; the choice is between different forms of pollution and risk.

I want to begin with some history and to show how various sources of energy have waxed and waned over time. Figure 1 shows the share contributed to the total by different sources of energy over the last 150 years. It is clear that wood, the original source, has practically disappeared, though it should be said that there is now an increasing resort to wood in the United States and that the increased price of oil must have caused a massive spoliation of forests in tropical areas. The most important feature to emerge from the diagram is that it has taken any one source around fifty years to increase its share of the market from 10 to 50 per cent. That is probably a law valid for all time – it takes around fifty years for a new technology significantly to penetrate the market.

Figure 1: Logarithmic Plot of Global Energy Substitution



Source: International Institute of Systems Analysis.

Turning from this view of the past, Table 1 illustrates the present contribution of the various energy sources. But the question I am requested to answer is how we move from here into the twenty-first century. The answer depends partly on the demand, partly on the supply. I estimate the likely growth in demand to be low, largely because it is dependent on the sources of energy available. The energy sources then are the important quantities.

Table 1: Estimated Global Primary Energy Supply, 1975

Type		Level (TWyr/yr)
Commercial energy		
Oil		3.8
of which oil from Middle East and North Africa	(1.6)	
Natural gas		1.5
Other		2.9
Total commercial energy		8.2
Non-commercial energy (e.g. fuel wood, agricultural waste)		0.6
Total energy		8.8

Source: Häfele, 1981.

Focusing first on oil, M. Desprairies of the Institut Français de Pétrole, in preparing from a vast range of estimates for the World Energy Conference of 1978, reached a median figure of 300 billion tons of recoverable resources. He was, however, working under the constraint of not exceeding in cost $20 a barrel. It may safely be assumed that further resources could be found, though at a higher cost. Summing up their own analysis, the International Institute of Applied Systems Analysis saw oil production reaching its peak between 2010 and 2020. A slightly more optimistic view might put the peak production between 2030 and 2040. The Institute foresaw oil as providing only some 60 per cent of the world requirement of liquid fuel by 2030. The rest would have to be found from synthetic or converted gas and coal.

Since natural gas is a relatively new discovery, considerable further exploration could be undertaken, and who knows what

the figure would be? For the sake of simplicity it may be assumed that oil plus liquefied gas could meet the world's need for liquid fuels up to 2050.

Thereafter coal would have to help out, and there is plenty of it. The total of the world's recoverable energy sources has recently been estimated by Sir Peter Hirsch. There is enough coal for much more than a whole century, while there is enough oil and possibly gas for only half a century. The shortage then is in the liquid fuel, oil. And oil is needed not only for transportation but also for certain chemical processes. True, coal can be gasified and liquefied, and so converted into oil. The technology is known and there are several operating plants in South Africa. It is more doubtful whether enough plants could be constructed in Western Europe by mid-2000. That then is the crisis.

Table 2: World Recoverable Energy Resources (10^9 tonnes coal equivalent)

Coal		Uranium		Oil[a]	Gas
Total	10,795	In fast reactors	14,378	951	302
50% recovery	5,398	In thermal reactors	172		
10% recovery	1,080				

Note: a. Includes natural gas liquids, bituminous sand and oil shale.
Source: *Nuclear Energy*, 1983.

But it is a crisis compounding another public crisis. Ever since the Industrial Revolution we have been emitting carbon dioxide and other combustion products into the atmosphere. According to a study commissioned by the US National Academy of Sciences (1983), the carbon dioxide concentration in the atmosphere has increased in the last generation from 315 parts per million (p.p.m.) by volume to over 340 p.p.m. This increase was ascribed primarily to the use of fossil fuels, though deforestation would also have played a part. It was estimated that the concentration of carbon dioxide in the atmosphere would exceed 600 p.p.m. (that is, double recent levels) by the third quarter of the next century, while some estimates suggest a doubling by 2035. This could increase temperature and 'carry our planet into largely unknown territory'. We know very little about climate changes, but there are those who consider that even a slight increase in temperature might render arid the Western part of the

United States, push into retreat the Northern ice-cap and raise the level of the seas. All this, however, is subject to great uncertainty.

In short, I foresee for the mid-twenty-first century a shortage of liquid fuels, an increase in the cost of all fuels as we dig deeper and harder for them, and possible changes in climate, the exact nature of which cannot be foreseen. In the face of this prospect our aim should be to contrive forms of energy which leave the environment unaffected or, to use the conventional term, do not pollute. Are such forms possible?

Hydro-electric power is often mentioned. This could possibly be doubled, but there have been horrific reports of the pollution produced by reservoirs in South America – for example, the production of hydrogen sulphide by rotting vegetation has caused large areas to be evacuated. Then there is the wind. The efficiency of a windmill cannot be much greater today than it was a hundred years ago, and there would have to be clusters, noisy and unsightly, way out at sea or on hilltops. As for radiation from the sun, it is dispersed and therefore difficult to collect. Thousands of sun-tracking mirrors could focus energy on a receiver placed on a hilltop in an arid area; the receiver could then produce super-heated steam to drive a generator. Suppose the chosen location is the Sahara. The electrical power generated in this way would then have to be distributed to the Northern regions. Think of the apparatus required and the international problems raised by transmission across frontiers. The alternative would be a mass of photovoltaic cells, of which the advanced example is the single-crystal silicon cell developed from aerospace activities. But the cost would be enormous.

I am forced to the conclusion that if the goal is a non-polluting form of energy the only alternative is nuclear power. It emits little into the atmosphere, although, of course, it leaves behind its radioactive waste material. This can be sealed and deposited in geological structures, such as clay pits, which are likely to be free from earth tremors. Such a treatment would render the waste material safe. It would not matter much which reactor we used; there is a case, however, for using the breeder or fast reactor. The original justification for a breeder reactor was a possible scarcity of uranium. We now know that uranium is not scarce. None the less there is the possibility that the price will rise and thus render the breeder reactor economic. In spite of its high

capital cost it is estimated that the breeder reactor will produce power more cheaply than any other reactor we know in the early part of the next century.

I do not propose to discuss fusion, for the engineering problems have not been tackled and, while some would see its advent in the next century, I am more sceptical, and would place its coming in the twenty-second century. It should be emphasised, however, that fusion would also leave behind some radioactive waste, though it would be different in nature from that left by nuclear fission and it decays very quickly.

We are therefore confronted with a choice. Either we continue to pollute the atmosphere as at present – and we now face the problem of acid rain as well as carbon dioxide – or run the risk which might arise from radioactive waste. For myself I would choose the latter. But the choice is that of the public and I cannot tell what it would be.

There is one final problem which I feel obliged to raise. Energy is inevitably going to become more expensive and require much larger amounts of capital. The present-day share of world capital stock in the energy system is 25 per cent or $2000 a head (Table 3). With new forms of energy designed to free us from reliance on the world's resources, this would need to be greatly increased to 33 per cent, according to the International Institute for Applied Systems Analysis. This would entail a tenfold increase per person by the end of the twenty-first century. How in a free economy, not noted for its high rate of saving, is this to be accomplished? Unfortunately, I do not know the answer to that conundrum.

Table 3: Energy Consumption and Capital Stock

	Energy Capital Input Ratio (W/1973$)	Capital Stock per Capita (1973$)
Developed market economies	0.71	8,500
Developing countries	0.77	380
Centrally planned economies (excluding China)	1.43	2,700
World	0.87	2,000

Source: Ströbele, 1975.

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ELECTRONICS AND COMMUNICATIONS

Peter Laister

In many ways, the 'health care' industry and the one to which I belong, electronics and communications, may collectively be seen as the new sorcerers – microsurgery and microchip conjure up visions of fantasy in the human imagination and psyche. Both fill our fellow human beings with wonder and fear: the one with the power to give life and to free mankind from pain, the other with the capability of capturing and transmitting information from the outer galaxies and from the depths of the individual atom, the building block of our very existence.

Even the terms employed by the two industries are barely indistinguishable to the layman: ion implantation, heart transplant, cellular radio and neuro-transmitter, all illustrating with clarity the convergence of science and technology, joining together to illuminate the undiscovered regions of ourselves and the world we inhabit.

Nevertheless, although all of us must from time to time seek refuge or enlightenment in the realms of philosophy and metaphysics, this lecture has as its objective an attempt to explain the effects of advances in communications and electronics on the economy and the nature it serves.

It was not until 1884 that Arnold Toynbee used the phrase 'the Industrial Revolution'. It was not until 1984 that we perceived the irreversible nature of the second 'Industrial Revolution' with its seemingly unlimited power to create wealth and to destroy jobs simultaneously.

The transistor, the practical consequence of decades of research and discovery in solid-state physics, had come of age. In less than forty years it had created an industry which by the end of the century will be larger than the automobile industry and oil industry combined.

For communications and electronics not only herald the coming of the truly automated factory and office, but lie at the heart of the political and military struggle to determine the nature of human society in the rest of this century and beyond.

Their power, excluding the possibility of nuclear war, can bring a new golden age or a world in which social unrest leads to ever greater social control and fulfils the worst predictions of George Orwell's *Nineteen Eighty-four*.

Medicine today deals with the whole man; communications and electronics deal with systems – office automation systems, building control systems, command and control systems, medical systems, flexible manufacturing systems and weapons systems. All of them have the relentless ability to increase wealth with fewer and fewer people. A recent university study shows that from 1961 to 2001, the available workforce in the UK will grow from 30.9 million to 34.5 million, while employment in manufacture, construction and agriculture falls from 11.9 million to 6 million.

It would require a high degree of pessimism to predict a growth in our gross national product between now and the end of the century of less than double. So whatever bad dreams we may have, there will still be an unending stream of automobiles, consumer electronic products and packaged holidays available for the working members of our population to buy. Even in the health professions, which in 1980 numbered 968,000, the study forecast an increase of at least 20 per cent by the year 2000. When one combines this with an ever-increasing flow of miracle drugs from an enlarged and flourishing biotechnological industry utilising fifth-generation computers incorporating advanced Intelligent Knowledge-based Systems, the resultant increase in life expectancy will compound the problem of finding work for all.

Until 1984 it has been the blue-collar worker who has borne the brunt and provided the casualties of the second Industrial Revolution. It has been largely the unskilled and semi-skilled worker who has widened the customer base for minor mental illness and increased market demand for new and non-addictive, low-cost tranquillisers. But studies by the Siemens company demonstrate that with the hardware and software available today for office automation, there could be a 25 per cent reduction in the EEC's white-collar workforce by 1990.

In summary, 10 million white-collar jobs, covering the clerical to middle management grades of the job spectrum, will have vanished. And yet in terms of the fifth-generation computer which will allow a human being to communicate directly with it in his own language (no finger trouble in operating the keyboard),

the systems identified below are technologically primitive:

(1) Document production – word processing and printers
(2) Filing and information retrieval – data base and file management systems, query methods
(3) Communications – electronic mail
(4) Decision support – spreadsheets, modelling, access to information.

With these basic elements, plus ever more powerful and faster computers, intelligent indexed data bases and the availability of low-cost and reliable voice and image processing, the possibilities for higher and higher productivity are limitless. One can easily create in one's imagination not only the paperless office but the Industrial Relations Manager's dream of it being peopleless as well!

My company recently acquired a semiconductor company called INMOS. At the centre of this company's product line is a 32-bit microcomputer called the Transputer. The Transputer is designed to provide all the resources of a computer including processing, memory and concurrent communication on a single chip. The memory can be extended off chip to both static and dynamic RAMs to provide data rates of up to 25 megabytes per second. Four high-speed serial communication leads enable interconnection with other Transputer products.

In other words, if this product fulfils its promise, every home could have its own main-frame computer interconnected through a national optical fibre cable network to all major industrial, professional and commercial institutions. It is then only a matter of cost and time to interconnect on a global basis by a system of communication satellites. But long before each home has one, networks will become available to each profession so that if we collectively will it, there will be equality of access to the world's store of knowledge on every conceivable subject.

Networks have already become an indispensable cliché in the jargon of information technology. They come in all varieties, Local Area, Metropolitan Area, National and Global and act as the nerve fibres of all major electronic systems with transmission media covering the whole electromagnetic frequency spectrum from a few cycles per second to gamma ray satellite-borne sensors used to detect cosmic radiation from distant galaxies.

It is interesting that the new Jodrell Bank Radio Telescope called MERLIN has an 'invisible dish' size 133 kilometres across, but in fact consists of six radio telescopes electronically linked. The whole array is thus a multi-radio telescope linked interferometer. Networking has truly come of age, embracing a range of systems from a 16-workstation multi-user super-microcomputer used for administration in an average-size general hospital to an integrated management and financial control system using 22 distributed minicomputers and hundreds of workstations now being installed in one of my company's product groups.

The two main human interfaces to these networks, namely keyboard and visual display units (VDUs), are not wholly ergonomically satisfactory. To improve matters we have developed keyboards which require almost zero force to operate and have a tactile feel. To make life easier for people, particularly senior executives and higher professional staff, we have developed simple keyboards (almost idiot proof) with a limited range of commands.

In VDUs using colour cathode tubes we are developing higher resolutions, flicker-free screens with freeze frame and zoom features. All will provide hard copy using laser-based, high-speed printers. The fifth-generation computer will almost certainly use voice commands and have most of its software embedded in its wafer size (tens of millions of semiconductor elements) VLSI semiconductor circuitry. It will have a powerful inference engine capable of providing probabilistic as well as deterministic answers to complex problems.

Yet nearly all of this power and flexibility are derived from the ubiquitous dynamic random access memory, the 'jelly bean' product of the semiconductor industry. Storage density will quadruple every three years with costs falling dramatically as the industry proceeds merrily down the learning curve.

Although we almost regard them as commonplace, each element has to be regularly refreshed at precise time intervals if we are to avoid memory loss and ultimate system failure. All complex electronic subsystems must be treated with the respect they deserve. The analogy with the human brain with one litre of blood flowing through it every minute readily comes to mind.

As I see it, the second Industrial Revolution is only at the beginning. We already have within our nation's research laboratories transistors with dimensions of 100 atoms. Combine

these with the discoveries and products of biotechnology and the next major advances in therapeutic medicine become a practical possibility. We believe we know how to store four years of recorded TV programmes on a few square centimetres of storage medium. In the new field of molecular electronics using doped multilayer synthetic membranes we can envisage optical computers of immense power and versatility.

Wealth creation is not our problem; if we are to survive as an industry and as a nation with influence and the ability to help others, we must accelerate progress – not retard it. We cannot provide freedom and opportunities for all our people by selling packaged computer software and exhibiting our crumbling heritage to a flood of American, West German, Japanese and South-East Asian tourists taking advantage of our ever-depreciating currency. Neither can we have a polarised society in which the high priests of the new technology and science enjoy the prodigality of its riches in status, personal choice and mobility, while a steadily increasing number of economically disenfranchised members of our new society sink into apathy or plot the downfall of that majority at work.

The risks must be shared: by longer periods of education; lower retirement age; and adding to the growing numbers of self-employed who provide the icing on the cake in a society where there is a surfeit of mass-produced consumer goods.

The Judaeo-Christian ethic with its emphasis on work (paid work in employment) will have to be modified to include work in all its forms, whether voluntary in service of the family and community or salaried in the service of government, the professions, commerce and industry.

We cannot tolerate a submerged 20 per cent, doomed never to work (in the old sense), without choice, without status and without hope. Those of us who are privileged to be a member of the working 80 per cent must use our imagination, our skills and our energy to benefit all. Structuring a society which has to compromise between freedom, equality and opportunity for reward will always be difficult. We all seek status, freedom of choice, financial independence and exclusivity, yet in a civilised society our object must be that all must win, if some win a little less than others.

Advances in science and technology, of which communications and electronics form only a part, provide the first real

opportunity in human history to create a world of plenty in which all can share. To achieve this end we do not need to sell our souls to the devil or the ideologies he has spawned. Communications and electronics have created systems which are designed to serve man. They are no more than tools created like the wheel and inclined plane to expand man's horizons beyond his short-term survival.

We are left then with a challenge: a technical future beyond our present imagination but a present-day situation already unable to cope in an organised way with the problems that this future will create. Technology can create wealth and a better environment but not jobs in the traditional sense. Can we then solve the social problems at a pace to match the speed with which technology is moving? Those who believe that the solutions lie in the traditional patterns of the past will fail, but there is every hope of making the same advances in social structure and engineering as have been made in medicine and electronics if we are willing to project and understand the reality and scale of the change and then give it the priority it deserves.

CHEMICALS AND PHARMACEUTICALS

Peter Cunliffe

I should like to start with somewhat of a personalised view, an anecdotal view, or, I suppose I should call it, more elegantly, an historical view, based on experience from my own chemical company. Selectively, from this experience, I think I may be able to justify some broad generalisations. I believe I can justify the word 'historical' since I have drawn heavily on the 1,200 pages of Dr Reader's two-volume *History of ICI*.

Since we are all speaking in the present glow of sunrise industries, I might usefully start the first part of my talk with a line from a poem by Clough which accurately but somewhat sadly encapsulates ICI's entry into the pharmaceutical industry:

> The sun climbs, slow, how slowly.

Lest you get too depressed, I should remind you that the story is going to get better since the poem from which I have taken the quotation is entitled 'Say Not the Struggle Naught Availeth'.

ICI came late to the pharmaceutical business. When ICI was founded as a chemical company in 1926 by the merger of Brunner Mond and Co. Ltd, Nobel Industries Ltd, The United Alkali Co. Ltd and British Dyestuffs Corporation Ltd, its technology was, as would be expected, tremendously biased towards heavy chemicals, towards the sort of product which is produced in thousands, indeed in hundreds of thousands, of tons a year. There was little sympathy within the new company for the small-batch processes of the dyestuffs industry which dealt with the mere hundreds of tons a year, and very little recognition that a high-added-value product was the result of high scientific ability and could produce a rather different return on capital from that of some of the heavy chemicals.

Small was not, at least in those days, seen to be beautiful. But there were other constraints, blinkers. The following other quotation is taken from Reader's *History of ICI*:

> When ICI was founded, it was almost entirely a group of businesses supplying materials or finished products required not by the final consumer but by other producers. This was what the founders thought of as the proper function of ICI. They did not see ICI . . . as makers of finished goods to be sold under brand names to the public at large. Indeed, in the general ICI attitude to such matters, for a good many years, it is possible to trace disdain.

And there was more, and there was worse:

> The leaders of ICI were inclined to regard the manufacture and, still more, the advertising and marketing of consumer goods with contempt.

One could not regard this as an auspicious background for the development of a pharmaceutical business. How could the sun ever rise over those dark Satanic mills? But, nevertheless, ten years later, the first glimmer of light appeared. The dyestuffs business of ICI, with its small-batch processes, was already on the fringe of the pharmaceutical industry with a few gaudy chemicals like brilliant green, crystal violet and mild silver proteinate, and, in 1936, the Board of ICI authorised the expenditure of £15,000 a year, for a period of five years, for research by the Dyestuffs Group 'in regard to synthetic organic pharmaceuticals, particularly original research to discover new remedies'. The research was undertaken by six PhD chemists and it was made clear that this research was to be terminated if not successful. However, outside events intervened before the five-year period expired and the Second World War put an end to the prudent timetable so that, by 1942, there were 20 PhD chemists and already a group of biologists.

With the stimulus of war, results came fairly quickly, a sulphonamide and an antimalarial, a trypanocide and an antiseptic, but the chemical company still did not appear completely to understand pharmaceuticals. The late forties and fifties marked a great leap forward in the pharmaceutical industry but ICI's approach, said the historian, was 'curiously half-hearted'. It did not take over an existing business. It did not take out licences. It relied on its own resources 'on the consideration

that the best way thoroughly to master a new field of endeavour is to learn by one's own efforts at all stages'. As the historian said: 'This was magnificent but was it wise?'

Clearly, it was not wise but, perhaps surprisingly, it worked. Because of the determination and the skill of the researchers – and I think I should more properly acknowledge their determination and their skill by referring to them as drug hunters – inventions came forward in the central nervous system area, in the anaesthetic field and, of course, in the big leap forward into beta-blockers. The £15,000 a year voted by a far-sighted, albeit perhaps unbelieving, Board began to pay off.

The development of a pharmaceutical business within a major, well-established and confident chemical company encountered, as I have indicated, some cultural problems. But it also inherited some substantial benefits and one major strength was the provision of cash at monotonously regular intervals and a willingness to wait for a surprisingly long time for the cash to come back. If you were to look at the profit and loss account of ICI's pharmaceutical business since 1936, you would see that whilst there were a few sporadic years in which the pharmaceutical business edged into a tiny profit, in most years the business plunged into loss. It was 1959 before ICI's pharmaceutical business began to turn in a reasonably sustained profit. Patience, allied with faith, had for a long time to be its own reward. It was 23 years from the date ICI started its pharmaceutical research before it moved into a profitable situation.

What does this mean in today's terms? I reckon that if we were to start our pharmaceutical research today from scratch, we would feel that we should hedge our bets and set up four different project teams. The cost of this would be in the order of £8 million in the first full year. Assuming some success and a product, or products, coming out of this research, we should have to step up the development effort and we should want to do this world-wide – in Europe, in the USA, in Japan. So, how much would ICI have to invest now in R and D if it were prepared patiently, faithfully, to wait 23 years for its reward? And the cumulative sum is staggering – something like £600 million in 1984 values and, allowing for inflation, perhaps £1.5 billion.

A fairly expensive dawn vigil! And it has to be asked which company could invest this magnitude of cash in the hope that it

might one day see the sun rise?

From this selective anecdotal background to ICI's pharmaceutical business, I want to draw out three generalisations which I shall refer to as the 3 Rs of the pharmaceutical business.

The first one is Research. The pharmaceutical industry, or at least the part to which I belong, and the part which may have a future, is heavily dependent on research. So, for that matter, is the health of humanity. The industry seeks to make new advances in medicine. In the past it has achieved a remarkable record of success in inventing medicines which have benefited mankind. The list is lengthy and the cost/benefit ratio to the world is healthy. And the search goes on. But the road is longer. There is agreement that there are major diseases and disorders to overcome. There is confidence that the industry has the brains and the will to solve the problems. But it will take longer and it will cost more. Firstly, because the problems are greater. Secondly, because the development time – the time from invention to marketing – has gone out from between two and six years to something like ten to twelve years. But research is still necessary because there are diseases, many diseases, yet to conquer.

And research will, I believe, continue to rely heavily on chemistry which is, just like biotechnology, a technique. In the human body, we are dealing with an infinitely complex chemical system and the chemist, in collaboration with other disciplines, is well suited to tackle these problems. What is still needed is a chemist's intuitive flair. Dr Spinks, a former Research Director of ICI, said, 'I do not know how to recognise it exists except by its results and so often the results have shown that the theory behind the flair was erroneous'. And this leads me on to query what is the sort of person to whom we entrust our confidence in research. There was a small book published by John Maddox some years ago which dealt with the question of pharmaceutical research and, in this, he said, 'Successful research directors are inspired intellectual gamblers.' They have to balance the advantage of concentration of resources on projects with the best chance of success against the prudent hedging of bets over several projects. They have to be deeply involved in the scientific background and argument. Intellect and inspiration, of course, but note, in addition, they have to be prepared to gamble, to back their scientific judgement, and this leads to the second R – Risk.

The pharmaceutical industry is unquestionably a risk industry. All of us in the industry say this – sometimes to the disbelief of our critics – and we say it because we live daily with these risks. Quite apart from the risks which affect all businesses, we have a series of risks peculiar to ourselves.

Firstly, we have the risk of our heavy investment in research. A company can go for ten years or more without being successful in making any significant invention. (It can, of course, go on even longer, much longer, but then it will tend to cease to be a pharmaceutical company.)

Even if the research appears successful and a major advance is produced, there is still considerable risk, the risk of last-minute signs of toxicity. Almost all companies have suffered from this. (There is even, alas, the risk of toxicity being revealed only after the product is marketed and this is the most savage and traumatic risk of all.)

And, of course, there is the risk of competition which, in spite of the assertions by some critics, exists in the pharmaceutical industry. A pharmaceutical company is in competition with all other pharmaceutical companies. No individual, no company, has a monopoly of brains and it frequently happens that a new advance in medicine by one company is rendered rapidly obsolete by a breakthrough made by another company. This is, of course, how it should be in a healthy competitive society.

But there are suggestions from time to time that the risk may become so inflated that the risk/benefit ratio may become asymmetrical. At a symposium on 'Medicines for the year 2000', Max Tiefenbacher, then President of the International Federation of Pharmaceutical Manufacturers Associations, put this point quite starkly and quite brutally in an intervention when he said:

> At Monte Carlo blue chips are the highest value and if you bet blue chips you expect to get them back if you win. Regulatory authorities have seen to it that companies engaging in drug research and development play only with blue chips. The smaller denomination of chips no longer goes. But what will happen to the drug company that is fortunate to hit the new drug jackpot? Will it be short-changed? Will it receive, say, yellow chips for the blue chips it has put on the table?

How then should research be rewarded? This leads to the third

R – Return on Investment.

The pharmaceutical industry finds itself in a peculiar position. Governments have an interest in the health of their citizens and, in many countries, find themselves paying for, or subsidising, the cost of health. Government can then have a dual interest in the pharmaceutical industry. Firstly, as a principal customer, it feels an obligation to keep down the price it has to pay. Secondly, it has taken on the obligation to make sure that medicines are safe so it requires data, an increasing amount of data, which in turn increases the cost of pharmaceutical manufacture.

Society, quite reasonably, wants to avoid risk, and politicians who try to anticipate, and even exaggerate, the aspirations of society, put the whole burden of risk back on the industry.

A pharmaceutical company which is successful in research is relatively profitable. Note, I used the word 'relatively'. If you look at the chemical industry over the past few years where prices, volumes and consequently profits were knocked silly by the recession and by over-capacity, you will see that the pharmaceutical segments of diversified chemical companies held up better and, indeed, in some cases, appeared to prop up the entire chemical business. You might think that an industry which invests heavily in research in order to invent new products for the treatment of disease should, when successful, be encouraged to carry on making a profit in order to pursue, and indeed extend, its activities. But you tend to run into an attitude which is as old as the Greek myths. Procrustes exemplified it with his bed. Everything has to fit or be made to fit. It is the justification of the average. You used to hear it from time to time in trade union negotiations where an official, with a perfectly straight face, would say that his members had to increase their incomes because they were below average – onwards and upwards, a process of perpetual motion. You can get the same compulsive regard for averages with government where government, at least in this country, says that because the industry's return is higher than average it should be reduced. If it is higher than the average of all industries, even in a time of recession, then it should be brought down. Again, the initiation of a process of perpetual motion but this time backwards and downwards. We may, in the past, have been called a nation of shopkeepers but apparently we have now lost the facility of understanding how the cash register works. If the prices of products resulting from heavy investment

in research, in successful research, are pushed down rapidly to permit only an average industrial return on investment, then the whole basis of research collapses.

There is an increasing tendency in the UK to praise the basic virtues of the 3 Rs in education. It might, perhaps, be prudent for administrators to remember that Research, Risk and Return on Investment are 3 Rs which are basic to the pharmaceutical industry.

I want now to return to my theme of chemicals and pharmaceuticals. ICI can be divided into a group of heavy chemical businesses and a group of light chemical businesses which ICI, in its more heavily facetious moments – it does, from time to time, make jokes – calls the Heavy Brigade and the Light Brigade. Incidentally, reference to the Light Brigade reminds me of a comment by one of our former research directors who, when told that management had decided and that debate should, therefore, stop, remarked that if he had been in command at Balaclava, the Light Brigade would not have charged. He was speaking from the sort of research environment where a management decision is taken as the opening proposition in a new and ongoing debate and this is conceivably a reason why some quite brilliant inventions came from this pharmaceutical research. But that is a proposition for separate debate.

The example of the chemical industry over the past few years has shown a marked divergence economically between heavy commodity chemicals and light speciality chemicals – the large-volume commodities have plunged into economic disaster, thus causing many companies to look towards small-tonnage, high-value-added products such as pharmaceuticals, for their future salvation, or even existence. (It is interesting to note that many companies who are not in the pharmaceutical industry are trying to diversify into the industry whilst many pharmaceutical companies who are already in are trying to diversify out. There is, of course, a third category of pharmaceutical companies who have diversified out and are now trying to return. One is reminded of Horatius:

> For those behind cried 'Forward'
> And those before cried 'Back'.)

The pharmaceutical industry is beginning to face a situation

similar to that of the chemical industry – the division between commodity products and speciality products in the chemical industry, the division between generics and innovative breakthroughs in the pharmaceutical industry. The OK political word in the second half of the 1980s appears to be generics and this is a sort of twentieth-century variant of Gresham's Law. Generics are attractive to those who confuse price with value, to those who are willing to live in the 'here and now' and let the future go hang. (There is a resemblance to the references made by some consumer associations to the World Health Organization's essential drugs list and their implication (not WHO's) that all anyone needs are the 200 or so essential drugs. I do not think the consumer associations have read the preamble to the essential drugs list, or if they have, they are certainly not willing to acknowledge it because it does say 'that exclusion does not imply rejection'. Too bad if you are not suffering from an essential disease. You will suffer; you might die.) Similarly with a generic drug policy. If you are suffering from a disease for which there is no past cure, hard luck; because the new medicines may not be invented.

There is, currently, a condition which has been styled 'intellectual ignorance'. This affects a generation of educated people whose life has been spent in an environment where they may believe that the only requirement for clean water is to install a tap; that it is proper to use tons of paper to spread the idea that cutting down trees is wicked; and that efforts to produce new medicines to combat diseases which threaten life, or diseases which deny enjoyment of life, are both immoral and unnecessary when they have enjoyed protection from the former and are not yet old enough to suffer the latter.

The pharmaceutical industry will have to face up to the problems of the chemical industry and decide whether it wants to rely on generic drugs or whether it should devote its best endeavours to research, to invention, to breakthroughs. If it chooses the latter, it will have to have money to do so. And it will have to make a return which justifies the risk of research.

The chemical industry is looking for new fields, that is new businesses where it can use its skills. It needs these new businesses to back up, or even, in some cases, to replace, the older businesses on which it built itself – the businesses which were

modern and innovative in their time but which the world has passed by.

The chemical produced by the pharmaceutical industry is different from the commodity chemical – the tonnage plastics, caustic soda and so on. It is, as it were, a simple conduit to a massive amount of sophisticated technology. It is, to use a homely analogy, a bit like a postage stamp – only a tiny, coloured piece of paper but look what it does, look what service it supplies. (Think also of the basic cost of the raw materials of the postage stamp and then think of the price you pay for it.)

The pharmaceutical industry has the inherent ability to seek new fields within itself, to conquer the diseases and disorders for which there are no existing satisfactory treatments. It has the ability, if allowed, to regenerate itself year after year.

The pharmaceutical industry has, I believe, been more successful than universities and research institutes because it has learnt to manage multidisciplinary activities, of which chemistry is only one. Chemistry, as I have already indicated, is a basic science which is essential to all living processes and one which has shown a remarkable adaptability to impinge on other sciences to affect the quality of human life. If other sunrise industries are as successful as the pharmaceutical industry in melding chemistry and other sciences, for example biotechnology, new materials, electronics, then the human race is in for a shining future.

DISCUSSION

Maurice Goldsmith

We have had a wealth of proposals, suggestions and new information made to us. I have selected from these some aspects of what I consider to be part of a necessary vision for the future, and I begin with a thought about the question of the definition of sunrise industries that was raised by Sir Bruce Williams. It is clear that today's sunrise industry is tomorrow morning's noon industry and tomorrow afternoon's twilight industry. Thus, there are only industries with technology in process of becoming outdated, and I believe that approach concentrates our attention on what requires urgently to be our major concern.

Two, I cannot tell what the future will be, but it seems obvious that our society in which, for example, the engineer is downgraded by comparison with the classics scholar – that is only one example – will never enable us to move as leader into that high-technology future.

Let me consider the information technology industry. In 1986, it will be the world's largest industry. By 1990, world-wide the industry will have a turnover of £1,000 billion. However, the UK industry by 1990 will have its share of the world trade shrink to 1.5 per cent as against the current 4 per cent. By 1992, the information technology trade balance figures for leading countries may be as follows: Japan + £42 billion, the USA + £20 billion, the United Kingdom − £5 billion. Over the period 1982 to 1992, direct employment in the information technology industry will increase from 0.6 million to 1.2 million in Japan, and will reduce from 1.3 million to 1.1 million in Europe. Those figures are taken from the 'Little Neddy' Report on information technology which has been published recently.

Three, how do we get from the present to the future that we know can be? I agree with Peter Laister that those who believe that solutions lie in the traditional patterns of the past will fail, and that is being demonstrated at the moment. It is the story of this past century. Britain's first Industrial Revolution did not transform our social fabric. We were left with a cultural

inheritance which is still crippling us. The practical consequences of the continuance of a pre-modern mentality are seen everywhere in our persistent economic retardation.

(There is a story told of Heinrich Heine. It is almost certainly apocryphal, but it is rather nice. He was asked one day where he would like to be when the world was coming to an end and he replied, 'In England of course.' 'But why in England?' 'Obviously, because England is always a hundred years behind the times!')

Four, to get from here to a defined future, we need a cultural revolution, and one in which science and technology are seen as essential elements in a one culture, and it will be a one culture which will enable us intellectually to work on the future and to make our wishes come true.

Five, let us not be modest. We are all seeking to build the future: we want to make the whole world rich: we want health for all. In ten years from now my chauffeur may be a computer. In thirty to fifty years we may be mining the moon and the asteroids. We may be keeping heart patients alive by free fall. Many industries will be out there in earth orbit. The earth may become a one-world park. The fact is that we do live on a finite earth but we live also in a system of 9 known planets, 36 moons, a million asteroids, a billion comets, and a very large thermo-nuclear reactor radiation source. I suggest that within half a century these resources will take care of the necessary warnings given by Aubrey Jones about resources, pollution and energy needs.

Six, the three major industries are information technology, biotechnology and space technology. I am not sure about the future of nuclear technology despite Aubrey Jones plumping in favour of nuclear energy. I think that the question of where to put the radioactive waste is going to be a key factor, as indeed will be the whole question of the use of and development of nuclear weapons.

But I would not be surprised if within a comparatively few years the researches and applications of those sunrise industries make clear that biologically we are at an evolutionary dead end, and that the kind of 'mechanical man' – if I can use that phrase – with the kind of intelligence that Peter Laister mentioned may be a break in organic evolution and will be more in the true tradition of setting a pattern of further evolution.

Seven, what then? I agree with the background statement to

this Symposium published by the Office of Health Economics which calls on us to tackle head-on the anti-intellectualism which seems to lie behind many of the misunderstandings about the better world which can be created if the sunrise industries are encouraged to prosper.

Eight, how can we do this? We have to recognise that our vision of nature, which includes us, is undergoing a radical change, and there are new conceptual structures emerging which are redefining the old distinction between scientific and ethical values. We do live in a dangerous and uncertain world, based upon scientific and technological advances which do not inspire confidence but anti-intellectualism. There is a sense of doom in this world of sunrise miracles. But can we, dare we, abandon the idea of progress? To do so is to make an irreversible decision to abandon ourselves to the intellectual equivalent of a nuclear winter.

Nine, we know what the challenge is. The challenge was expressed in some verse by Cecil Day Lewis:

> Green fields were my slippers,
> Sky was my hat,
> But curiosity killed the cat.
> For this, did I burst
> My daisy band –
> To be clapped in irons,
> By a strange hand?

Or, as Peter Laister put it: 'We are left then with a challenge: a technical future beyond our present imagination, but a present-day situation already unable to cope in an organised way with the problems that this future will create.'

We know what the challenge is, I have just said, and I rephrase it in the striking words of the Mexican poet, Pablo Neruda: 'Shall we be able to emerge from the lightless suburb in which the poetry of everything is vanishing, or shall we be left standing among the ruins with only sorrow to bite on, or shall we be able to see again with new eyes of hope?' The new eyes require a new kind of vision. There is not much time in which to secure this, but, after listening to Peter Cunliffe, I suggest it may well be that the pharmaceutical industry in its international

behaviour as a multinational corporation is already showing us a possible way forward.

DISCUSSION

Michael Kenward

In my role as discusser I want to highlight some of the important points raised by the speakers in their presentations this morning. Focusing first on an issue which emerged from Sir Bruce Williams' paper, it is my belief that more careful consideration must be given to the 'need' for unrelenting technological advance. In other words, is progress being sought for progress' sake rather than in response to clearly identifiable demands? Furthermore, if the latter can be satisfied by 'middle- low- and no-technology' industries, we may be better able to resolve the unemployment problem faced by many Western nations.

Aubrey Jones mentioned in his paper on energy sources that in the United States there appears to be a fresh resort to the use of wood. However, I understand that in Oregon the repopularisation of wood burning is producing one of the worst environmental problems for many decades. Turning to other 'alternative' sources, I think that Aubrey Jones' paper tended to overemphasise the environmental problems associated with solar energy. The construction of power stations in the Sahara is clearly a non-starter but orbiting space stations, which would get round the environmental problem, may present a more viable solution. The United States is now investing heavily in this idea which, incidentally, was universally dismissed when it was first floated twelve years ago.

Windmills were also mentioned as a possible supplementary source of power. However, problems such as the electrical disturbance to which they give rise imply that they would have to be established in isolated locations. My final comment in the context of energy sources is a warning not to place too much faith in estimates of future energy reserves. There are many examples of the fallibility of such estimates and perhaps we need to concentrate on the requirements of, say, just the next 25 years, during which time new solutions will probably emerge in any case.

Peter Laister's contribution referred to the hundredth anniver-

sary of the Industrial Revolution and this reminded me that it is just ten years since the advent of the microcomputer. And the point that this thought emphasises is how difficult it is to make accurate forecasts. At the beginning of the microcomputer, hardware and software costs were so high that there was a widespread belief that there would be very little market potential for the product. Yet technological advance coupled with the economies gained from large-scale production have substantially reduced prices and demand is booming. The problem that this rapid 'mini-revolution' has conferred upon us is, instead, one of coming to terms with, and exacting the full potential from, the technology that is now available.

Another point that I believe deserves to be highlighted is that high-technology equipment and systems are not immune to the interventions of the 'human factor'! An example of what I mean may be drawn from British Telecom's admirable new electronic mail system. It is a system of great value to me as an editor: I have correspondents scattered around the world who are able to meet my Tuesday morning deadline even with stories they are filing last thing on Monday night. Recently, however, the system experienced a snarl-up – I believe a tractor was driven through a cable and the system was put out of action for a day!

Peter Laister also raised the question of technological progress and employment opportunities. In this context I should like to draw upon my own experience at *New Scientist*. Each weekly issue of the magazine contains approximately 30 pages of classified job advertisements – yielding several hundred employment opportunities. Yet they have little relevance to the millions of unemployed because the majority of them demand only people with experience. Even new graduates from university are excluded. In this sort of situation, how are new generations to gain the experience necessary to take advantage of the few opportunities that do exist?

Finally, Peter Cunliffe referred in his paper to the vast sums of money that a pharmaceutical company would now need to find in order to undertake a new research programme. Setting aside the difficulties which would be involved in obtaining this volume of finance, the question that intrigues me is whose judgement would decide the direction of the research initiative? Would it be the views of the scientist or the marketing people or some other department that would prevail? The point implicit in this

question returns to what seems to me to be a key requirement in the context of technological advance – the meeting of need rather than the pursuit of progress simply for its own sake.

GENERAL DISCUSSION

Two principal topics emerged during the period for general discussion. The first concerned future economic progress and was raised initially by Sir Douglas Black (President, British Medical Association) who questioned rhetorically the desirability of indefinite economic growth. Both Aubrey Jones and Peter Laister championed sustained advance: the former returned to one of the themes he had elaborated upon in his paper and argued that future energy supplies are dependent upon capital investment and that this will not be forthcoming unless there is growth. Peter Laister, however, argued that attention should be focused on change, which is both desirable and inevitable, rather than economic growth as it is traditionally understood. Having made this distinction, he commented that he could not imagine a static society. Furthermore, he argued that there is a need to plan for change, referring, as an illustration of this requirement, to the growth of the semiconductor industry and its pervasive effects upon all modern technology and especially that in information, communications and entertainment. And, he added, such forward thinking cannot simply be confined to changes of a 'technological nature' – the social sequelae of the latter will have to be accommodated and this problem requires considerably more thought than is being given to it at the present time.

Otto Nowotny (Hoffmann-La Roche, Switzerland) sought to provide some degree of reassurance for those fearing the consequences of indefinite economic growth by pointing out that the latter is, in fact, a chimera and does not exist in any context. He referred to Salk, the inventor of the polio vaccine, who had shown that if two fruit flies are placed together in a glass jar, they will start to multiply and continue to do so until a certain point in time at which exponential growth ceases. This pattern of development, portrayed by the S-curve, also characterises economic growth. Furthermore, Mr Nowotny argued that the model applies equally to population growth so that stabilisation may be predicated by 2050 (at around 10 billion people). Hence fears of pollution on a catastrophic scale resulting from exponential population growth may be unfounded.

In the context of pollution, Dr Maurice Goldsmith also expressed some degree of optimism based on the observation that there appears to be increasing understanding of the importance of operating in closed systems – that is, in systems which ensure that pollution is not allowed to escape into the external environment.

The second broad area of discussion focused on the implications of progress in electronics and communications for information quality, storage and flow. Dr David Conning (British Industrial Biological Research Association) questioned whether the development of artificial intelligence might help to raise the quality of available information by rejecting the 'useless' material that manages to get published today. Peter Laister expressed confidence that in the future intelligent computers could be taught – or perhaps could train themselves – to identify information which has a high probability of application or use. Consequently, there would be no diminution in the input of worthless data, but the other end of the system output would probably contract, with its content becoming restricted to only high-quality data. Michael Kenward viewed potential development along these lines with some concern because of the danger that floods of new data, albeit of seemingly high quality, may be rapidly and widely disseminated to individuals whose understanding of the information's limitations (arising, for example, from its method of construction or problems in interpretation) may be incomplete.

In closing the discussion period, Lord Swann raised the general question of society's responsiveness to change. He reminded the meeting that in any sort of living organism there exists a prodigious number of negative feedback systems (for example, temperature control) which are effectively designed to promote stability. He then suggested that a form of negative feedback also appears to operate in relation to the acceptance of new ideas. And, perhaps contrary to popular opinion, science does not rapidly advance because scientists are extremely receptive to new ideas. Indeed, Lord Swann maintained that scientists tend to be as dogmatic as other groups in society and many famous practitioners have failed to gain acceptance of their ideas during their lifetime.

This state of affairs is, of course, not necessarily harmful. Moreover, it may be argued that a degree of resistance to change

is required to prevent a slide into chaotic disorder. However, Lord Swann expressed concern at the possibility of the development of too much resistance. The effect of new technologies over the last century or so has been in general to raise people's socio-economic status and with that their expectation of life. Consequently, we now have a much older population which in general means that it is more resistant to change. Paradoxically, therefore, the greater the technological progress, perhaps especially in health care, the more resistant to change society may become.

SESSION II:

THE INTERNATIONAL SCENE FOR PHARMACEUTICALS

CHAIRMAN'S INTRODUCTION

Graham Wilkins

Lord Swann, in his introductory remarks opening the Symposium, characterised this second session as dealing with the macro-political aspects of the pharmaceutical industry. This seems highly appropriate judging from the titles of the papers to be presented this afternoon. It is also clear that we are concerned with the pharmaceutical industry and its operations in an international context. The international scene facing the industry is ever-changing and thus requires continuous review by pharmaceutical manufacturers leading to modified or new responses as and when necessary. Yet I am not sure that in the past the pharmaceutical industry has been prepared to change as rapidly as it ought to have been and this point, coupled with the need for appropriate action, will perhaps emerge from this session as a key issue.

POLITICS AND THE PRESENT PATTERN

George Teeling Smith

After the discussion so far on the 'sunrise industries' as a whole, this paper focuses down on to the specific problems of the pharmaceutical industry. At the time that the Symposium was planned early in 1983, the prospects for the pharmaceutical industry looked generally very favourable. Its growth as a proportion of total world gross national product from 0.58 per cent in 1960 to 0.78 per cent in 1980, for example, reflected the continuing success of the industry's innovation (Table 1). Since 1983, however, the political climate has become distinctly more hostile, and this Symposium can no longer merely focus on the achievements and the potential for the industry, but must inevitably look also at the problems with which it is increasingly faced. Later papers will pick up this theme more clearly; the present task is to set the scene by describing the international pattern of pharmaceutical innovation and the political environment in which that pattern has been created. Most specifically, this paper will focus, in an historical context, on the political problems and pressures which seem to have developed so strongly over the past two years.

Table 1: Pharmaceutical Consumption and World Gross Domestic Product

Year	Pharmaceutical Consumption[a] ($ billion)	GDP ($ billion)	Pharmaceutical Consumption as per cent of GDP
1960	6.5	1,126	0.58
1970	18.0	2,503	0.72
1975	36.0	5,055	0.71
1980	76.0	9,708	0.78

Note: a. Manufacturers' prices.
Sources: Pharmaceutical sales: Intercontinental Medical Statistics; GDP: United Nations.

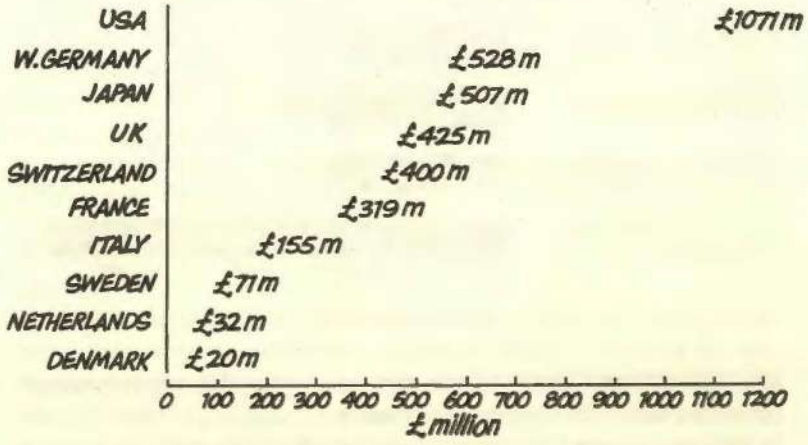
The international pattern of the pharmaceutical industry

should already be well known, but it is worth recalling that the concentrations of research investment, on the source of new pharmaceutical products and of pharmaceutical world trade each present an essentially similar picture. Only six countries have been mainly responsible for the world-wide growth of the pharmaceutical industry. These are centred in the United States, in Western Europe, and, more recently, in Japan.

Figure 1 shows that the pharmaceutical industry's research is concentrated in the United States, West Germany, Japan, the United Kingdom, Switzerland and France. Figure 2 shows that the same countries – the United States, the United Kingdom, Japan, West Germany, Switzerland and France, in that order – were the source of the largest proportion of the world's leading pharmaceutical products in 1982. For comparison, Figure 3 shows the corresponding data for 1980, when Japan lay in fifth position. Its rise to third place in 1982 is undoubtedly significant. It indicates the inescapable interrelationship between that 'sunrise nation' and this 'sunrise industry' in the future.

Figure 4 shows that, with the exclusion of Japan, it is once again the same six countries which dominate world trade in

Figure 1: Pharmaceutical Research and Development Expenditure in 1982



Source: OHE.

Figure 2: Country of Origin of Leading International Pharmaceutical Products – 1982

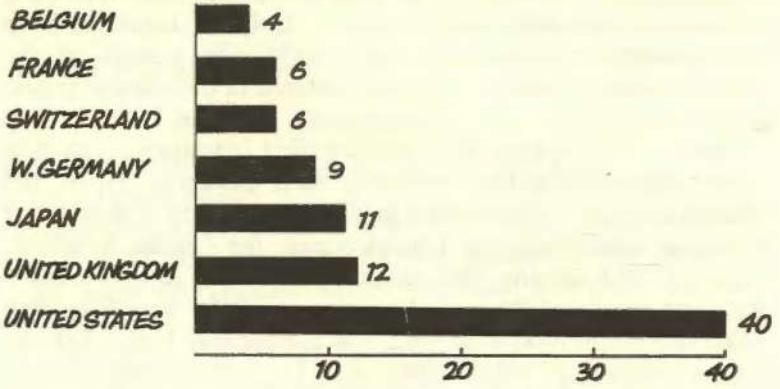
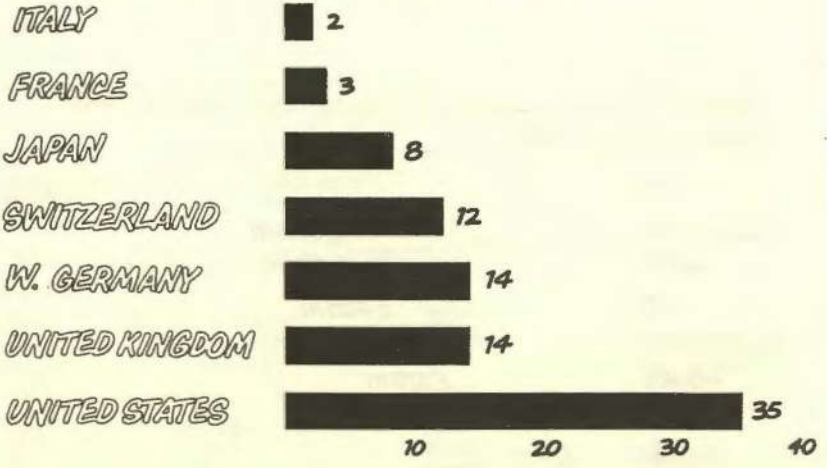


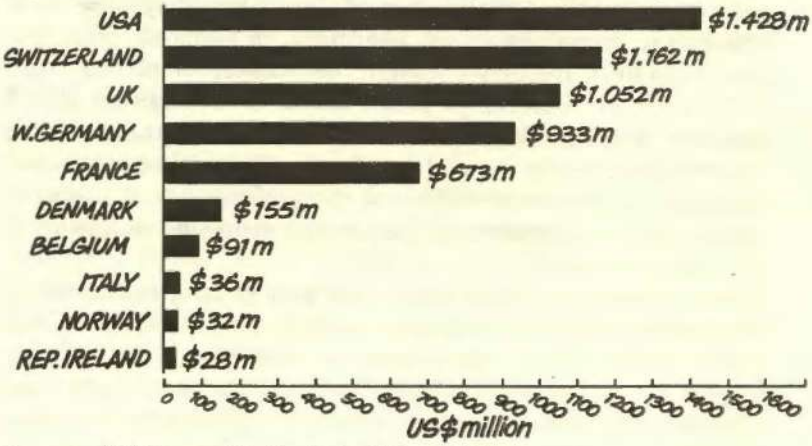
Figure 3: Source of the Leading International Pharmaceutical Products in 1980



pharmaceuticals. Japan seems certain to join this small band of countries with a strong positive balance of trade in pharmaceuticals in the near future. Meantime it is the other five national centres of pharmaceutical innovation which enjoy the economic benefits

of a substantial trade surplus in pharmaceuticals. Undoubtedly, pharmaceutical research and development has brought prosperity to the countries which have encouraged and fostered it.

Figure 4: Pharmaceutical Trade Surplus by Country – 1982



Source: UN Commodity Trade Statistics, 1982.

Turning from the pattern to the politics, one essential prerequisite for pharmaceutical progress has been a sound basic scientific infrastructure in the universities and in the government research institutes. From these the industry's pharmaceutical research scientists have been able to gather fundamental new ideas and to interchange scientific theories. However, the fact remains that in each country it is the industry, rather than academia, which has had the resources and the expertise to turn these basic scientific theories into marketable medicines.

The other less obvious prerequisite for a country to have emerged as a successful centre of pharmaceutical innovation has been a liberal economic policy towards the industry. To a greater or lesser extent, this has applied in each of the six successful nations.

In the United States, the predominant philosophy has always been that 'what is good for American industry is good for the American people'. The inroads of the Anti-Trust Laws and Ralph Nader and others, in their attacks on industrial freedom, have done little to dent the overwhelming American belief in private enterprise. Specifically for pharmaceuticals, the stringency

of the Food and Drug Regulations and the introduction of universal substitution laws to permit generic dispensing have done surprisingly little to undermine the essential prosperity of the United States research-based industry. For example, although cheap substitution is permitted, patients have generally chosen to pay for the original brand of medicines when they have been offered the alternative in the pharmacy. In financial terms, the pharmaceutical industry's 'return on capital employed' runs consistently five percentage points above the average for all US industry. It has no price control and very little restraint on free competition in sales promotion. In the United States, despite continuous consumerist sniping at the pharmaceutical manufacturers, their contribution to human and economic well-being is generally recognised and rewarded.

West Germany, again, has in the past given great economic and scientific freedom to the pharmaceutical industry. There is no price control, and no restrictions on competition. Admittedly, doctors can be penalised if they over-prescribe; there have been voluntary restraints on price increases by the industry; and some less important types of medicine are no longer reimbursed. However, in general, the Federal Republic of Germany has enjoyed a healthily liberal climate.

Switzerland has perhaps the strongest tradition of all of an economic alliance between government and industry, in order to promote national economic prosperity. For pharmaceuticals, this has resulted in this very small nation becoming a world leader in the industry.

The Japanese government, also, has until recently offered strong scientific and economic protection to its indigenous pharmaceutical industry, and, despite recent price reductions, local prices remain well above the world average. These high prices have enabled the Japanese pharmaceutical industry to fund its expanding research programmes.

In the United Kingdom, the Pharmaceutical Price Regulation Scheme specifically recognises a dual function:

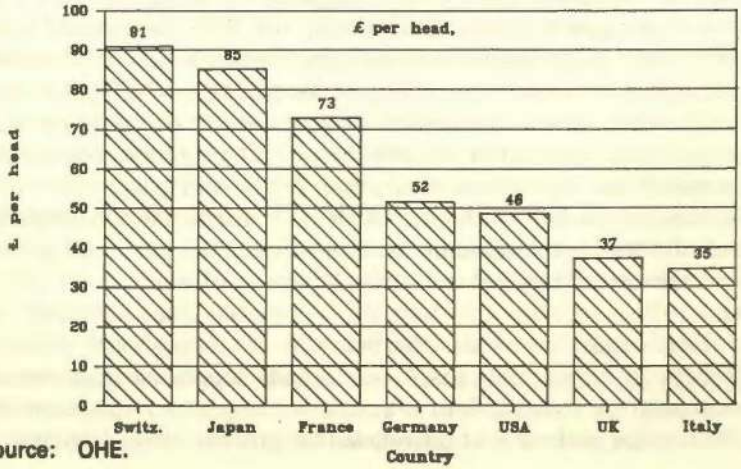
> in securing not only that safe and effective medicines are available on reasonable terms to the National Health Service, but also that a strong, efficient and profitable pharmaceutical industry in the United Kingdom is capable of such sustained research and development expenditure as should lead to the

future availability of new and improved medicines, both for the National Health Service and for export.

Although controls on the level of marketing expenditures were imposed by government in 1976, and greatly strengthened in 1983, Health Ministers continue to reaffirm the government's intention to maintain a strong and profitable industry in Britain.

France, on the other hand, represents something of an enigma among the six most successful innovators. The French government has always imposed, at least in name, strict price control on pharmaceuticals. In the 1950s and 1960s these nominal controls could often be circumvented by legitimate commercial devices within the industry, and it was widely suspected that government willingly connived at such practices. However, more recently, French pharmaceutical price controls have operated more effectively, and now French prices are so low as to be an embarrassment both to the local and to the international industry. Surprisingly, the French industry's export performance has been maintained, but possibly this too has been achieved with uneconomic pricing. Nevertheless, Figure 5 shows that France has a higher per capita consumption of pharmaceuticals in money terms than many other European countries. Perhaps this very high local consumption, despite the low prices, will be able to sustain the French industry even with the present restrictive price controls.

Figure 5: Pharmaceutical Consumption per Capita – 1981



Source: OHE.

In general, therefore, the picture in the past has been one of national governments supporting their pharmaceutical industry in the countries which have become centres of international pharmaceutical innovation. More recently, however, governments have tended to respond to consumerist pressures and to exert a less benign influence. The relationship between government and industry is, therefore, indeed a delicate one, which will no doubt be much discussed in later papers.

Here, an historical analogy may be of interest. The example is the early development and the later economic difficulties of rail transport in Britain. It is a splendid example of the initially supportive and finally restrictive intervention of government. Although the type of economic activity is very different from pharmaceutical innovation, the lessons to be learnt may indeed be relevant.

Railways were first conceived of in Britain as a form of transport in the early nineteenth century. In order to overcome local obstacles, Acts of Parliament were required. In those days, as now, innovation was suspect, and the first Railway Bill of 1819 was defeated by the lobbying of a local Master of Foxhounds – who presumably feared that the railway would frighten either the foxes or the hounds. The first Railway Act was eventually passed in 1821, and this, together with a further Act of 1823, enabled the classic Stockton to Darlington Railway to open in 1825.

The first 'inter-city' train – from London to Birmingham – was also the subject of controversial legislation, but an enabling bill was finally passed at the third attempt in 1833. Subsequent Acts authorised a plethora of competing railways and of funding operations to finance them. Thus in the early days Parliament and the private railway companies worked together to develop and extend the innovation of rail travel. The private companies provided the innovative drive, and Parliament passed enabling legislation. In the 1840s and 1850s, that particular 'smokestack' industry was in the same innovation phase which pharmaceuticals and the other 'sunrise' industries have experienced in the 1960s and 1970s.

But – just as with pharmaceuticals throughout Western Europe in the past few years – an initially supportive government was soon to develop into a restrictive regulatory influence. In 1889, price control was introduced to prevent alleged abuses of

monopoly power by the railways, and an Act of 1894 further reduced the railway industry's flexibility in pricing. By 1914, according to the economic historians Dyos and Aldcroft (1974), the railways had become the 'most regulated form of economic activity' in Britain.

Ironically, this strict regulation to prevent the supposed abuses of monopoly coincided with the emergence first of the internal combustion engine and relatively cheap road transport, and later with the development of inter-city air travel. Vigorous innovative competition compounded the problems which had already been introduced for the railways by bureaucratic economic controls. To add to the industry's difficulties, government responded to the railways' consequent economic problems by further regulation. An Act of 1921 called for rationalisation, and set targets for 'standard revenues' from the railway companies – a horribly similar principle to government's attempts to control pharmaceutical revenues in the 1980s.

By the 1930s, according to Dyos and Aldcroft, 'to a large extent, the [railway] companies were prevented from operating their undertakings as commercial concerns by the statutory obligations with which they had been encumbered'. In particular, they were prohibited from pricing competitively in order to earn maximum profits from the sort of goods for which the railways could compete effectively against road transport. Drawing a particularly sinister analogy, this paved the way for the nationalisation of British Railways in 1948. The legislators had first strangled the industry's entrepreneurial freedom; this in turn provided a justification for their taking control of it, once it had been driven into financial difficulties by the dual forces of bureaucracy and competition.

Looking more broadly at the lesson from Britain's railways, how easy it seems to be for well-meaning attempts to control a sector of economic activity, supposedly in the public interest, to end up by simply making it uneconomic. The political implications arising from this thought lead on naturally to a review and to a discussion of the political forces which have so stridently attacked the pharmaceutical industry in the past two years or so.

Particularly since the late 1970s, a series of organisations purporting to represent the broad public interest have launched a massive and concerted attack on the activities of the pharmaceutical industry throughout the world. These organisations

include Oxfam, War on Want, the World Council of Churches and Social Audit, as well as the international umbrella organisation, Health Action International. They are supported by politically motivated doctors and their objectives are mirrored in the health policies of Britain's two socialist parties – Labour and the Social Democrats.

There is little doubt that all these organisations sincerely believe that they are acting for the public good. Unfortunately, their basic philosophies are founded on two fundamental misapprehensions. The first stage in their philosophy is that stricter government control and more rigorous price competition would be in the public interest. This exactly mirrors the beliefs of the nineteenth-century 'do-gooders' who wanted more competition and more control on the British rail system in the 1880s. It runs counter to the economic principles expounded in the twentieth century by Schumpeter (1942), Chamberlin (1933) and Robinson (1933) which describe the favourable conditions necessary for an innovative industry to compete and to develop.

But much more dangerously, these critics of the free-enterprise pharmaceutical industry may not be aware that stricter bureaucratic control of the industry coupled with the fierce innovative competition which exists for pharmaceuticals could easily create a financial crisis in the industry, and produce an exactly similar political and economic climate to that which led to the nationalisation of the railways in Britain in 1948.

This would delight the more extreme consumerist groups such as Oxfam and the World Council of Churches. They seem to believe that multinational capitalism acts against the interests of the mass of the world population, and that state-owned national enterprises would in some way be 'more responsive' to public needs. Although, for many people, personal experience of state-controlled organisations belies this touching faith in the benefits of nationalisation, the real arguments against excessive bureaucratic controls 'in the public interest' are more fundamental than mere public inconvenience.

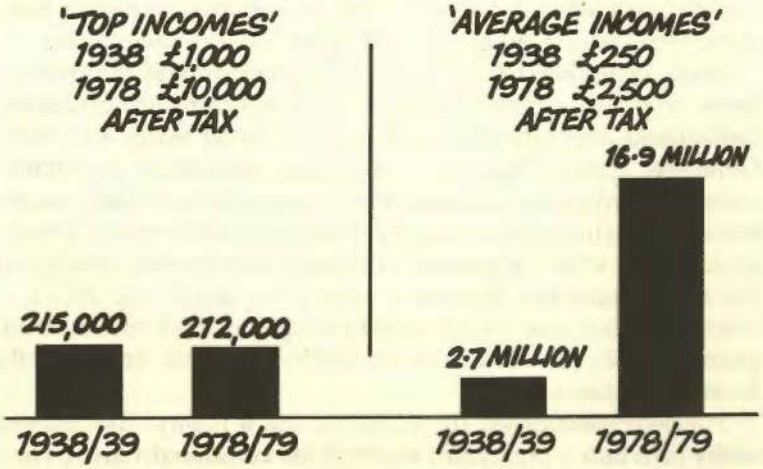
Harping back once more to the example of the railways, their financial problems stemmed in part from the existence of government restrictions which prevented them from maximising their profit on successful lines. The price control schemes for the pharmaceutical industry in the 1980s have a similar effect. They knock the tops off peaks of profitability, and create an economic

climate for financial mediocrity. The broader underlying philosophy seems to be that high incomes for a few lead to profligate extravagance and, at the same time, deprive the masses of their fair share of spending power.

In other words, the belief is that high income creation is inimical to fair income distribution. In fact, economic history demonstrates the opposite. When the technological entrepreneurs are generously rewarded, extra real money is created and this quickly spills over to benefit the less-well-off. British experience over the past forty years illustrates this point.

'The poverty lobby' has often implied that generally rising incomes in Britain have been concentrated for the benefit of a privileged few. It is interesting, therefore, to look at the facts, comparing 1938/9 with 1978/9, as shown in Figure 6. At the top end of the scale, in 1938/9 there were 215,000 net incomes after tax in excess of £1,000. Allowing for tenfold inflation, the equivalent figure in 1978/9 was 212,000 incomes over £10,000. Thus, at the top, the picture has remained static. But for the majority of people, there has been a dramatic change. Taking £250 a year as a minimum viable net income in 1938/9, only 2.7 million incomes exceeded this level. By 1978/9, taking £2,500 as the equivalent cut-off point, 16.9 million incomes exceeded this figure – a fivefold

Figure 6: Redistribution of Incomes in Britain: 1938/9 to 1978/9



Source: *The Economist Diary* (1984).

increase over that in 1938/9. Thus higher real incomes for the British population as a whole have been paralleled by a massively wider distribution of the total income. The creation of greater earning power by technological progress has selectively benefited the less privileged majority of the population. In simple terms, making money is a 'good thing' for society as a whole; it is not something which should be controlled or restricted.

Unfortunately, in practical terms, the consumerist bodies consider that pharmaceuticals should be an exception to this general rule, and they have been remarkably successful in persuading governments that strict price controls are desirable in order to reduce public spending. This is the problem facing the international industry in practically every country. Alarmingly, the pressures seem to be increasing. Oxfam, for example, has recently increased the share of its budget devoted to its politically conscious Public Affairs Unit from 5 per cent to 6 per cent (Melrose, 1984). They use isolated examples of undesirable practices in the industry, often from the past, to justify their demands for stricter control. They dismiss the industry's response that self-regulation and long-term competitive objectives will eliminate the cause of these criticisms more effectively than government regulation. They keep demanding government intervention, backed by more legislation and stricter enforcement, as their preferred solution. According to their own opinions, they are doing this with the best of intentions. Their attitude recalls the aphorism which a doctor I knew once applied to his sister-in-law: 'She is a worthy woman; and I can say no worse of her.'

Thus, returning to the pattern of international innovation, there is a real choice facing the five governments of Japan, Switzerland, the United Kingdom, the United States and West Germany. Either they can continue to provide a favourable economic environment for free-enterprise success, or they can go down the pathway followed by the nineteenth-century British government when faced with criticisms of monopoly abuses by the British railways. For the French government, the choice is whether to continue on an already dangerous path of restrictive price control, or whether to reintroduce a more economically favourable climate.

For pharmaceuticals, the sunrise is still a reality. But it could easily turn into a premature sunset if the consumerist groups and left-wing politicians were to have their way. When later papers

look more specifically at the prospects for the industry over the next few years, they must do so against the stark reality of these alternative scenarios for the political future of world-wide pharmaceutical innovation. Supportive co-operation between science, government and industry has provided the infrastructure for successful pharmaceutical innovation since the 1950s. If governments were now to become restrictive economic regulators, it would spell disaster for the future of pharmaceutical innovation.

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THE ROLE OF THE EUROPEAN COMMUNITY

Tom Garvey

I would like to begin my remarks this afternoon by emphasising the positive economic and social contribution made by the pharmaceutical industry to the European Community. The industry employs approximately 300,000 people, of whom about one-fifth are university graduates. In 1982, exports of pharmaceuticals from the Community exceeded imports by 2,700 million European Currency Units, equivalent to approximately £1,600 million. Quite apart from purely economic considerations, the products of the industry have brought relief to millions of people, both in the Community and the rest of the world.

At the present time, we appear to be on the threshold of major changes in human and animal therapy. Recent scientific advances in the field of biotechnology hold out the prospect of an important new range of medicines and the possibility of treating many diseases more effectively than in the past.

Indeed the potential of biotechnology is already being realised through medicines which are now on the Community market, such as human insulin, or which are about to come on to it, such as the interferons and synthetic vaccines. However, innovation is also occurring outside the field of biotechnology: new drug delivery systems will permit the more precise targeting of medicines within the body; new manufacturing procedures will permit the easier synthesis and purification of certain medicines. Clearly the potential of the pharmaceutical industry is vast. The challenge lies in realising that potential and ensuring that the European pharmaceutical industry does not fall behind its competitors, particularly in the United States and Japan. The Commission attaches great importance to the future of the pharmaceutical industry, for it is a sector where we have been strong in the past and where we are reasonably well placed for the future. My objective in this paper is therefore to explain how the Commission perceives its responsibilities in meeting this challenge.

A comparison of the relative position of the Community pharmaceutical industry and that of its major competitors in the US and Japan shows that the European industry is disadvantaged by the absence of a truly unified large internal market. Leaving aside economies of scale, the larger the market the easier it is to recover the substantial investment incurred in bringing a new product on to the market. For this reason, the Commission's first task must be to fulfil the mission conferred upon it by the Treaties, the creation of a unified single Community market for pharmaceuticals.

The difficulties involved are considerable. We are dealing with a highly regulated sector in which public health interests are paramount and where complex scientific assessments must be made, sometimes on the very frontiers of human knowledge. Not unnaturally, industry executives and academics are often more familiar with national legislation than with the Community texts on which that legislation is based, but there is often a surprising ignorance of our work in this field. I therefore propose to outline what has been achieved and what remains to be done.

However, there are other problems confronting the industry, and so I shall also briefly examine national price controls, restrictions on the social security reimbursement of pharmaceuticals, parallel imports, patents, the protection of know-how and the second applicant problem and research in general.

Harmonisation of Legislations

In principle there are two methods of attaining a single Community-wide market for pharmaceuticals. The first method would be to create a single, centralised Community licensing authority to grant approvals for new drugs for the Community as a whole. Although at first sight this seems the simplest approach, some thought will show that its administrative, legal and financial implications would be considerable. The alternative approach is to leave decision-making at the national level and to work towards the mutual recognition of national decisions. Thus once a new product has been authorised in one country, authorisation would normally follow in the other Member States unless there were valid reasons for a refusal. Discussions on the most appropriate way of proceeding took place at Community level for

many years, but the most recent Council Directive, adopted in October of 1983,[1] seems to have settled the debate in favour of the approach based on mutual recognition, at least for the time being.

To date, five substantive directives on proprietary medicinal products for human use have been adopted by the Council,[2] and two relating to veterinary medicinal products.[3] Although the principles underlying the human and veterinary medicines directives are similar, there are some important differences between the two and the following comments are confined to the human directives.

The manufacturer of a medicinal product must obtain a marketing authorisation from the authorities of each country in which the product is to be marketed. Authorisation can be refused only on grounds relating to the quality, safety or efficacy of the product, and the directives set out the requirements the manufacturer must satisfy in order to obtain authorisation. In particular a directive on standards and protocols sets out detailed requirements for the conduct of analytical and pharmaco-toxicological tests and clinical trials. Therefore it is no longer necessary to repeat tests and trials in order to obtain authorisation in the different Member States. In fact, provided language requirements are satisfied, the same dossier may be submitted to all the Member States. This aspect of the Commission's work is therefore now largely complete, although the detailed test requirements must be kept under constant review, and, if necessary, adapted to take account of technical and scientific progress. Thus in October 1983 the directives were amended to provide for mutagenicity and bioavailability tests. More recently we have proposed that the use of LD_{50} in the acute toxicity test be replaced by the notion of the approximate lethal dose in order to avoid any unnecessary use of laboratory animals.[4]

So far as manufacturing operations are concerned, we have been able to make substantial progress without having to spell out the duties of manufacturers in great detail. Thus the directives already provide for the mutual recognition of national authorisations for manufacturers. However, if the authorities of the importing country are in any doubt about the quality of a particular manufacturer's process, they may ask the authorities of the exporting country for the information necessary to satisfy themselves that the legal requirements have been complied with.

Individual batches of pharmaceuticals, accompanied by the manufacturer's batch control reports, are exempted from systematic inspection or testing when they are imported to another Member State.

Much has therefore been achieved, but one fundamental problem remains. Although the directives set out in some detail the information to be supplied by the applicant for marketing authorisation, there is no guarantee that the authorities of the Member States will evaluate this information in the same way. There is therefore a danger of divergent decisions, with a product being authorised in some countries but not in others. In order to overcome this problem, a double approach has been employed.

First, two expert working groups, one on the safety of medicines and the other on the efficacy of medicines, have been working on detailed guidelines for the testing of medicines. The objective of these guidelines is to give the considered opinion of all the national authorities on the manner in which the requirements of the testing of medicines should be interpreted and applied, and thus provide clear guidance to industry on what is expected of it. A first series of guidelines was promulgated by a Council Recommendation to the Member States in October 1983,[5] and the Commission has recently proposed the adoption of a second series of guidelines to the Council.[6] In consultation with the industry, priority subjects for inclusion in a third series have now been identified and work on these is in progress.

Second, in 1975 the Council created the Committee for Proprietary Medicinal Products. The main task of this Committee is to promote a convergence in national evaluations of pharmaceuticals through the discussion of concrete dossiers. Since it became operational in 1977, the Committee has discussed more than 100 products referred to it by Member States. Of particular interest is the 'multi-state' application procedure. A firm which has already received authorisation in one of the Member States may apply for authorisation in at least five other Member States through the Committee. Following receipt of the dossier, the Member States have 120 days to lodge objections to the authorisation of the product. These objections are examined by the Committee, and after 60 days at the most, it issues an opinion of the quality, safety and efficacy of the product. The opinion is not binding, but the Member States must announce their decision within a further 30 days.

Since 1977, the Committee has examined 38 dossiers in this way. It is perhaps regrettable that this number is not greater, but realistically it must also be accepted that there were certain shortcomings in the procedure which made it unattractive to the industry. However, in 1983 the Council agreed to certain changes which will come into effect in November 1985 at the latest. In particular the threshold number of Member States will be reduced from five to two, and for the first time the applicant will be given the right to a hearing before the Committee.

Nevertheless, on the basis of the progress then achieved, in 1980 the Commission considered that the time was right to propose the mutual recognition of national marketing authorisations. Thus a product authorised in one Member State would, at the request of the firm, be authorised in other Member States save in exceptional cases which would be submitted to the Committee for Proprietary Medicinal Products for its opinion. Unfortunately, the Council was not prepared to go this far. Nevertheless the 1983 Directive does require the Member States to take the original authorisation into due consideration. To facilitate this, the directive also requires Member States to elaborate and exchange assessment reports on pharmaceuticals containing a new active substance. This solution, a compromise, is clearly transitional, and the Commission is required to submit new proposals to the Council in 1989 to eliminate the remaining barriers to intra-Community trade in pharmaceuticals. In the meantime it can only be hoped that the industry will find the new Committee for Proprietary Medicinal Products procedures sufficiently attractive. If there is one thing that experience to date has shown, it is that progress towards the free movement of pharmaceuticals can only be made by establishing mutual confidence between the national administrations. One of the few ways of establishing that confidence is through the detailed discussion of particular cases. Unless the pharmaceutical industry itself is prepared to help us, by submitting good-quality, carefully presented dossiers through the Committee for Proprietary Medicinal Products, further progress will be difficult.

The Biotechnology/High-technology Proposals

For medicines derived from biotechnology and other high-technology medicines we considered that we could not afford to

wait until 1989 before taking action. Bringing these new products on to the market requires a considerable investment, which is extremely risky, and is usually financed by the industry itself. In February 1984 we received from the European Federation of Pharmaceutical Industries Associations, EFPIA, an important discussion paper entitled 'The European Pharmaceutical Industry and the Development of Biotechnology'. After studying that report and the other available evidence we became concerned that firms were deferring necessary investment decisions with the result that the Community industry was in danger of falling behind its US and Japanese competitors.

The Commission has therefore recently proposed a package of regulatory measures to favour the marketing of biotechnology and other high-technology medicines.[7] One part of this package is a proposal for a directive to improve the present co-ordination procedure so that we can arrive at uniform decisions on the marketing of biotechnology and other high-technology medicines. Under this proposal the Member States will be required to refer systematically to the Committee for Proprietary Medicinal Products all applications for marketing authorisation for biotechnology products. At the same time they will be required to send to the Committee a summary data sheet on the product, a summary of the documents contained in the application and any existing evaluation reports. In addition the firm will be able to send to the Committee whatever information it considers appropriate and it may request an oral hearing before the Committee. The Committee may either examine the application itself or entrust the work to an *ad hoc* working group or to outside experts, who will of course be required to respect the confidentiality of all the information they receive. At the end of the procedure the Committee will deliver an opinion on whether the product should be authorised and while this opinion will not be binding, we hope that it will lead to a greater convergence in national decisions.

For other high-technology medicinal products, such as major new drug delivery systems, or important new drug substances, the procedures are essentially the same as for biotechnology products. There is, however, one important difference. For biotechnology products we considered that the wider interest justified the systematic referral of all new products to the Committee for Proprietary Medicinal Products. However, for

other high-technology medicines it was doubtful whether this was necessary, and so the matter will be referred to the Committee for Proprietary Medicinal Products only if the firm or a Member State so requests.

In addition to provisions relating to individual decisions, the proposal also contains provisions designed to prevent the unilateral adoption by Member States of technical regulations governing biotechnology and other high-technology medicines which might have the effect of creating new barriers to trade within the Community. Each Member State will be obliged to notify all new draft technical regulations to the Commission and the other Member States, and to take account of any comments they receive. Where a Member State or the Commission considers that a technical regulation will result in unnecessary barriers to trade, the Member State will be obliged to delay adopting the measure for six months unless it is urgently necessary for the protection of public health. If the Commission decides to propose Community legislation on the matter this period is extended to twelve months.

Two points should be emphasised about this proposal. In the first place, there is no question of setting up a centralised Community decision-making system. All we are trying to do is to strengthen existing well-established co-operation and co-ordination procedures. Second, it would clearly be counter-productive if Community co-ordination procedures resulted in additional delays in getting new products on to the market. For this reason, the examination at Community level takes place at the same time as the examination at national level and the Committee for Proprietary Medicinal Products is obliged to respect the same time limits as the national authorities.

As a second part of this package, the Commission is also proposing major changes to the procedures for amending the technical standards and protocols for the testing of human and veterinary medicines. At the present time these standards and protocols can only be amended with the unanimous agreement of all the Member States. The search for unanimity makes the procedures long and cumbersome, lasting on average four to six years, when what is required is flexibility and the possibility of rapid change to reflect changes in the state of the art.

For this reason, it is proposed that henceforth these changes should be made by what, in Community jargon, is called a

qualified majority vote. Such a change will, of course, mean that each Member State will lose the power of veto and, predictably, there are many who argue that in areas where public health is involved each Member State must retain a right to veto changes to which it is opposed. To that argument, there are two replies. First, the qualified majority system offers considerable safeguards. The votes of the Member States are weighted, with the four larger Member States casting 10 votes each, Belgium, the Netherlands and Greece 5 votes, Ireland and Denmark 3 votes, and Luxembourg 2 votes. A measure is adopted only if it receives at least 45 votes out of a possible total of 63. Thus a large measure of agreement is required before any directive can be adopted. Second, and perhaps more importantly, the present unanimity rule itself poses a danger to public health. How much longer are we to tolerate a situation in which a single Member State, possibly even a single national official, can prevent or delay the changes which are necessary to bring the detailed test requirements into line with scientific and technical progress?

A criticism which is sometimes made of the Commission's work is that it has become so immersed in the details of product registration that it can no longer identify the wider problems confronting the industry. With that criticism in mind, I would like to consider briefly some of these problems and our response to them.

Price Controls

In the majority of Member States pharmaceuticals are subject to direct or indirect price controls of varying degrees of severity. The industry argues that price controls limit its ability to finance research into new products. Others reply that the link between high profits and research innovation is not clear, or that the best way to encourage research into new products is to reduce the prices of older products. The setting of the overall level of finance which a given society is prepared to devote to its drugs bill involves an element of political choice which at the present time can only be exercised at the national level. The harmonisation of national drug pricing systems will become possible only when a much greater degree of general convergence in the economies of the Member States has been achieved. Thus the

Court of Justice has ruled that Member States may take measures to control the prices of pharmaceuticals, provided that they do so in accordance with the Treaty,[8] which in practical terms means that they must not discriminate against imports from the other Member States.

It is the responsibility of the Commission to ensure that these rules are applied. When the national regulations governing prices openly distinguish between domestic products and imports, our task is a relatively simple one. We simply have to demonstrate that the regulations are capable of putting the marketing of imports at a disadvantage compared with similar domestic products. Thus in the past we have been able to secure certain changes in national pricing systems without having to take the matter before the Court. At the present time proceedings are in progress against three of the Member States. Obviously I cannot discuss these cases in detail, but one of the points we are pressing strongly is that when setting the prices of individual products, a Member State must treat the research expenditure incurred in the other Member States in exactly the same way as research expenditure arising within its own territory.

Our position is much more difficult when the national regulations appear to apply equally to domestic products and to imports, but it is alleged that their practical effect penalises imports. In this type of situation we must be able to prove to the satisfaction of the Court that the application of the regulations either makes the marketing of imports at a profit impossible or that it makes the marketing of imports more difficult than the marketing of comparable domestic products.

Given the limited investigative powers of the Commission in this area, it is extremely difficult to collect the necessary evidence without the co-operation of industry. While I can understand the reluctance of individual firms to antagonise the national authorities or to provide data which may be considered commercially sensitive, I must emphasise that without the necessary information it will remain extremely difficult to resolve allegations of this type satisfactorily.

Social Security Reimbursement

Another cause for concern in certain quarters is the use by some Member States of positive or negative lists of products eligible for

or excluded from social security reimbursement, particularly when price considerations are taken into account in the establishment of these lists. The industry fears that such lists will result in a yet further downward pressure on prices and favour generic products over innovatory products. However, one can also understand the desire of the national social security institutions to get the best value for money out of the limited resources available. In fact the Court of Justice has ruled that the Member States are entitled to take price considerations into account in establishing negative lists of products excluded from reimbursement, provided that these lists are non-discriminatory and are established according to objective criteria which are verifiable by each importer.[9] My services are currently examining whether there is really sufficient transparency in the market and in national decision-making procedures to satisfy the criteria set out by the Court. However, this is a complex problem which requires careful consideration.

Parallel Imports

At the present time there is a considerable variation in the price of pharmaceuticals between the different Member States, resulting in parallel importing into the higher-price countries, Germany, the Netherlands and more recently the United Kingdom. I must emphasise at the outset that the Court of Justice has ruled on several occasions that responsible parallel importing is a perfectly legitimate commercial activity.[10] Since these decisions were based upon the interpretation of the Treaty, they can be reversed only by the Court itself.

One must nevertheless recognise that the recent increase in parallel importing of pharmaceuticals into the United Kingdom has given rise to fears that public health will be endangered. A particular cause for concern has been that patients will be confused by the absence of clear labelling or instructions in English. I would like to deal with this point of detail straight away. Under our directives the labelling of medicinal products must be acceptable to the competent national authorities; any package insert must be approved by them and certain essential user information must be given in the language of the country in which the produce is marketed. These rules apply to parallel

imports just as much as to other pharmaceuticals. The national authorities are responsible for implementing and enforcing them.

On a more general level it is clear the Community law permits the Member States to ensure that parallel imports provide the same public health guarantees as other pharmaceuticals. What they cannot do, however, is to lay down methods of compliance which cannot readily be satisfied by the parallel importer, for example by insisting that he produce documents to which he has no access. In an attempt to provide the Member States with guidance in this admittedly difficult area, in 1982 the Commission issued a communication to the Member States.[11]

There is a danger in exaggerating the potential danger of parallel imports. It was with some surprise that my staff read reports in the British press which almost appeared to be suggesting that the products sold in Continental Europe were less safe than the same product sold in the United Kingdom and produced by the same company or group of companies. That would be a quite remarkable admission for a major pharmaceutical company to make.

The other major concern expressed in industry circles about parallel importing is that funds are being diverted away from productive research into the hands of parallel importers. Clearly, as long as significant price differentials remain, the phenomenon of parallel importing will continue. Although estimates vary widely, the overall level of parallel imports into the United Kingdom appeared to be in the region of £50-80 million a year shortly before the introduction of the licensing scheme. However, in the absence of concrete evidence, we have no way of knowing the long-term effect that parallel importing at this level is having on the development of innovatory products.

Patents

The Commission as an institution has always attached great importance to the patent system as a means of encouraging and protecting innovation. Thus, for example, we have recently set up an inter-service working group to consider the complex

problems of patenting and biotechnological inventions in consultation with acknowledged experts from the Member States and industry. In July of this year, after many years of discussion, the Commission adopted a regulation on the exemption of patent licensing agreements from the Community competition rules which should go a long way to resolving uncertainty in this area.[12] But perhaps the most pressing question for the pharmaceutical industry is the problem for the erosion of patent life caused by delays in obtaining regulatory approval for new products. The industry's position in seeking an extension of effective patent life is well known, and considerable interest has been generated by moves to prolong the patent life of pharmaceuticals in the United States. However, I doubt whether similar initiatives are feasible at the European level. Before the entry into force of the Munich Convention, patent life in Europe varied between 14 and 20 years and the Convention itself opted for the maximum life of 20 years. To ask those countries which then agreed to a six-year increase to patent life to accept a further substantial increase does not appear politically feasible. Moreover, there are also considerable technical difficulties attached to this problem. How much of the delay between patenting and marketing should be attributed to regulatory delays and how much to necessary research and development? How are third parties to be informed of extensions of patent life? Rather than tinkering with the patent system, it would be better to attack the fundamental causes of the problem: to ensure that applications for marketing authorisation are processed as quickly as reasonably possible and to ensure that once a product is authorised in one Member State it gets rapidly on to the market of the other Member States so that the manufacturer has the widest possible market in order to recoup his research and development costs.

Protection of Know-how and the Second Applicant Problem

A controversial problem of increasing topicality is the question of whether the copier of an innovatory product should be required to repeat the pharmaco-toxicological test and clinical trials carried out on the original product. The position of the industry, as expressed in a document, recently submitted to us,[13] is that we must in no circumstances authorise the release or use of company

confidential data for third parties. I can fully understand the desire of companies to protect the investment involved in compiling the information contained in an application for authorisation, particularly in cases where patent protection for the original product is not available. However, at the same time we must be aware that there is an important body of public opinion, which I may say is increasingly shared in regulatory circles, which regards such an attitude as unacceptable if it will result in the unnecessary repetition of toxicological or pharmacological tests in animals or even of clinical trials in man. Thus I would urge the industry to be realistic in its demands and to take account of the very real ethical problems which arise. For our part we have recently submitted a proposal to the Council as part of our overall package, which is intended to regulate the second applicant problem more clearly at Community level. The main objective of the proposal is to protect the innovatory manufacturer by re-establishing the principle that the second applicant should obtain the consent of the original manufacturer before the authorities refer to the original dossier. The conditions under which consent would be given would normally be a matter for negotiation between the parties. The second applicant will also be entitled, as he can now, to rely upon published data. In cases where the second applicant cannot obtain the consent of the first applicant, or where the published references are not available, he will be able to submit an abridged application only after ten years have elapsed from the authorisation of the original product. This ten-year delay, which follows the rules relating to the notification of dangerous substances, will enable the original manufacturer to recover the greater part of his research investment, without imposing an unfair burden on the second applicant.

Research

I would like to conclude my remarks with a few words on the role of the Community in encouraging research in the pharmaceutical sector. In fact the absence of a single market produces adverse effects not only on the marketing of products but also at the stage of basic research resulting in a duplication and diffusion of research efforts and the absence of the critical mass necessary to secure effective industrial exploitation of research results. Thus

for several years now the Commission has been working on programmes which are intended to improve the basic infrastructure for research in Europe and to co-ordinate different national research activities. The latest initiative is the programme for a multi-annual research programme in the field of biotechnology (1985-9) which is currently before the Council[14]. The benefits of these programmes far outweigh their costs, and I therefore hope that the Council will reach a decision rapidly. At the same time work on the block exemption from the competition rules for research and development contracts is at an advanced stage and it is hoped that the final regulation will be adopted soon.

Notes

1. Council Directive 83/570/EEC of 26.10.83, amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ No. L 332 of 28.11.83, p. 1.

2. Council Directive 65/65/EEC of 26.1.1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ No. 22 of 9.2.65, p. 369/65.

Council Directive 75/318/EEC of 20.5.1975 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products, OJ No. L 147 of 9.6.65, p. 1.

Second Council Directive 75/319/EEC of 20.5.1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ No. L 147 of 9.6.75, p. 13.

Council Directive 83/570/EEC of 26.10.1983 (see note 1).

Council Directive 78/25/EEC of 12.12.1977 on the approximation of the laws of the Member States relating to the colouring matters which may be added to medicinal products, OJ No. L 11 of 14.1.78, p . 18.

3. Council Directive 81/851/EEC of 28.9.1981 on the approximation of the laws of the Member States relating to veterinary medicinal products, OJ No. L 317 of 6.11.81, p. 1.

Council Directive 81/852/EEC of 28.9.1981 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products, OJ No. L 317 of 6.11.81, p. 16.

4. COM (84) 437 of 25.9.1984.

5. Council Recommendation 83/517/EEC of 26.10.1983 concerning tests relating to the placing on the market of proprietary medicinal products, OJ L 332 of 28.11.83, p. 11.

6. COM (84) 437 (see note 4).

7. COM (84) 437 (see note 4).

8. Case 181/82, Roussel *et al. v.* Netherlands, Judgement of 29.11.1983.

9. Case 238/82, Duphar *et al, v.* Netherlands, Judgement of 7.2.1984.

10. Case 104/75, de Peijper, Judgement of 20.5.1976.

11. Commission communication on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted, OJ No. C 115 of 6.5.1982, p. 5.

12. OJ No. L 219 of 16.8.84.

13. *Encouraging Pharmaceutical Innovation in the European Community* (EFPIA, 1984).

14. Proposal for a Council Decision adopting a multi-annual research programme of the European Economic Community in the field of biotechnology (1985-9), COM (84) 230 final, 26.4.84, OJ No. C 182 of 9.7.84, p. 7.

PHARMACEUTICALS AND THE THIRD WORLD POOR

Sanjaya Lall

What is the role of the modern research-based pharmaceutical companies in those countries of the world whose per capita incomes are low and where the large majority of the population cannot in their lifetimes afford the benefits of modern drug innovation? What sorts of policies should the governments of these countries adopt to this industry? If we assume (and often the assumption does not hold good) that they are acting without ideological preconception and in the best interests of their population, what is the best set of policies towards the innovating companies, the large multinationals (MNCs) which dominate the industry but which are regarded with suspicion and nationalistic hostility?

These questions are extremely complicated. They grow more complicated and thorny over time and, after years of puzzling over them, I must admit that no straightforward answers emerge. The dialogue between the governments and the international drug industry is often hostile and based on mutual misunderstanding. Governments in poor countries pursue several objectives which conflict with the free operation of the multinationals (and market forces more generally). Some of these objectives are rational and morally defensible but others are not. The drug companies, for their part, tend to regard all interventions as undesirable and fight them with vigour. Of course, host governments wield the ultimate power and the companies usually lose the important battles. Depending upon whether the objectives have been rational or irrational, the country as a whole gains or loses from its policies. Ultimately, the lack of mutual understanding proves costly to both sides.

In this paper I want to explore whether a more sensible set of policies cannot be found. I shall therefore run through the preoccupations of the Third World (as I interpret them) and then suggest what I see to be appropriate economic policies for the international drug industry in poor countries.

Needless to say, I am only talking of those Third World countries which are not ideologically opposed to private enterprise and market forces. In particular, I am referring to the most advanced among them, the so-called NICs, or 'newly industrialising countries'.

There are certain inherent features of the international pharmaceutical industry which invite an extraordinary degree of regulation in both rich and poor countries. However, the content and emphasis of regulations in both are rather different. In developed countries the major concerns are the safety and efficacy of new pharmaceutical products and the regulation of prices (at least in certain sectors of publicly financed health programmes). To a lesser extent, there is concern with the cost and effects of the powerful promotional mechanism deployed by the industry. However, continued research and innovation coupled with free international flows of information and investment are believed to be in the interests of those countries. It is also realised that innovation is increasingly expensive. Further, it is accepted that the promotion system does, with some control (largely self-imposed by the industry) and despite its cost, serve as the most effective system of disseminating information about new drugs to prescribers. These beliefs counterbalance the concerns that make for intervention and hold back efforts to regulate prices and profits too tightly.

In the developing countries, by contrast, the safety of new drug innovation and the need to maintain industry vitality by promoting innovation play a minor role in policy formulation. The overriding concern of policy makers is to reduce the cost of medicines to the population, and particularly to the state sector and the primary health care system. The industry lends itself to such policies more than other sectors providing a 'basic need'. Why is this? Drug innovations are relatively easy to copy if the patent system is ignored and established brand-named drugs can be substituted by generic substitutes: in both cases, it is always possible to find cheaper drugs in the short term than provided by the international drug industry. But there may of course be problems with buying cheap drugs. Drug quality and bioavailability may not be secure. Their procurement and subsequent distribution may be inadequate. Information about their effects and uses may not be effectively provided. It may be difficult to take remedial action if drugs are faulty and have been purchased

from large numbers of small producers abroad or within the country.

Nevertheless, the facts that drugs are a 'basic need' for the mass of the population, that drug purchasing resources are very limited and that it is possible to economise by buying cheap substitutes raise almost irrepressible pressures to regulate or bypass the drug MNCs. Small and less industrialised countries try to buy cheap medicines in bulk from the cheapest sources in world markets. More industrialised countries, with most of their drug needs manufactured at home, largely by affiliates of MNCs, try to hold down drug costs by a combination of other measures. The main one is a wholesale, and often punitive, policy of price control. This is supplemented by measures to dilute the patent system, promote local ownership of enterprises and foster price competition by replacing brand names by generic names.

The normal counterbalance to this, in the industrialised world, is the need to finance innovation. Both high-priced new drugs and older brand-named drugs, for which substitutes exist (but which fetch high prices because of the brand loyalty they command), contribute to the financing of innovation. A necessary part of realising the profits from innovation is the powerful promotion mechanism by which branded products are brought to the market. It is not possible to break any of the links in this complex interlocking system of innovation, commercialisation and further investments in R and D without affecting the flow of innovation itself. Of course, changes on the margin are always possible. Promotion expenditures can be pruned, but not drastically curtailed. Brand-named drugs can be exposed to more competition from generics but brands cannot be abolished. The patent system cannot be further weakened; on the contrary, many governments are accepting that it probably needs to be considerably strengthened and its life extended, to take account of the lengthening period of drug testing and trials. These are the elementary economics of the drug industry, yet they are not obvious to, or accepted by, most Third World governments.

The crucial point is that the innovation process is not considered important to the developing countries, for three reasons. First, the centre of innovation is the advanced countries and much of R and D is directed to diseases which do not directly affect the bulk of the Third World poor. Second, specific diseases of the poor do not attract much R and D in the rich countries – in

fact, given the hard 'bottom-line' economics of tropical disease research, it is perhaps surprising that it attracts any at all. Finally, even for drug innovation which is of direct interest to developing countries, any individual country is of such marginal importance in the global market that it may feel that its opting out of the innovation system will not affect the progress of innovation. In fact, for some of the important areas of pharmaceutical research today, it may even be argued that if the whole Third World ceased to be a potential market the profitability of innovation would not be affected.

The marketing practices of MNCs in the Third World are another area which invites severe criticism, though in fact it has not attracted so much regulatory control. Developing countries do not see the value of powerful promotion as an integral part of the innovation and information dissemination system. They regard innovation as irrelevant or, at best, of little direct value to their populations; even if its value is seen, they feel that it would continue even if they did not contribute. The informational value of promotion has been gravely compromised by the notoriety achieved by MNC affiliates through instances of misleading promotion and discrepancies in advertising content between different countries. Brand names have emerged as the main villain of the piece, and many governments now believe that their abolition would, at one fell swoop, reduce drug prices and eliminate promotional malpractices.

In view of these perceptions, the question is – why do Third World countries allow MNCs to invest and produce medicines at all? What benefits do they receive from the MNC system? First, the MNC is undoubtedly the most efficient system of drug production and marketing. In terms of sheer production efficiency, quality control, managerial skills and marketing know-how, it is difficult to match the drug majors. Second, MNCs provide the most direct access to new product and process technologies. Despite their protestations, and their unwillingness to pay for innovation, any Third World country with a respectable industrial sector and a well-informed medical profession and consuming elite would feel dreadfully deprived if in fact it got left behind in new technologies. Third, MNCs provide investible resources and project execution skills to countries which are short of these. Thus they play a valuable role in starting and expanding the industry. Finally, in the more technologically capable host

countries, MNCs stimulate local technology by launching local R and D, training local personnel and providing sophisticated equipment and know-how for local innovation.

It is the superior efficiency and technology of the MNCs which make them attractive to the NICs. Furthermore, over time, after experiments have been tried with other forms of drug production, many governments are veering back to a more favourable attitude to MNCs. There is a general liberalisation towards MNC activity in various industries. However, the basic areas of conflict remain. Poor countries really want cheap drugs for large sections of the population. They want to market them economically and with correct information. They want increasing national participation in drug production. And, with lesser urgency than the problem demands, they want new tropical drugs.

Each of these conflicts with some interests of the major drug multinationals. For example, MNCs cannot afford to cut prices to the extent that their profits and R and D commitment are seriously diluted. The danger is twofold: to the profits earned directly in the Third World, and to prices charged in the industrialised countries if they make concessions to the poor countries. The latter may be the more important threat than the former. However, unless some compromise can be reached which lowers drug prices in the poor countries and yet retains the leading companies' profitability, we face the worst of both worlds. Developing countries for their part would continually chip away at the prices and profits of the MNCs, sometimes going too far and deterring production and investment. MNCs, for theirs, would automatically resist all regulation and price controls, and face political and consumer hostility.

The threat to profitability in the Third World, reinforced by similar threats in the rich world, would adversely affect investments in innovation. The population at large would pay the price.

Developing countries, especially the more advanced ones with trade and technological aspirations, must accept that they have to contribute to innovation and strengthen their patent systems. How they fit this in with their need for cheap basic drugs is a matter of negotiation and compromise. They cannot afford to buy drugs at free market prices and distribute them for free. They should not tax the purchaser in favour of consumers by imposing punitive price controls. Some other reconciliation must be

sought. One way, which I have advocated before, would be to let MNCs charge free market prices for new drugs but foster a fully fledged generic market in which MNCs compete freely with small firms for established drugs. Generics are not exactly embraced with warmth by the MNCs, but they do enter and compete in them as vigorously as elsewhere if they have to. In the Third World, they should not oppose generic markets but accept them and even work actively towards them. This may create a great deal of good will and forestall less attractive alternatives like price control or brand-name abolition. It would shift the burden of financing innovation more to new drugs and to the rich countries – but this may be a desirable outcome.

A more positive move to help the poorest sections of the Third World would, of course, be along the lines of the cheap drug scheme of the least developed countries launched by European firms. I understand this scheme is just starting to be implemented, but its scope should be considerably broadened if it is to have a real impact on the Third World. Many political factors, however, probably prevent a very large scheme of this sort.

Ultimately, however, MNCs have to accept some form of price reduction in the Third World as the cost of continued operations there.

The marketing problems of the industry are probably easier to tackle. Some combination of internal regulation (such as the International Federation of Pharmaceutical Manufacturers Associations code) and international information cum guidelines would seem to be the answer. It is unfortunate that this relatively easy problem has been allowed to create so much ill feeling and misunderstanding.

What about policies to stimulate R and D into tropical illnesses? The price mechanism by itself simply cannot achieve this to anything like the required extent. Aid is clearly the answer – but how should it be distributed? Complicated schemes for paying for innovation, with a lot of 'fine tuning' to pay firms exactly the right price for innovation, would probably be less effective than a simulated free market. Here innovators would compete for high-priced innovations, and successful firms would reap a reward just as they do in normal markets. The only difference would be that aid would make up the gap between free market prices and low prices charged to the developing country. In many ways that would be a far more effective use of declining

aid money than large infrastructural and industrial projects.

This paper has ranged over a vast and complicated range of issues. I have simplified drastically in order to highlight some of the major areas of conflict between the international pharmaceutical industry and the developing countries. And I have hinted at some possible ways of resolving the conflicts.

Let me conclude by asking a question most economists tend to ignore: how feasible are these recommendations? Will the newly industrialising countries accept the basic premise that market forces and free international flows of investment and technology are desirable for their own development? Will they accept that research-based pharmaceutical companies have a role to play in their economies and allow them adequate prices and profits?

Obviously not all the developing countries will. Different NICs have very different attitudes to market forces and MNCs. India is extremely interventionist and hostile to MNCs, but may be moving in a more liberal direction. Mexico and Brazil are much more open to MNC investment, but seem to be moving in a more interventionist direction. The fast-growing countries of South-East Asia, like Korea, are more pragmatic and market oriented, and their fast growth itself testifies to the success of this orientation. Countries further behind are tending towards interventionism. A messy picture, where no clear tendency emerges.

I believe, nevertheless, that in the long term some compromise of the type suggested will emerge. How much effort it will take and how many lapses will occur along the way is really anyone's guess. What may be crucially important is a positive and constructive response by the leading companies and by the governments of the developed countries. The last may be as difficult as the first if the earlier speakers in this session are right.

PROSPECTS FOR THE 1990s

Ron Wing

Following the sunrise portrayed in the opening session of this symposium for the twenty-first and even the twenty-second century, and as we are now considering some of the issues of the approaching sunset of the twentieth century, as a practical manager in the pharmaceutical industry I have been asked to look at the situation which will face the industry in the 1990s.

Fifteen years ago, largely based on 1967 figures, the Office of Health Economics published a paper entitled *Medicines in the 1990s – a Technological Forecast*. Two significant things about the document give it away; one is the cover price of ten shillings and the other is that it did not foresee the enormous inflation of the mid-1970s. If the corrections are made for those factors, the book reads extremely well today and apart from some things emerging a little earlier than predicted, the rest is largely realistic as seen now in the mid-1980s. Possibly, the surprising thing is that it was written immediately after the historical document *The Sainsbury Report* and before the momentous regulatory changes which followed in the Medicines Act.

I do not intend to comment on that treatise or to make any further technological appraisal. Instead, I propose to examine the circumstances of today and to suggest what conditions may influence the 1990s environment as technological evolution in pharmaceuticals continues to take place.

As I considered the principal influences on the situation, it curiously emerged that virtually all the words began with 'co' and made my primitive scientific mind think of carbon monoxide, which is a bland but noxious gas, and left me with some sense of premonition. However, I did appreciate that most of the subjects themselves were neutral and therefore it was the application of the political will behind these subjects which would have the principal effect on the prospects for the 1990s.

The four subjects which dominate the situation as I see it are as follows:

(1) Communications: Computers – compilation of data, analysis, evaluation transmission.
(2) Constraints: Costs, fiscal containment, statutory regulation.
(3) Co-operation: Cosy, Collateral, understanding, working together.
(4) Community: EEC – The problems of agreement on what basis?
'the lowest common denominator' or the 'highest common factor'
Third World – Health for all by the year 2000: less than twenty years to advance communities through changes which took the rest of the world over two hundred years.
Community in that sense where peoples try to work together outside the constraints of selfish nationalism and endeavour to find a new identity and commonality of purpose and endeavour.

I propose to address each of these topics in turn, commencing with communications. This is a subject which is changing most rapidly because of the advances in other 'sunrise' industries. Electronic microprocessors and transmission, with fibre optics and space relay stations etc., allow masses of information to be readily generated from numerous locations, according to decision or decree. It is becoming clear that in the complex area of health care, considerable attention is being directed towards the assembly of data regarding disease, diagnosis, therapy, prognosis, patients and management issues.

Consideration is already being given in the UK to the proposal that everyone should have a health credit card with an appropriate number which would enable all data on his/her health care history to be produced at a selected terminal and for new data to be added on consultation, including diagnoses and treatment. Precribing would be recorded automatically and a prescription issued. This in turn would be electronically recorded in the pharmacy where it would be dispensed and credited and charged as appropriate. This system of management will be highly effective in facilitating control and efficiency. The recent rejection by government of an information system link between British Telecom and IBM is only a postponement of the

commercial revolution which will impact at the end of this decade.

Beyond this, it is possible to envisage the development of standard diagnostic programmes which on access will assemble information and give back diagnostic options, and possibly even provide approved therapeutic responses. Such packages are in fact already becoming available. It should be emphasised, however, that there is a genuine risk of clinical freedom becoming constrained unless safeguards to individuality and innovation are built into the system. Consideration would also need to be given to a host of other matters – the Data Sheet programme, for example, would need to be allied to a therapeutic rather than manufacturer's classification.

Early last month a leading article in the *British Medical Journal* by David J. Spiegelhalter of the Medical Research Council in Cambridge discussed the question of computer-aided decision-making in medicine. He commenced his analysis by stating:

> Though computers are established in signal processing, data analysis and physiological modelling and are slowly coming into recorded systems, they have been used only rarely for explicit help in medical decisions. Recent articles, however, argue that a critical time has arrived.

He concluded that:

> As micro computers become familiar in routine practice, we may expect many more applications of automatic interpretation of information – but, as appropriate for any new technology, the medical profession would be right to be sceptical until benefit has been proved in vigorous evaluations. When that happens, computer aids may well come to be seen as basic tools in the art of clinical medicine.

During the next ten years, the inevitable thrust of progress in information processing and technology will create a very new environment in which the practice of medicine and use of pharmaceuticals will operate. The decision-making circumstances for the physician will require a coherent and logical information flow which will involve the industry, regulatory authorities,

physicians and all concerned in health care.

The innovative pharmaceutical industry is well geared to accommodate and even lead change and thus contribute to this revolution. In fact many companies are involved in planning their participation. The Squibb Captopril ADR programme in the UK provides an example of an initiative that is already in action. These and other developments should generate by the 1990s a rapid information flow on products in use both experimentally and in the immediate post-marketing phase, thereby enabling rapid assessments to be made of utility and limitation.

In summary, the recent Anderson report commissioned by the DHSS in the UK to evaluate the role and utility of computers in medical practice states: 'The strategy for the mid-1990s and the widespread introduction of practitioner computing provide opportunities for considerable improvements in health care'. Nevertheless, there remains a further issue in the context of communications and that is the question of communication with the patient and general public. Whilst traditionally it remains unethical for companies to communicate with the public about their products, the demand for more information grows all the time. The mystery surrounding therapy is slowly being removed and the informed enquiring patient seeks much more information than is readily available, incuding details on possible side-effects as well as the benefits to be expected. Evidence of this is available from the recent Milpro survey on the pharmaceutical industry in the UK which shows that 77 per cent of patients wish to have more information about their medicines. The comparable figure only four years ago was 50 per cent. Information to patients in the coming decade will become of greater importance as a better-informed populace with home computers becomes the norm. There will be a major shift in medical opinion and the industry has a new role to develop regarding the patient. Medicines will be supplied in manufacturer's original packs, properly coded and labelled and consequently automatically entered for reimbursement and payment. The old-fashioned home medical encyclopaedia will give way to video cassettes, computer programmes and cabled programmes of greater comprehensiveness to meet more effectively general and educational needs than is the case today.

This greater access to knowledge and the resulting enhanced levels of awareness will increase the demand for more reliable

and successful therapies than are presently available. Whilst it may be expected that statutory authorities thoughout the world will move closer together on preclinical data, the major problem of how true clinical evaluation and post-marketing monitoring may be carried out will only be resolved through these new technologies and greater standardisation.

It is vitally necessary that the industry co-operates in the creation of this information environment and flow with health authorities and medical institutions. In this way comprehensive and balanced data will become available to the professions and the public and thereby avoid leaving its supply to the small number of arbiters who, under a consumerist label, currently assume they are the natural conduit for such data.

The 1990s will not see pharmaceuticals being less in the public eye. Instead the opposite trend may be more likely as the competition in information flow increases beyond today's already seemingly saturated levels. Nevertheless, a more extensive and balanced information flow should help to widen understanding of the true role of medicines and allay much of the near hysteria which occasionally breaks out.

I want to focus now on my second subject – constraint. During times of high economic growth, up to the mid-1970s, resources were fairly readily found to increase health care and welfare levels. However, during recession and modest growth, it is much more difficult to find new resources to match identifiable need and to provide for expansion into innovative endeavour. It is not possible today to look forward to the periods of strong economic growth enjoyed at times since the war – the 1990s do not hold out those high prospects. Consequently, as inflation is barely controlled, unemployment is at a high level and the pressures of an ageing population are beginning to make themselves felt, the cost of health care will remain under stringent scrutiny as of necessity.

Nevertheless, the contribution of the innovative pharmaceutical industry will be more necessary in the 1990s than today as a wider range of disease and chronic disorder challenge for effective remedy by pharmaceuticals. The problem with the UK style of a 'free' Health Service is that it encourages under-valuation of the improvements and benefits available from therapy. The public expect effective health care but lack appreciation of its cost. And when economies need to be achieved, attention has focused on

pharmaceuticals, especially by liberal idealists with little or no understanding of the role of the industry and the direct contribution it makes. Consequently, from an international perspective, UK doctors remain relatively lowly paid and pharmaceuticals under-valued.

This seemingly particular UK confrontation is likely to remain as critics persist in trying to discredit the industry in a country where standards have been set and leadership given. At the recent Labour Party Conference, the following statement was made from Basildon: 'People do not like big business being involved in health care. They think it wrong to make profit out of people's health.' And from Wakefield: 'What sort of a system is it that allows the pharmaceutical companies to be the leeches and parasites of the health service?' Apparently it is legitimate to make a profit out of making people ill with tobacco or alcohol or even satisfying people's hunger, but not in making them well. It is therefore possible that in continuing political circumstances like these, even British-owned companies in the 1990s may begin shifting more resources abroad as scientific and technical competence increases in territories overseas.

In this way, the industry in the UK could emulate the experiences of the electronics and engineering industries, but for a different reason. Not the competence of the industry, but an indifferent political will, as typified by recent ministerial comments that it is easier to damage an essential industry than contain the lack of realism in some employees in the Health Service. Constraint may be chiefly fiscal, but the anxiety is that it becomes political, and the vision is lost.

The recent book by the late Lord Vaizey, entitled *National Health* contained a chapter on rising expenditure where he compared differing attitudes to innovation and its cost between the electronics industry and pharmaceutical industry:

> Medical innovation . . . rests primarily upon the pharmaceutical industry, which is an industry that is concerned primarily with innovation.
>
> The difference between electronics on the one hand and high technology medicine on the other is that the first is sold in the market and the second is provided largely by the public sector. The electronics industry is thus seen as adding to economic output, while high technology health care is seen as

adding to public expenses and as a drain upon the economic output to which the electronics industry is contributing. Clearly, there is conceptual error in this way of looking at things: health care, after all, is not a 'drain on output' if people need it . . . and rising expenditure is desirable if it gives people what they want – more comfortable, happier lives with less ill-health.

It would be true to say, however, that the development of high technology medicine has led to increases in outlays, whether these be called an 'increase in costs' or 'expenditure' or whatever; furthermore, it is virtually certain that high technology medicine will accelerate for two main reasons. First, the pharmacological revolution which we are now witnessing is based on breakthroughs in science, especially biochemistry and biophysics, and it is from this scientific development which is itself still accelerating, that the fuller understanding of immunology, of the treatment of viruses, of cancer and of genetic malfunctioning will come. These breakthroughs will lead to pharmaceuticals and other innovations, which will in turn make possible new medical and surgical procedures.

Second, the main strand of high technology is the application of contemporary developments in micro-circuitry and new materials to medical matters ranging from the use of the computer in diagnosis and in epidemiology, to the use of tiny catheters in surgery. These various developments – and there are many of them – enormously increase the likelihood of the effective treatment of illnesses. The demand for treatment is certain to grow, therefore, even were the incidence of illness to diminish, since it is the concept of the treatable illness that determines demand rather than the actual amount of illness – which (according to the definition of the World Health Organization) is virtually limitless.

If attitudes presented at this time by certain would-be opinion formers prevail, the UK will in the 1990s begin to lose its current prominent position in the world league and markets will be relinquished to the USA and the rising strength from the East. Although it will remain a net contributor, it will be at a continuing reduction in level, as the balance of investment moves inevitably in those directions. The sunrise will remain, but

possibly in the land of the rising sun, and the Pacific basin, rather than Europe and the Atlantic. To the politicians I will paraphrase the biblical prophet: 'Lift up your eyes unto the hills from whence cometh our help.' There you will see the sunrise.

The third theme I want to raise concerns co-operation. The industry has never been an isolated fully independent unit – it is dependent upon external agencies through which it must work. The primary one is of course the medical profession, who ultimately and independently must pioneer the prospective therapies in clinical practice. They alone with their own ethical committees and colleges exert a powerful influence on the industry. This is not just because ultimately they are the users, but also the evaluators and provers.

Thus the relationship between industry and profession must remain strong. It must also remain above reproach. Pressure to cast suspicion on the relationship in a media environment of scandal seeking will require an alert industry and profession to understand and conform to the ethic of our responsibility. It is regrettably going to be necessary to introduce more guidelines on 'systems of working', 'codes of practice' and possibly, though hopefully not, more regulations to ensure the transparency of the relationships between the parties.

It is also vital that our academic institutions are not forced to cut back in those highly successful areas of biological science which have serviced health care and this country so successfully in the past fifty years. Industry will need to continue working with academia in fields of original thought and experimentation to foster knowledge, exploit opportunities and to ensure that the benefits become available to the community.

It is vitally necessary that the industry works with governments and international bodies to ensure that success follows its endeavours. It would be much easier if it could function in the market place without their arbitrariness, as most politicians are frightened of the industry and respond negatively to defend their political image rather than positively to lead the country into a fairer evaluation and appreciation of the resource. Sometimes this prevaricating can be understood, particularly where it concerns the Third World. Nevertheless, it is encumbent upon those who have the opportunity, whether governments or voluntary agencies, to endeavour to find ways with the industry to establish reliable systems and infrastructures to meet local and

particular needs.

The medicines produced by the industry cannot be fully utilised without the local political will to work with the industry to ensure that treatments reach those in need. It is also interesting to speculate how much greater progress would be achieved in India, which potentially has a sound technological base, if it had a system of protecting intellectual property.

The danger for the 1990s is that a continuation of today's unbridled and simplistic criticism by the partially informed, whether in fields of animals rights, Third World, or even the management of Western health care programmes, will produce a diminution of the resource available to discover, develop and distribute the benefits which science can realistically achieve in the next decade. It is a risk, however, that I believe the industry which holds so much promise will resist and overcome by meeting genuine criticism and adapting as appropriate.

Finally, I want to focus on the fourth of the subjects identified at the beginning of this paper – Community. The drawing together of people into wider communities, irrespective of nation, creed, ethnic origin or race is slowly happening, though it certainly appears to be occurring at only a snail's pace and sometimes there are setbacks; nevertheless, it is happening and it should and will continue.

Out of the continuing evolution of the EEC will emerge wider mutual recognition of produce licences and developments. Also the current scale of interchange between regulatory authorities barely envisaged ten or twelve years ago will be far more integrated by the mid-1990s as countries can less afford to be out of step today than they could ten years ago. It will need continuing work by both authorities and companies to get the balance right not only on scientific and medical regulatory matters but also on fiscal matters to ensure that price control systems do not vary to the point where the source of innovation is prevented from receiving a due return, thereby jeopardising further investment.

Although there remains much to be done, particularly in the Third World, clear progress has been made in public health and servicing the communities. The pharmaceutical contribution, which is growing steadfastly all the time, has provided many of the opportunities for progress over the past thirty years. This thrust will continue in association with national and world

authorities. Industry has constantly contributed, and will continue to contribute, to the dialogue and will continue pragmatically investing in the Third World, training and developing the emergent resource and market it represents.

To impose a rigid system would slow down development, but to foster mutual recognition and participation will gradually produce increasing standards and results.

In conclusion, the 1990s still beckon the pharmaceutical industry, as it remains the one organised resource in the world which can still bring together all the disciplines necessary to devise and introduce the advances and improvements in treatment and health care sought throughout the world on a virtually limitless scale.

The co-ordination of the new communications and data management technology will revolutionise health care management and the pharmaceutical industry's role, but the pharmaceutical industry will continue to seek the best environment and opportunitites to fulfil mankind's aspirations of a long life with minimal adverse impact or impediment from ill health.

Its success will be improved by increasing knowledge and greater efficiency and the promise of that success will keep those seeking discovery and those leading the enterprises united in pursuing that goal.

The 1990s will present an ever more stringent environment, an increasingly knowledgeable, curious and even critical mankind, and constant opportunity to seek many a new sunrise.

DISCUSSION

Balu Sankaran

I am not an economist or a social reformer. I am a physician with a modicum of experience in health planning and with a brief exposure to international thinking on health and related subjects. I have read with great interest Dr Sanjaya Lall's paper and I have, in fact, been reading his papers since 1974. I have also listened with particular interest to Tom Garvey, Ron Wing and Professor George Teeling Smith.

The pressures on the pharmaceutical industry have been increasingly evident over the past few years, particularly since 1981. Considering the response that industry has made to such pressures, I think the effects have been beneficial.

When I look at *IMS Pharmaceutical Marketletter* and *Scrip*, I have the impression that it is possible for the pharmaceutical companies to achieve an economic bounce-back in spite of the activities of Health Action International, Peter Lind's report to the EEC, and various threats from other organisations.

Following a resolution adopted by the World Health Assembly last year, a meeting will be held in 1985 to discuss the more rational use of drugs. All concerned parties, including governments, pharmaceutical industries, patients' and consumers' organisations, will be involved.

I believe that this session of the Symposium has generated many thought-provoking arguments about the move towards a major pharmaceutical and pharmacological revolution, and how this could be the sunrise industry of the future. I have no doubt in my mind that this will be possible. I am sure there is widespread awareness of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases where efforts are being concentrated on six tropical diseases (malaria, schistosomiasis, filariasis, including onchocerciasis, trypanosomiasis, including both African sleeping sickness and Chagas' disease, leishmaniasis and leprosy).

The results have been remarkable and research carried out both within and outside the Special Programme has brought

about significant progress. Some new tools for disease control have already reached the state of actual application in the field, while others are close to it. Examples of major developments towards the control of the diseases include:

- A biological agent, *Bacillus thuringiensis* H-14, to control the flies that spread river blindness is being used extensively in West Africa and is being tested against malaria-carrying mosquitoes. A new drug, mefloquine, for the treatment of malaria infections resistant to standard therapy has been registered for use. Vaccines which may treat and prevent leprosy are in the early stages of testing in man.
- Simple kits to measure the sensitivity of malaria parasites to drugs to assure the correct choice of treatment are being used widely. A simple test to diagnose sleeping sickness (African trypanosomiasis) at the village level, and thus permit early intervention, is ready for widespread application.

Among significant achievements at earlier stages of development are the following:

- Vaccines against malaria are now a real possibility following the identification and production of the substances in the parasite responsible for man's immune reactions against them.
- A totally new family of compounds for the treatment of malaria, based on a traditional Chinese remedy called Quinghaosu, has been synthesised and testing has begun.
- Drugs for the treatment of river blindness, critical for the control of this disease, are being synthesised and tested.
- Natural biological agents are being tested in the field, such as *Bacillus sphaericus*, which will destroy the larvae of disease-transmitting insects and recycle themselves and in this way prolong their effectiveness.
- Simple and effective diagnostic tests – vital to all disease control programmes – are being developed for Chagas' disease, schistosomiasis, malaria and leprosy.

The Onchocerciasis Control Programme also has excellent backing from the pharmaceutical industry: there has been a reduction of 14 million in the number of cases of blindness in the area of the Volta River Basin.

Over a period of ten years, this is no small accomplishment and I would like to say, in all humility, that the contribution of the pharmaceutical industry to various WHO programmes has been considerable. But, at the same time, much more has to be achieved.

Between sunset today and sunrise tomorrow about 1 million children will die because of malnutrition, neonatal tetanus, malaria, or other communicable diseases. At the rate of population growth of developing countries this number of deaths will be offset by a birth rate of approximately 3 per cent. However, 14 per cent of the children born will have a birth weight of below 2,500 grammes. That shows why, here at least, the sun should never set.

DISCUSSION

Frank Münnich

I am supposed to comment on the papers of this session. I am afraid, however, that I shall have a hard time in trying to do so for two reasons. On the one hand, so many topics have been covered that it seems almost impossible to touch on even the most important propositions. On the other hand, I find myself in agreement with almost all of them, except of course with those favourable remarks by George Teeling Smith on my country, which to me looked more like a historical reminiscence than a description of the present let alone a prospect for the future! So I just want to underline four points which in my understanding and with the background of the experience from my country seem to me the most important in framing the next five to ten years for the pharmaceutical industry.

Firstly, the single most important development will be the increasing importance of the political as opposed to the product market place for the economic success of new products, both nationally and internationally. This is not to say that technology and marketing will lose their importance but that changing regulations will have a growing direct and indirect influence on the returns of new products and, considering the political pressure on generic prescribing, of long-standing products as well. So demand and supply for regulation, the political market place, will be one of the most important factors shaping the industry. The demand for regulation will increasingly be exerted not by the industry itself but by the population in general and by people who pretend to represent the interests of the population.

There are two psychological factors which have increasing importance in my country. One is the development of a new social responsibility. This new social responsibility has been put forward by intellectuals, people whose business is to produce sense, philosophical interpretations. They may be journalists or priests or very often they are poets, writers and artists. These people give sense, interpret sense and deny sense to social, technological and scientific phenomena. Of course, they are

generally critical of all technological development and as they are very influential, they are to a large extent responsible for the highly critical attitude which now prevails in most of our population, especially among young people.

This new social responsibility has also attracted scientists and physicians who have discovered the exciting feeling of giving social assessments besides their own business. They have transcended their own professions and become amateurs not only in philosophy but also in economics, restricting of course the idea of maximising returns to their private applications.

So we have quite a few physicians as well as pharmacologists who do research on the economic consequences of the use of pharmaceutical products and whose results suggest that there could be enormous savings in that market place, perhaps 50 per cent, by such easy and very simple solutions as parallel imports, generic prescriptions, formulae and essential drug lists. They are unable to consider all of the negative and positive interrelationships and feedbacks which exist in the economic system. They never consider whether the capacity exists for producing generics in the required amounts. They never even mention the cost which is involved in not serving people who are sick but for whom there is no cure as yet, so they underestimate the gains which would result from new products.

The other psychological factor is a new anxiety within the old population and therefore these critical remarks by intellectual opinion leaders easily succeed in getting large acclaim. So like other sensitive areas – nuclear energy, insecticides and herbicides, even traditional agriculture – the production of pharmaceuticals is under general attack.

My second point is that not only psychological factors but also hard economic facts influence this political market. Thus the financial situation of the social health insurance funds which in all of our countries provide for the largest part of the market – in my country for approximately 85 per cent – is an important factor. As a result of the slow-down of economic growth and the consequent shrinking of the contributions to the sickness funds, coupled with the increasing scope for medical intervention, the financial situation of the sickness funds has deteriorated progressively. Quite understandably they try to make ends meet and therefore buy as cheaply as possible.

This presents a special problem for the pharmaceutical market

because of the public character of all progress, that is the development of new products. There normally are no people who demand products which are not yet developed and who are willing to pay for progress in advance. To some extent physicians may have asked for or prescribed products with the special intention of helping or sustaining research, though nowadays they are compelled to prescribe the cheapest generic. But the normal demander – and I would count the sickness funds as normal demanders – looks for the cheaper products. It may well be that we have to develop a specific market order to deal with the problem of pharmaceutical progress.

My third point is that economics does not, unfortunately, provide very good tools for analysing this specific situation. The economics profession to a large extent and all those politicians who rely on this part of the profession are stuck to the concept of perfect competition and the market failure which derives from this idea of perfect competition. This idea of market failure is used to justify political action for increased regulation. So the idea of price competition is over-emphasised, while that of innovative competition, put forward by Hayek or Schumpeter, is under-emphasised in the shaping of political action.

I come to the conclusion, therefore, that it is necessary for the pharmaceutical industry to put much more effort in terms of resources, expertise and creativity into the political market. I am quite convinced that the industry will be able to cope with the problems of a technological and marketing nature, but it will have a very difficult time on the political market.

Finally, I want to express one minor point of disagreement. It seems to me that in an international comparison not all societies show the same development. There are quite a few, especially lesser developed ones, where attitudes and the mental climate are different. I am convinced that the six countries to which Professor Teeling Smith has drawn attention will not achieve the same success in the future if the political market is not changed, because nothing moves as quickly as capital and ideas.

I want to conclude with a personal remark. Today's papers and discussions have impressed me with the unbroken confidence in technological progress which almost all of them have demonstrated. I am used to much more seemingly endless discussion of whether we should look for such progress at all. Listening to today's proceedings has been very refreshing.

GENERAL DISCUSSION

The speakers' and discussers' contributions to the second session of the symposium generated comments from the audience which focused on the political and public standing of the pharmaceutical industry and the problems of the Third World.

Taking the first of these topics, David Crouch (Member of Parliament) expressed astonishment that an industry which has contributed so much to the well-being of mankind should be under seemingly constant attack from all points along the spectrum of political opinion. He pointed out that the industry was not alone – agriculture was currently experiencing similar hostility. Recognition of the latter's success in substantially increasing productivity and in reducing imports has been replaced by criticisms relating to the environmental impact of its activities. However, farmers' representatives are now seeking to restore a more appropriate balance and so too should the pharmaceutical industry. Mr Crouch argued that drug manufacturers must start to channel greater efforts into marketing their achievements – in saving and prolonging life, in alleviating pain and in emptying hospitals – and into emphasising how closely the industry works with the medical profession, a fact which is insufficiently appreciated.

Focusing on Third World issues, Dr Robert Maxwell (King Edward's Hospital Fund for London) was concerned that the world's poor were not getting value for the resources they allocated to pharmaceuticals. He referred to a study in Bogota, Colombia, which had shown that poorer families were spending 25 per cent of their income on health care and that half of this amount went on pharmaceuticals. Yet, Dr Maxwell claimed, the quality of these products may be in doubt and, more fundamentally, he questioned the need for many of the medicines in the first place. Against this background he considered that it is in the long-term interests of the pharmaceutical industry to be concerned about such problems and to work towards their resolution.

In response to this point, Professor George Teeling Smith agreed that the pharmaceutical industry has to be responsible, and be seen to be so, in the very difficult area of the Third

World. Manufacturers have admitted in recent years to marketing excesses and errors in some poor countries and this seems to have stemmed principally from inadequate local management control. Nevertheless, he believed that the industry has taken and continues to take steps to ensure the cessation of marketing of ineffective products. And beyond this, as Ron Wing pointed out, the industry is actively seeking ways in which to co-operate with Third World governments to establish appropriate infrastructures in order to promote appropriate use of its products.

At the same time, Professor Teeling Smith considered it essential to recognise that the problem now derives much more from the behaviour of indigenous manufacturers than from the activities of the multinationals' subsidiaries. In his view, government failure to exercise control in this matter has resulted in a degree of freedom for local firms to sell their products resembling that which enabled the market-place hucksters of Victorian Britain to be so successful. The balance has therefore shifted and it is no longer appropriate to attribute a large part of the blame for the problems identified by Dr Maxwell to the multinational industry.

A further question which was raised in relation to the problem of pharmaceutical supply in the Third World concerned the possibility of governments purchasing all the drugs required by their populations and then distributing them free of charge. This policy had been adopted by a number of national authorities for contraceptive preparations. Dr Sanjaya Lall pointed out, however, that no developing country has sufficient health care resources to pursue such an approach for more than a handful of drugs at most. Furthermore, every newly industrialising country regards the development of a drug industry as one of the pillars of industrialisation. Consequently, domestic production is encouraged – resort to purchasing all requirements at the cheapest possible price on the world market being eschewed.

Dr Balu Sankaran, replying to the same question, observed that many countries operate systems which attempt to distribute essential drugs for primary health care on a no profit/no loss basis. He also concurred with Dr Lall that no developing country could afford to supply drugs free of charge. Finally, in response to a separate comment concerning the problem of raising the standards of medical education in Third World countries, Dr Sankaran referred to the World Health Organization's develop-

ment of an essential drugs list. To date, 50,000 copies of the document in five languages have been distributed to as many medical schools as possible. He pointed out, however, that in the developing countries there is frequently considerable resistance to the introduction of such initiatives into the curriculum from the local medical hierarchy.

In what turned out to be the final contribution to the session, Mr Malcolm Barlow (Smith Kline & French Laboratories International, USA) provided a shaft of optimism regarding pharmaceutical industry/government relationships in the developing countries. He referred to a conference sponsored by the World Health Organization and the Harvard School of Public Health in spring 1984 to discuss the essential drug programme. From this meeting, it emerged that there is a surprising degree of support for the private sector from many Third World governments. In addition, he pointed to the co-operation between several United States pharmaceutical companies and the government of Gambia which resulted in the setting up of a highly successful drug distribution scheme in that country. He added that the companies are now introducing the project into Sierra Leone and that perhaps one of the most encouraging aspects of this new initiative is the offer of continued assistance from the Gambian government. These developments clearly signify that real progress is now being achieved.

SESSION III:

BALANCING RISKS AND BENEFITS

CHAIRMAN'S INTRODUCTION

Elizabeth Ackroyd

As members of the audience who are experienced conferees will know, the morning's session following the banquet dinner is usually the kiss of death! However, we have some lively speakers who, I am sure, will put some zing into the proceedings. In the programme, the title of this morning's session is 'Balancing Risks and Benefits', and as you will also have seen from the programme, I come from the Patients Association. Before calling upon our first speaker, I would like to point out that most people in this country, as in many others, are fully familiar, in their gambling and betting capacities, with balancing risks and benefits. I do not think therefore that it should be too readily assumed, as perhaps the pharmaceutical industry is apt to do, that people are incapable of taking on board the fact that there are risks, as well as benefits, involved in their use of medicaments.

THE ROLE OF THE CONSUMER MOVEMENT, AND ITS CHALLENGE TO THE BRITISH PHARMACEUTICAL INDUSTRY

David Taylor

This paper examines three main areas. First, it looks briefly at the historical development of the consumer movement in the UK, and attempts to define its role and the extent to which its leaders genuinely represent consumers' views. Second, following on from this last area, it outlines recent research conducted by the Association of the British Pharmaceutical Industry (ABPI) into consumer attitudes relating to pharmaceuticals and some of the factors which may influence them, particularly in the context of drug risks/costs/benefits. Finally, it suggests some ways in which the pharmaceutical industry might appropriately respond to the serious challenges presented to it by the modern consumer movement.

The Development of Consumerism

Table 1 indicates that the historical evolution of organised consumer representation can be usefully divided into four overlapping stages.

Table 1: Stages of Consumer Movement Development

'State' consumerism – the middle ages to date
'Market' consumerism – from the 1930s
'Radical' consumerism – from the mid-1960s
'International' consumerism – of the 1980s?

'State' consumerism began in the middle ages, with legislation on matters like the weights and measures used by traders and publicans. 'Consumerism' in this sense was an amalgam of political process and the social forces which have created legal structures in all societies.

In the nineteenth century, as Britain became a more sophisticated economy, legislative interventions designed to protect consumers in areas like the insurance market also became more complex. And in the current century the emergence of a large public sector stimulated still more elaborate forms of legal provision and representative 'state' consumerism. Examples of the latter include 'user' councils of the nationalised industries, the National Consumer Council, and the NHS Community Health Councils.

By contrast, independent 'market' consumerism has a much shorter history. It dates from the early 1930s in the USA, and from the 1950s in the UK. As people gained more spending power and the range of consumer goods to choose from increased, bodies like the UK Consumers' Association emerged. They have tried to improve the working of the market place by giving consumers better information, with the latter being treated almost like a consumer product in itself.

However, although 'market' consumerism is self-funded, many people working in it are idealistically motivated. It is of note that in the UK the state was quite clearly associated with the emergence of the independent consumer movement, which politicians encouraged because they feared that wartime experiences had blunted British consumers' powers of discrimination to an undesirable extent.

Turning to what may be termed 'radical' consumerism, this too was first an American development. Leaders like Ralph Nader and theorists such as J. K. Galbraith channelled the energies of many people in the 1960s into looking more critically at the nature of market places, at how 'demand' is created, and at the nature and behaviour of multinational companies. This may justifiably be seen as simply a logical extension of market consumerism into a more aggressive mode.

Now, in the last few years and particularly in the UK and some other European countries, consumerism seems to be moving into a new, 'international' phase. Against the background of the public debate and international action taken in respect of the world-wide sale of baby-milk formulas in the 1970s, some consumer groups and/or charities have taken the radicalism of the 1960s a stage further. They are pressing for comprehensive, international controls on industry operating in areas like pharmaceuticals. On occasions they seem to be searching for

alternatives to, rather than improvements in, the market place. This in many respects brings the cycle of consumer development back round to an expanded form of 'state' consumerism.

In summary, it may be said that, as far as the UK is concerned, it is the tone and the aims rather than the fundamental composition of the consumer movement which have changed in the last few decades. Its leaders were, and are still, members of a paternalistic,* semi-political elite who wish to use their power and position to improve the lot of the less fortunate mass of consumers. There is nothing wrong in that. The doubts relate to how competent that elite is to judge the best interests of those they mean to help.

Inasmuch as the modern consumer movement is moving on from traditional 'market servicing' – providing information, lobbying law makers to define fair trading practices – towards identifying market failures and influencing directly (international) policies in areas like health care, questions must be asked about how representative would-be consumer leaders are. For if market forces are no longer relied upon to indicate the collective will of the population, then the processes underlying any alternative means of preference expression deserve careful attention.

Recent ABPI Opinion Research

In the summer of 1984 ABPI commissioned a four-stage research project into public, professional and 'opinion former' (MPs, journalists, professional leaders) attitudes on issues relating to health care and the pharmaceutical industry. Table 2 outlines the main elements of this programme, and Table 3 notes three of its key findings.

Perhaps somewhat to some observers' surprise, the survey made it clear that at all levels of society the pharmaceutical industry has a high standing. Its activities are seen as desirable and worthwhile. People do appreciate the value of medicines,

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* The emergence of the women's movement and its involvement in health care consumer issues has been another important development in the last decade or so. The application of the word 'paternalistic' to the leaders of this group may be injudicious, but it may nevertheless in some instances accurately describe their motives.

Table 2: The ABPI Opinion Research Programme – a Four-tiered Approach

'Opinion formers'	25 in-depth interviews
Professionals	Interviews with nine professional groups, i.e. 72 personal interviews
General practitioners	Interviews with a sample of 200 (based on pilots and Stage 2 observations)
The public	An interview-based survey involving 420 individuals (based on pilots and group interviews)

Table 3: ABPI 1984 Survey Findings: Key Points

The pharmaceutical industry has a high standing at all levels: its activities are seen as fundamentally worthwhile. *But* there is concern about a relatively large number of discrete 'consumer' topics, like prices and profits, safety, promotion, use of animals, product duplication and compensation for injury.

The public have a strongly expressed and rapidly growing desire for information on medicines. Fewer people are prepared passively to accept professional decisions on treatment.

'Opinion formers', and probably decision-takers, tend to believe the pharmaceutical industry to have a badly tarnished public image.

despite their risks. People do see the worth of innovation and the contribution of industry to society and the economy. Eighty per cent of the public said that, in overall terms, they have a fundamentally favourable view of the industry.

Yet against that, and again at all levels, there are a large number of discrete consumer concerns on topics like prices and profits, safety, promotion standards, use of animals, product duplication and Third World medicine supply where people do have significant worries. Also many members of the general public express very strongly a desire for more information about medicines and about the pharmaceutical industry and health care systems generally. This demand has grown very significantly over the last four or five years. About three-quarters of the population said they wanted more information about prescribed drugs in 1984, compared with a half at the start of the decade.

We have moved away from a situation where people behaved

with passive compliance towards their professional advisers to one where they are demanding active participation, not only in therapeutic processes but in the political processes surrounding the health care area. ABPI asked respondents whether they believed they should question their doctors if they felt there was something wrong with their treatment. And it is important to note that over 90 per cent said they had a duty to challenge medical authority in such circumstances.

In the middle seventies such findings might have been taken to indicate a total breakdown of traditional medical authority. But that is not the case. Rather, there is a changing pattern of authority, a redefinition of the ways in which medical authority can be tolerably expressed. There is no doubt that most of the consumers ABPI questioned still saw their doctors as their preferred source of medical advice and information, but they wanted such advice and information to be given in different ways and in different degrees of depth as compared with past practice.

Perhaps the most important understanding to draw in regard to the first two sets of information referred to in Table 3 is that the underlying pattern revealed is one of concern coupled with lack of knowledge. For example, 60 per cent of those interviewed said that they were worried about medicine safety regulations in one respect or another. At the same time, 80 per cent said that they did not know what the regulations are. Concern, coupled with what some might call ignorance, is a dangerous mixture. It breeds distrust and the sort of political instability which can lead to precipitate, ill-planned interventions.

Looking at the attitudes of 'opinion formers' – and consumer leaders – it appears that they tend to pick up, and feed back to the public, exaggerated criticisms of the pharmaceutical industry simply because they do not fully comprehend the balance between the specific worries and the overall confidence of the population. That is, in trying to aggregate the concerns of various discrete groups relating to matters like profits, safety, Third World health or animal testing, those in representative roles may tend to lose sight of what ordinary members of the public can more easily see – the industry's good overall record in contributing to economic and social welfare. This type of error may affect much thinking on the risks/costs/benefits of medicines at the political level.

Propaganda Campaigns and Allied Interventions

Against the background outlined above it is obvious that propaganda campaigns, direct action programmes, lobbying and the like, aimed at influencing the public and political attitudes towards medicines, can generate distorted or exaggerated views in the minds of even well-meaning 'consumerists'. In a continuing cycle such interventions may subsequently also allow the latter to propagate misleading opinions more effectively than the industry or the medical profession can put forward objectively more accurate counter-arguments.

Some individuals in the industry may believe that the media generally, and especially papers like *The Guardian*, themselves comprise an active propaganda campaign against pharmaceutical manufacturers. But such attitudes do not usually prove constructive.

There is some selective reporting, of course; particular journalists have their own set views. It is, by and large, their right to express them, however misguided those in the industry believe them to be. Yet overall the press and other media are fairer than may be claimed. The newspapers in a sense represent blank sheets on which those with enough skill and convincing arguments can put forward their case. The pharmaceutical industry's problem is that all too often its critics 'score' better in the media game than do its own chosen representatives.

Three examples of relatively large, and in part at least successful, 'anti-industry' or 'anti-drug' campaigns in the UK in 1984 were:

(1) 'Animal rights' protests against medical experimentation.
(2) MIND and others on minor tranquillisers and the risk of dependence.
(3) Health Action International's programme on pharmaceuticals and the pharmaceutical industry in the Third World.

It is not the purpose of this paper to go into any of these three issue fields in depth. But a few comments may prove valuable.

First, in the 'animal' context, ABPI's opinion research found that around 90 per cent of the UK population understands the role of animal experimentation in medicine, in development and testing. Of course people do not want to be unkind to animals,

but they understand and accept that experiments on animals are often necessary. Only about one respondent in a hundred spontaneously suggested that there should be new regulation in that area.

But supposing that even just one person in a thousand is truly committed against 'vivisection' in any form. There would still be a UK-wide pressure group of 50,000 activists, an enormously significant number. If they were to demonstrate and act in concert over writing to MPs and the media, such activity could well lead 'opinion formers' to believe that a groundswell of public opinion against animal experimentation exists. The vulnerability of our type of political system to subtly organised 'mass' lobbying is one reason why political judgements may become distorted.

Second, the MIND campaign on tranquillisers has been extensive, and carried by media ranging from Esther Rantzen's BBC programme 'That's Life' to the magazine *Woman's Own*. The latter conducted a survey on tranquillisers, the forms for which were headed 'You can Help Fight this Menace'. The objections to such work are obvious, although this is not to say that there are no problems associated with minor tranquilliser use.

Perhaps the most relevant factor to draw out about this debate is that the conflicts in this context are, first, about prescribing policies and, second, the clash of views between people like psychotherapists on the one hand, who have a 'social' model of mental distress, and traditional psychiatrists on the other.

Members of the medical profession are said by their critics to have an 'organic' model of such conditions, although many in fact seem to combine the physiological and the social views pragmatically. The point is that tranquillisers, and the pharmaceutical industry, are used as scapegoats in a complex dispute which ordinary people would find hard to understand.

Finally, with regard to the Health Action International (HAI) campaign on Third World medicines, there can be no doubt that this has been on occasions unduly hostile, and damaging, to multinational pharmaceutical companies. But counter-attacking HAI members as if there were some Falklands-style confrontation decisively to be won or lost seems futile. Rather it would seem more useful to take a balanced view of their activities, good and bad, and to try to understand the basic reasons for their actions.

It may be universally accepted, for example, that the

improvement of the Third World population's health is one of the key tasks for humanity in the late twentieth century. Against the magnitude and importance of this goal there can be little question that some actions by some companies seem at best trivial and at worst anti-social. But this does not make the pharmaceutical industry, as a whole or in part, a prime cause of Third World ill health, or its 'reform' a major step towards solving Third World health problems.

A major reason for exaggerated claims in this context is the need of pressure groups and charities like those in HAI for a viable platform in the Third World. If they went to an African, Asian or Latin American country and said, 'Your professionals do not care sufficiently for the poor' or 'Your government has not planned health care adequately,' they would not be likely to get a friendly response, officially at least. Yet if they say, 'Our multinationals are at fault; they have distorted health care in your country,' it is a viable position from which to offer aid and advice.

Another factor underlying the generation of exaggerated attitudes in relation to HAI's work is linked to the realities of the rich world. ABPI's opinion survey showed, with no room for doubt, that relatively few people in the UK (and this would also go for most other developed nations) are passionately concerned about Third World health *per se*. But if rich world issues can be linked to Third World concerns HAI members believe that they have a better chance of making an impact.

Thus the campaign against the industry here on issues like generic substitution. The aim is to link into pharmaceutical and other health questions relating to the Third World. And they have done this with great competence. This last is a central message of this paper.

Much resentment of HAI and its members, such as Oxfam, is arguably based on jealousy. They have done an excellent job in getting their message across and have in certain contexts achieved some good as a result. What the pharmaceutical industry needs to do is to distinguish accurately between the valid and invalid elements of HAI's arguments, and to internalise the skills which have made those associated with it such successful communicators. At present, whilst they radiate concern for the well-being of consumers across the world, the industry all too often seems worried only about financial matters.

An Industry Response

Table 4 outlines the potential consequences for the pharmaceutical industry of failing to understand the nature of the challenge confronting it in the public arena at this time, and/or failing to take appropriate action.

Table 4: The Consequences of Underestimating the Consumer Movement Challenge

Loss of public sympathy?
Loss of political sympathy?
Revenue decreases
An unduly restrictive environment
Loss of independent managerial control

First, there is the loss of public and political sympathy. So far it seems from ABPI's research in the UK that the position is not so serious as some people fear. The 'bad news' should not be overstated. Nevertheless, in an era when the industry's activities and income seem ever more to be influenced by political forces rather than market variables and straightforward product characteristics, the danger cannot be ignored.

This opens up the second question, that of revenue decreases. Again, the losses to date, such as the cuts made under the PPRS and allied cuts imposed by the Conservative government in 1983, have not been so severe as to risk destroying the industry 'overnight'. But in the longer term it may be that the rewards of current research efforts could take longer to emerge than we hope. Suppose, for example, that the major products of the current 'therapeutic revolution' do not materialise for a decade, or even two. Some companies may survive to see the sunrise, but the cumulative effects of intervening income reductions could kill many before their research programmes have had time to come to fruition.

Similarly, if unduly restrictive regulations on promotion and experimentation are imposed, many potential new therapies may never get to see the light of day. This may happen if too many people come to believe the extreme 'consumerist' message, which is that those in charge of the pharmaceutical industry today are not socially responsible and should not have the freedom

effectively to run the existing free-enterprise structure. That is the fundamental challenge – to be able to convince the broad majority, and those in political control, that the industry does have the right to independent managerial control. A legitimate right, won through socially responsible action.

Table 5 outlines the principles which the author believes should clearly govern the industry's approach to winning the respect it needs. First, its commitment to good health care right across the globe should be unequivocal, which in the British context means a commitment to the NHS.

Table 5: A Pharmaceutical Industry Response to the Consumer Movement

A clear commitment to health care
A commitment to freedom of information
The professionalisation of public affairs

One of the most important understandings to be drawn from ABPI's opinion research programme at the 'opinion former' level was that although the industry has a good case it is not being communicated precisely because of doubts in this area. That is to say although the industry and its products have contributed greatly to health care, it sometimes sounds as if the only motive behind such contributions to human well-being is sectional financial profit. In an area which is so emotional, and where simple market mechanisms may be distrusted and inefficient, the industry must be seen directly to be comprehending welfare considerations.

The second proposed guiding principle is a commitment to freedom of information. This applies not just to the critically important area of prescribed medicines and their side-effects, of which virtually all consumers now demand knowledge. It relates much more broadly to company and industry affairs.

The point is that if the Western, democratic system of a market economy backed by fair and balanced government regulation is to be preserved, and work efficiently, public and political debate on all aspects of the community's life must be properly informed. Sir John Hoskyns, formerly Mrs Thatcher's policy adviser and now of the Institute of Directors, has argued

the case for freedom of information with particular force and eloquence.

Finally, there is the question of the professionalisation of public affairs departments. Of course, many people responsible for this type of work in the pharmaceutical industry can already claim, with much justification, that they today achieve very high standards of practice in their established fields of activity. But the real issue here is the extension of the operations being undertaken into new areas, involving new skills.

The aim should be to internalise the good practices of groups like Health Action International: the obvious commitment to consumer interests; sociological insight; empathy with the disadvantaged. To take such elements and create a fresh image and reality for and within the pharmaceutical industry, a reality which combines emotion and compassion with scientific and medical skills and economic realism.

Again, we can to an extent look to the record of Mrs Thatcher's administration in this area, at least inasmuch as under the Conservative government of the last few years information directors have acquired a much higher status than was previously the case in departments of state. Generally speaking, the reforms that this author is urging for pharmaceutical public affairs departments comprise:

(1) The appointment of information directors with at least equal status to individuals like research and marketing directors. They should have free access to all company decision-making processes and the personal qualities needed to fully protect and encourage the professional work of their staffs.
(2) The creation of integrated programmes of social and economic research and policy development; consumer advice/contact and in-company consumer advocacy; and decision-taker, opinion leader, media and direct public communication.
(3) A de-emphasis of top-down control in operational contexts. Once overall policy is established, excessive controls on individual actors, often falsely justified with claims that the organisation needs 'one voice', should be removed. Pressure groups benefit from their plurality within the umbrella of common long-term goals, and so should the industry and its member companies.
(4) Objective performance analysis, particularly with regard to

matters like television and press interview performances, is essential. Rank alone should not protect incompetent people.

The introduction of the above concepts and values into the organisational structure and day-to-day functioning of some pharmaceutical companies, not to mention other associated bodies, may not be easy, or free from conflict. But the long-term benefits could well prove to be very substantial.

Conclusion – the Challenge of Change

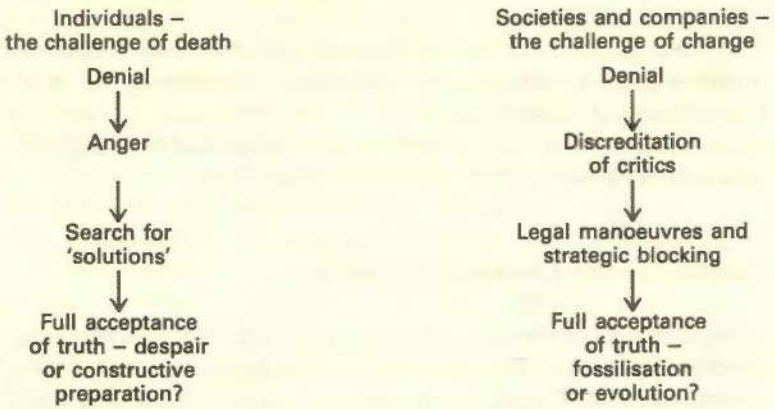
Some alarmist observers, inside and outside the industry, may contend that the days of the multinational pharmaceutical companies and of private-enterprise-generated medicines innovation are close to an end. But there is little reason to believe this to be the case. Whether or not the industry will ultimately live or die will be determined by the value of its products to society. And there is every reason to hope that the next decade or two will see many significant, life-protecting and -enhancing advances.

However, to the extent that the innovative sun may take longer to rise than we hope, there are problems to be faced in the pharmaceutical market place. The industry will surely have to adapt to new pressures and alter its practices as and when valid criticisms emerge. Whilst they should not attempt to appease groups like Health Action International when exaggerated or distorted views are put forward, companies must respond to shifts in broadly based social and political expectations.

They have done so successfully in the past and will be able to do so in the future, even though changes are not usually easy. Figure 1 attempts to illustrate the types of problem involved by comparing the processes an individual may have to go through in accepting his or her impending death with those a corporate entity may go through in responding to an adverse external environment. The point to stress, of course, is that while individuals must confront the finite limits of their existence, corporate bodies have an indefinite span, if they are capable of sufficiently rapid evolution.

An individual confronted with, say, a diagnosis of cancer may pass through first a process of denial. The information cannot be accepted. Then anger, rage and a desperate search for ways out

Figure 1: Processes of Adaptation



of the maze. Then a rational acceptance of the truth and a careful, planned approach to the personality's last great challenge, that of making a dignified exit from the world designed to maximise the chances of one's survivors being able to live on in a way which allows life still to be celebrated. Or alternatively a collapse into depression, despair and oblivion.

The comparable process for a company will not usually involve any sort of mortal issues. But suppose an organisation is confronted with evidence that it has harmed its consumers in some way, or is not acting in the public's best interest? Again the first-stage response might be denial. Then hostility, and attempts to counter or block whatever criticisms or new policy proposals are being made. Then a rational awareness of the facts and constructive programme of work to right whatever wrongs exist. Or alternatively a degeneration into a stolid defence of the *status quo*, which in time may lead the organisation only into the pages of history.

It may be suggested that the international pharmaceutical industry is already well on the path of constructive evolution. The task now is to maintain the momentum already built up with respect to issues like the improvement of Third World marketing practices; to maintain such momentum and at the same time acquire new skills so that future policies may help to generate even more individual and collective welfare – and be seen clearly to be so doing by all groups in society.

THE PUBLIC AND ANTI-SCIENCE

John Maddox

A few weeks ago I was sent a copy of *The Wrong Kind of Medicine* by its authors, who had spotted that I was going to talk to this Symposium. They obviously thought it would be a good idea if I read it first. In all kinds of ways, I found it interesting and illustrative of the kinds of problems that Mr Taylor was talking about. It is a vivid illustration of the paranoia that persuades your critics that you are engaged in a conspiracy against humanity.

I share many of the anxieties expressed by Mr Taylor but, at the same time, differ very much from him in the way in which I think these problems should be met. I want to begin with a few simple examples. Some years ago at a dinner party somebody asked me what my job was. I told her – she was a very distinguished architect – and she said, 'Good Lord, you must be one of those dreadful Darwinists.'

More recently, a very distinguished company in North America which is a major supplier of radioactive isotopes and chemicals incorporating radioactive isotopes has become known by the name of NEN Inc. It is, of course, the New England Nuclear Company, but it has thought it prudent to change its name so that it will not attract criticism for having the word 'nuclear' in the title. There is even a proposal that the familiar technique of nuclear magnetic resonance, widely used in almost every modern chemistry laboratory, should be changed to something else, and I have no doubt that as soon as a suitable alternative can be found, the name will be changed. In other words, we live in a time when people try to meet a great many criticisms of the kind that the drug industry faces by devices which entail the renaming of familiar things, rather than by devices that meet the problem head on.

I would like briefly to remind you of how we have got to where we are. Those who can recall the decade immediately after the war will very clearly remember that in this country, in that part of Europe that had not been devastated, and in the whole of

North America, science was highly regarded. It was reckoned to be one important reason why the Allies had successfully survived the war. Indeed, at that time people respected radar, nuclear weapons, jet engines, penicillin and pesticides as some of the ingredients of what had been a successful war. For a decade afterwards there was no doubt in the public's mind that science was not merely a device whereby in an emergency you could hope to win a war, but was also a means by which all kinds of then current social problems could be solved: the supply of energy, the control of population – you name a problem and science would cure it. On top of that, people had every expectation that science and its methodical and deliberate application would increase human happiness in all kinds of marvellous ways.

Even now, there are few people in societies like ours who question the value of science as a way of tackling intellectual problems. Science's esteem, in the world at large, is as great now in this academic sense as it ever has been. The problems we have now are entirely to do with the application of science, and it is very easy if you think back to tell where the problems have come from.

After the first marvellous decade following the war, all kinds of things began to go wrong. In the early 1960s, Rachel Carson published her book *Silent Spring*, which was a clear and, to some extent, an accurate indictment, although it was grossly overwritten as a book and, in my opinion, irresponsible in the way it drew attention to entirely hypothetical schemes by which pesticides might cause cancer. But it was an accurate indictment of the way in which the US Department of Agriculture had set about encouraging farmers to use pesticides widely in North America, without considering the consequences, because the consequences were partly unknown and partly ignored. In my opinion, Rachel Carson's book was a turning point. But that was also the period when thalidomide was being widely used in this country and in West Germany but not, as it happens, in the United States. It was when people were for the first time concerned that the scale of industrial pollution might become so large that the integrity of the environment in which we live might be endangered.

I think that for all kinds of reasons, many people may disagree with that extreme environmental view of the 1960s, as I do myself. But we have to recognise it as an historical phenomenon.

That period in the early 1960s contrasted sharply both with the years immediately after the war when science was riding high and with the intervening years when all kinds of splendid schemes were launched in this country. We were going to have a massive nuclear power programme. We were entirely unmoved in 1957 when the nuclear reprocessing plant at Windscale caught fire and caused a release of radioactivity much greater than that released from Three Mile Island, the American power station that went wrong five years ago. We took that in our stride, so to speak, as indeed we did all kinds of other technical developments, many of them failures, such as the Comet aircraft which fell out of the sky and the thermonuclear machine at Harwell which the people there claimed was going to produce inexhaustible cheap electricity and which turned out, in fact, not to be working as they had supposed.

The transition from the 1950s to the 1960s was very sharp. I would like to suggest briefly some of the underlying causes of this sharp change in public attitudes.

First of all, there had been excesses in the claims made on behalf of science and its application, some of which I have mentioned.

Another reason why the 1960s could engage in a period of controlled scepticism about the application of science was that they were, of course, exceedingly prosperous years not only in this country, but also in North America, West Germany, Italy and many other countries in Western Europe. One of the essential needs, if one wishes to be sceptical about the application of science, is that one must be prosperous enough to afford such a luxury. In addition, the Vietnam war did enormously colour American attitudes in the 1960s, particularly as the decade went on. It created a great sense of disenchantment in the American voters for the American government, and it cannot be left out of account as one of the reasons why by the end of the 1960s the mood of scepticism about the application of science was very strong.

Another development during that same period was the discovery, particularly in the United States, that there were multinational companies that were not confined in their operation or even legally within the boundaries of single countries. Until that time, and it really was a very new discovery, it had always been possible for a government to speak of 'our manufacturers',

but suddenly it emerged that manufacturers were no longer tied to national boundaries in the old-fashioned mercantile way of the eighteenth century. To the extent that this has challenged the power and the potentially absolute power of governments, it has been a worrying development for a great many people. In all the arguments in the past few years about the rights and wrongs of the operations of multinationals, this almost psychological factor, the way people have been disturbed by the discovery that multinationals, however small they may be in turnover, are actually larger legally than the governments that contain them, has been very important. You must recognise this as a real dilemma for many governments and many voters. They need multinationals for economic reasons, but they fear them because they are not legally confined.

In talking about the causes of the great change of attitudes in the 1960s, one cannot leave out the importance of the messianic characters who helped the movement of scepticism along – Ralph Nader is now well known: there is a man called Barry Commoner, who was so eloquent in proclaiming that Lake Erie was dead from pollution that I even made a journey to see it one cold December in the middle of the 1960s and discovered, to my surprise, that the fishermen were still dragging fish out of the lake. There were people like those who belonged to the Club of Rome. There were people who warned us that the world would soon collapse because population growth would get out of hand. The population bomb was the kind of slogan that they used. These messianic people, quite apart from being very influential in the 1960s, are still with us. To some extent the authors of the book *The Wrong Kind of Medicine*, the people who run Social Audit, are that kind, as are those nowadays who tell us that a nuclear war would be followed by a nuclear winter, and so on. They are people who believe that they have a special message, have a special understanding of the world in which we all live which, if it is communicated effectively, will enable them to save mankind from what would be otherwise a dreadful effect.

Those, I think, are the reasons why the 1960s saw the emergence of a movement that can loosely be called an anti-science movement but which is the development of vigorous and, in many cases, exaggerated scepticism about the application of science in all its forms.

But things have got better since the 1960s. In the early 1970s

the newspapers were full of talk about how economic growth would soon have to be brought to a halt and worries about whether the Third World could become as prosperous as Western society without consuming so much coal and steel and copper, and goodness knows what, that we would all run short of resources. There were predictions that in a hundred years, perhaps less, some would say – 55 years from 1972 was one estimate – atmospheric pollution would be so great that the atmosphere would be poisonous.

This was a tremendously exaggerated period which, nevertheless, had understandable roots. I think that things have got better since then for several reasons.

First of all, the exaggerations of the movement in the 1960s did frighten people into sobriety. If things were indeed as bad as the extremists said, surely their listeners had to think hard and long about whether the problems were as real as they had been told. Sober reflection by a great many honest people in the early 1970s did, I think, produce a reaction against the extremes that the environmental movement and the movement of scepticism had earlier been preaching. It also became plain that it was no longer possible to do what had seemed in the 1960s to be essential – to do away with anything that appeared to be an offence against human nature. If there is sulphur dioxide in the atmosphere, then install scrubbers in every power station to remove it. If there is something wrong with this industrial process, then make it safe by spending however much money we may have. I think that now people are more worried at the prospect that the Japanese will beat them to it unless they do something energetic themselves. So we have come to a much more robust understanding of where science stands. It seems to me an understanding, after the ups and downs of the optimistic 1950s and the cataclysmic 1960s, that is now tinged with a great deal of scepticism. People do rightly say, and why shouldn't they, that they would like the benefits of scientific innovation and would prefer not to have the disbenefits, the side-effects, whatever they are. That is a legitimate expectation. The fact that the expectation cannot be realised, except in very few circumstances, is the problem around which these arguments persist and are likely to continue.

To take one issue – the issue of drug safety and side-effects – people want the drugs but not the side-effects. We tell them two

things: this drug has been well tested, it has been put through all the procedures that the government expects of a new drug and therefore, in some sense, it is safe. But we also tell them, or should tell them, that all drugs may have side-effects, many have serious side-effects, many have unexpected side-effects that become apparent only in the course of the usage of a drug. The argument as it is conducted now, in the general newspapers, particularly those in the United States and in the US law courts, unfortunately does not take account of the truth that side-effects are almost always unavoidable in the long run, even though there may occasionally be some drugs that have none. With the kind of legislation that exists in this country and in the United States, these arguments can never be conducted rationally. In this country there is still a system whereby the Committee on the Safety of Medicines examines proposals for the testing and licensing of drugs and a licence is eventually issued by the Department of Health, but if there are side-effects, then the manufacturer is still to blame. And under the strict liability laws likely to become uniform in Europe in the near future, this liability on manufacturers will be strengthened.

So long as such a situation exists, there is bound to be litigation as in the United States; there is bound to be on the part of the public a sense of grievance every time an individual develops some untoward consequence of a medicine; there is bound to be a situation in which the manufacturing industry and the public are at loggerheads. Let me repeat: this happens in spite of the fact that people know that all drugs may have side-effects, some of them unpleasant.

My own opinion is that this argument cannot be conducted rationally unless the principle of the legislation is different. If a public authority and a drug industry together decide which drugs should be put on the market and if it then turns out that there are side-effects, both parties of the licensing process should share the responsibility. The move towards strict liability is a move in the wrong direction. In my opinion, ICI should not have paid out so quickly on its beta-blocker discovered to have side-effects, and the importance of this issue, both to the drug industry and also to the general public, is not sufficiently well appreciated. So long as we have this present system we are going to be in trouble.

The case for strict liability, that a manufacturer should be liable for whatever damage may be done by his products, is in my

opinion both inequitable and in the long run divisive. Suppose a manufacturer develops a new product, tests it carefully using the best available knowledge of what the risks may be and then puts it on the market with a licence from the appropriate regulatory authority, only to discover some years later that the product when in general use entails some unsuspected side-effect. The present tendency is to say that the manufacturer is responsible. The licensing authority stands back, washing its hands of the affair, reminding the manufacturer that its licence to put the produce on sale was not a guarantee of safety but, if you like, merely a licence to take the ordinary commercial risks that follow from selling something novel.

The cynics say there is no serious difficulty in this arrangement. Suppose a manufacturer honestly puts on the market a drug that turns out to have side-effects. He pays compensation to those affected, writes off the cost of development and marks up the price of his next product to recoup his losses. Or maybe he simply takes out an insurance policy against the risk, and marks up everything he sells. The flaw in this argument is that it is inequitable as among manufacturers, turning bad luck into a factor to be reckoned with in the balance sheet. It is less obvious, but no less true, that it is inequitable to consumers. For one thing, prices are higher than they would otherwise be, as manufacturers are from time to time required to pay compensation on inflated scales (or to insure against such payments). Fortunately, so far as I know, nobody has yet had to deal with the situation that would arise if a drug with damaging side-effects were identified long after the manufacturer responsible had been forced into liquidation for some quite different reason. Who would compensate those drug-users for their double dose of bad luck?

Let me make a few other points. Those in the pharmaceutical industry, rather like the people who work in the nuclear industry, have a sense of being misunderstood. They are producing splendid products which are of great benefit in the treatment of disease, and the general public, for whom these benefits are provided, is constantly complaining.

I do not think that the pharmaceutical industry has actually faced up squarely to one of the underlying questions that is a constant running sore. A patent granted in respect of a new machine or a new drug is in fact a licence to exercise an exclusive

exploitation for a certain period of time. It confers a monopoly right, and were it not for the patent system, innovation would be slow. But in the field of health, a monopoly right for an important drug is tantamount to a licence to charge what you like for it. In those circumstances it is unavoidable that there should be controls of some kind on the level of profits which are made. My own belief is that the particular formula we have in this country is not helpful; the formula applied in France is not helpful either and it is absurd that there should be all this anxiety about buying round, importing from Europe more cheaply, and so on. Nevertheless, the drug industry has been slow, first of all, to recognise the need for some kind of control and, secondly, to make constructive suggestions that would make more sense administratively than at the present.

The principles on which this should be done are easily spelled out. I do not quite know whether it is appropriate that the pharmaceutical industry should be called a 'sunrise' industry – it has been around a long time, after all. But it is certainly a high-technology industry, one whose success stems directly from research and development. Everybody acknowledges that. And now, there seems to be a more general recognition that the research and development, geared as it must be to commercial goals, has to be carried out competitively. What I have to say is based on the assumption that that principle will not seriously be challenged. So the problem is that of devising a mechanism for rewarding successful research and development well enough not merely to persuade the successful companies to carry on with their research enterprise but to be able to grow without putting them in the invidious position of seeming to make uncontainable profits from the sales of important drugs, pushing up the costs of health services as they do so. In my opinion, none of the arrangements so far reached between governments and national pharmaceutical industries is satisfactory. In Britain the government uses as a yardstick for fixing prices the rate of return on capital employed, which is not an efficient way of distinguishing between those whose research is effective and those who are consistently less successful. The whole question of promotion costs is legitimately a source of public anxiety. The international dimensions of this problem are more than merely taxing. It will be in the best interest both of the pharmaceutical industry and of the sick people whose lives will be

improved or prolonged by their products that there should be a seemly accommodation on this issue with the authorities responsible for public health (governments where there are national health services, as in Britain and France, insurance plans and state governments as in the United States).

I should like to make two other points. The first concerns the general public's complaints about the treatment of animals and the use of animals in research, particularly in the pharmaceutical industry. It is obviously a field in which zealots can exercise a powerful influence. Nevertheless, the welfare of laboratory animals has become a legitimate public interest. The sceptical part of that interest is fed by all kinds of problems that come to light. The University of California at Berkeley was recently fined $18,000 for having kept rabbits in appalling conditions and is being prevented from spending $25 million on a new animal house or a new life sciences building because of the trouble that it has run into. So long as the public has an interest in the welfare of animals and so long as that interest can be contained within the boundaries of the law, which is important, then it is essential that all those who use laboratory animals should go to some trouble to ensure that the public knows how they are being used.

Advertising is obviously another contentious issue. Companies such as Nestlé have been bitterly attacked in the press for advertising powdered baby foods and milk substitutes overseas. The argument has been: 'Isn't it dreadful that these people should be persuaded not to use natural mother's milk but instead to buy something from the developed world when they don't have the sterile water with which to make the formula?'

The influence of Nestlé in the Third World raises a dilemma both for us and for the critics of the drug industry. It is a dilemma for us because there are obvious possibilities whereby advertising could change unwisely the practices of people living in Third World countries. It is a dilemma for the critics because who is to say whether it is better or worse that a woman in Tanzania should look to Nestlé or to mother's milk to feed her child, particularly if she is not sufficiently well nourished to provide adequate milk, and particularly if, even in those circumstances, she wishes to share the freedom that women in this country enjoy?

The parts of advertising practice that I find unseemly are the promotional devices by means of which individual physicians are induced or at least are taken to play golf. Whether it has any

effect on their prescribing practice is another matter.

To sum up, industry's attitude to the problem of public criticism ought to be more positive, more constructive, but less terrified. And the reason for this is that the tale it has to tell is potentially even more exciting in the future than it has been in the past.

RISK FACTORS IN HEALTH CARE

Richard Doll

The title that I have been asked to speak to is one that could be interpreted in several ways. In a narrow sense it might be taken to refer to those causes of risk to which individuals are exposed when they seek professional advice for the care of their health. If, however, I were to interpret it thus I should be limited to discussing such factors as the imposition of bed rest (which was at one time so common and is such a prolific cause of vascular thrombosis), the adverse effects of drugs and immunisation (reports of which already fill the columns of the daily press) and the carcinogenic effects of radiotherapy and radiodiagnosis (which together are estimated to be responsible for some half a per cent of all fatal cancers in developed countries). I cannot, however, omit discussion of the adverse effects of drugs altogether, as it is of such concern to the pharmaceutical industry whose contribution to the physical and economic health of the country this conference seeks to discuss.

No one who has been involved, as I have been, with the work of the Committee on Safety of Medicines can be happy with the arrangements that now exist. No matter how carefully drugs are tested on experimental animals, it is impossible to be sure that no untoward effect will occur in humans and almost impossible to get any idea of the balance of benefit and risk – except of course by finding that the chemical is too toxic to consider using at all. If, however, we are to make any further progress in the treatment of disease and the relief of disability that we have been unable to prevent, new drugs will continue to be needed and we must find some better system than we now have for monitoring their use. We need in particular not only to be able to detect unforeseen adverse effects, but also to be able to compare the size of the risk with the size of the benefit obtained – something which the present system often miserably fails to do. This system relies heavily on controlled trials carried out on a small scale, combined with selective reporting of suspected adverse events and has missed major effects that make the use of a drug

unacceptable, such as those produced by practolol, and leads inevitably to scare stories that are liable to result in precipitate action which does not take account of the benefit that many patients are grateful to receive.

To assess benefits and risk in a scientific way in the interests of the whole population, we need three things: (i) controlled trials on a large scale when new drugs are introduced that are likely to be used by many people; (ii) an automatic system of quantifying any unexpected rare effects; and (iii) the goodwill of the media in reporting good news equally with bad. In this country we have a marvellous opportunity for organising an effective system of large-scale monitoring by using the records of National Health Service prescriptions, general practitioners' lists of patients, and the skill of interested physicians to follow up and check the reality of apparent ill effects. By such means it should be possible to avoid, for example, the loss of such a valuable drug as benoxaprofen, which cool assessment now seems to show was almost without serious risk, so long as overdose was avoided in elderly people with renal dysfunction. Without, however, the goodwill of the media even the most scrupulous scientific assessment can do little. Scare stories, like the one that Debendox caused congenital malformations, get so firmly fixed in the public mind that it proves almost impossible to eradicate them, despite the fact that the most intensive investigation showed that it almost certainly did not.

Discussion of the ill effects of treatment contributes, however, so little to our appreciation of the major risks with which members of the health professions have to deal that I have preferred to interpret my title more widely.

Consider, first, the changes in health that have occurred over the last hundred years and the way in which the current position in Britain compares with that elsewhere. This, according to the recommendation of the World Health Organization, requires us to think in terms of positive health and to measure the differences on a scale that culminates in 'complete physical, mental, and social well-being'. Positive health, however, remains elusive to quantification and we still have to measure progress by the extent to which we succeed in preventing, curing or relieving disease. Even this is a daunting project and there is no simple way in which all measures of morbidity can be combined. One index, which was made by combining hospital in-patient days,

out-patient referrals, general practitioner consultations, days of sickness benefit and loss of life expectancy, led Black and Pole (1975) to conclude that mental illness and handicap and respiratory disease headed the field, each contributing over 13 per cent to the total burden. It is difficult, however, as Black and Pole pointed out, to know what weight to give a consultation for a headache in comparison with a year's loss of life and there is no real alternative to the separate assessment of a variety of indices. Of these, mortality is outstanding, not only because of its overriding importance to the individual, but also because the measures that reduce it commonly reduce any corresponding morbidity as well. I shall, therefore, confine most of my comments to the factors affecting the risk of death.

Within England and Wales these have changed so greatly that the commonest age of death is now around 80 years instead of being under 1, and more than half of all newborn infants can expect to live to be over 75 years instead of under 50. The improvement (measured as the percentage reduction in mortality at each age) is, moreover, continuing as rapidly as ever, if not more rapidly, except only for the *anni mirabiles* that followed the introduction of the sulphonamides and antibiotics, as is shown in Table 1.

Table 1: Trends in Mortality in England and Wales, 1841 to 1982

Period	Infant Mortality	Per Cent Change in Death Rate in 10 Years at Ages			
		5-9	20-34	45-65	75-84
1841-5 to 1871-5	+1	−7	−1	+3	+3
1871-5 to 1901-5	−3	−18	−18	−4	−4
1901-5 to 1931-5	−23	−16	−14	−12	−2
1931-5 to 1951-5	−33	−50	−33	−12	−6
1951-5 to 1971-5	−16	−16	−18	−5	−9
1970-2 to 1980-2	−36	−34	−11	−12	−10

Source: OPCS.

The low rates that have now been achieved in England and Wales (which are generally slightly lower than those recorded in Scotland) are, according to the World Health Organization, already among the lowest in the world at ages 5 to 29 years, and

we may wonder how much further they can possibly be reduced. At other ages further progress is still obviously possible, as infant mortality is 40 per cent lower in Sweden and the rates in middle age (45-54 years) and early old age (65-79 years) are nearly 20 per cent lower in Holland and Japan. Moreover, we now know so much about the causes of disease that even in these low-risk countries it seems clear that mortality can be reduced still further.

All will, I think, agree that this improvement in mortality has been brought about partly by the social and economic changes that have resulted in better nutrition, smaller families, less overcrowding and better education, as well as by specific measures for the prevention and treatment of disease that have resulted from the increase in biological knowlege. I doubt, however, if anyone has a clear idea of the relative contribution that each has already made in the past or is capable of making in the future.

The part played by socio-economic factors in causing current inequalities in health was reviewed in great detail in the *Black Report* (Black *et al.*, 1982) and it would be impossible to add anything worth while to such a detailed review in a few paragraphs. Poverty has always been a major factor in the production and maintenance of disease and even in the most highly developed countries, where the diseases of affluence have become of major importance, the conditions of the poorer sections are still associated with significant detriments to health. How far these detriments are due to social drift, causing the socially deprived to be, for other reasons, the most susceptible to disease and the least capable of taking the measures necessary to avoid it, is still unclear. It is certain, however, that not all the detriments can be explained in this way and that some could be reduced by differential increase in the standard of living of the poorer sections, by targeted education, and by special efforts to ensure that those who were most at risk make full use of the services available to them.

A move in this direction was made recently in Britain when central funds were made available to recruit 70 Asian mothers with good knowledge of English and an Asian language who will be given the special task of encouraging pregnant women of Asian origin to attend antenatal clinics, thus helping to reduce the perinatal mortality in their communities to nearer the

national average. Other specific measures of this kind would certainly be desirable, but I agree with the medical authors of the *Black Report* that the amount of money that would be required to make effective 'education and preventive measures specifically directed towards the socially deprived' is too great to be obtained by diverting money from the acute services without doing correspondingly greater harm (Black, 1981).

The part that could be played by the application of increased biological knowledge is, I believe, easier to assess. For a large part of the loss of expectation of life that occurs under 85 years of age is due to diseases which, in one way or another, are known to be capable of control. This loss of life expectancy is now due to only a very small extent to death in infancy and childhood (11.2 per cent) and more than half is due to death in what I am increasingly inclined to call late middle age (that is 55 to 74 years of age). In this age group the principal causes of death are neoplasms and myocardial infarction, each of which is responsible for nearly a third of all deaths, as is shown in Table 2, and it is the risk of these diseases that we must make our principal efforts to reduce.

Table 2: Proportions of Deaths at Ages 55-74 Due to Different Causes (1982)

Cause of Death	Percentage of All Deaths
Neoplasms	31.3
Ischaemic heart disease	31.3
Cerebrovascular disease	9.4
Other circulatory disease	8.0
Chronic obstructive lung disease	4.7
Pneumonia	4.6
Violence	2.1
All other causes	8.6
All causes	100.0

Source: OPCS.

So far as the risk of cancer is concerned, there seems little doubt that in the immediate future the largest reduction is likely to be achieved by prevention. Approximately 35 per cent of all cancer deaths in this country are due to smoking tobacco,

particularly in the form of cigarettes, including 90 per cent of those due to lung cancer, some two-thirds of those due to cancers of the mouth, pharynx, larynx and oesophagus, and perhaps half of those due to cancers of the bladder and pancreas. The whole of this benefit can, of course, be obtained only when (if ever) we have a population that is composed entirely of lifelong non-smokers. A large part of it can, however, be obtained by stopping smoking, even after thirty or forty years of the habit, and a substantial proportion by switching to low-tar cigarettes. This is shown by the dramatic fall in the mortality from lung cancer that has already occurred among men under 50 years of age, who have smoked mainly, or only, during the period when the tar content of cigarette smoke has been, on average, less than half of what it was before the war and who now experience a mortality less than half what it was 25 years ago.

This, however, is not the only way in which we may hope to see a major reduction in risk, even though it is the only one that is now reliably proved (Doll and Peto, 1981). Substantial reductions can be hoped for by modification of diet, immunisation against viral infection, the manipulation of hormones and treatment of the clinical case.

Of these, the modification of diet is, perhaps, the one likely to have the largest effect, but the present evidence is inconclusive and apart from advising the avoidance of obesity, which would certainly reduce deaths due to cancers of the gallbladder and endometrium, recommending moderation in the consumption of alcohol (not complete abstention since a small amount may reduce the risk of vascular disease and in the absence of smoking will have very little effect on the risk of cancers of the upper respiratory and digestive tract to which it otherwise contributes) and advising the consumption of more cereal bran, which might reduce the risk of colon cancer and would certainly relieve constipation (thereby greatly increasing the enjoyment of life if not its span), there is little or nothing we can as yet propose with confidence.

The same, unfortunately, applies to the manipulation of hormones. This is a field for research which may yield rich returns and we can now only guess whether it will ever be possible to modify normal metabolism in such a way as to mimic the effect of, for example, having a full-term pregnancy under the age of 18 years and so materially reducing the risk of cancer of

the breast.

I have no doubt, however, that we shall, in the course of time, be able to prevent a number of cancers by immunisation against viruses. Active vaccines have been prepared against the hepatitis B virus and trials are shortly to begin to see if their use in infancy will prevent the carrier state and hence reduce the risk of cancer of the liver. Shortly, too, we should have a vaccine against the Epstein Barr virus, which apart from preventing infectious mononucleosis may be of use against Burkitt's lymphoma and nasopharyngeal cancer. None of these cancers are important here (though hepatitis and infectious mononucleosis are worth preventing for their own sake), but if it proves (as much recent evidence suggests) that the human papilloma virus helps to cause cancers of the cervix, vulva and penis, and perhaps also cancer of the bladder, and if a vaccine can be prepared against it (which is by no means certain) immunisation against this virus would free women from a major hazard (and possibly men from a small one).

Prevention, however, is only one side of the coin, and, although I believe it holds out greater hope for reducing the risk of cancer than we can ever expect from treatment, the better use of radiotherapy and new forms of chemotherapy have dramatically altered the prognosis for cancer of the testis, childhood leukaemia and Hodgkin's disease, have greatly improved it for other cancers of the lymphatic and haemopoietic systems, and are beginning to improve it for cancer of the breast. It would be pessimistic in the extreme to suppose that these complete the list of cancers that pharmacological research will discover how to cure.

Prevention also has more to offer in reducing the risk of vascular disease, although in the short run the contribution of treatment may prove to be almost as great. As with cancer, cigarette smoking is a major factor, particularly in the case of peripheral vascular disease and myocardial infarction under 55 years of age, the first of which, in the absence of smoking, would be almost eliminated as a serious threat to health. Complete abstinence would not, however, have much effect on the incidence of myocardial infarction and stroke over 70 years of age and it is not known whether the switch to low-tar, low-nicotine cigarettes will have any effect on the incidence of these diseases.

Improved forms of treatment combined with an effective screening programme to discover asymptomatic hypertension and

controlled trials to determine the level at which treatment should begin should reduce still further the rapidly falling mortality from stroke and might reasonably be expected to reduce the mortality from myocardial infarction by some 10 to 20 per cent. This sounds a small percentage, but the disease is so common that it actually means a substantial reduction in the total risk of death. Perhaps, however, I am being pessimistic and a judicious combination of hypotensives, anti-platelet drugs, beta-blockers, anti-coagulants, fibrinolytic drugs and perhaps (though more doubtfully) anti-arrhythmics – some of which might be given prophylactically to prevent thrombosis as hypotensives are given to prevent stroke – with coronary by-pass operations for the selected few, may have a greater effect than I have suggested. Unfortunately, however, half of all deaths from myocardial infarction occur so quickly that the patient never gets to hospital alive. Unless, therefore, more of these treatments can be given prophylactically than now seems likely, we shall have to rely on a more active policy of removing the prime causes of the disease.

The evidence that myocardial infarction is associated with a high-fat diet, particularly one that is high in saturated fats, is now overwhelming. We have been slow to accept this in England and even slower to accept the impressive (though less compelling) evidence that a high-salt diet contributes to the development of hypertension. People have been much quicker to react in America, and as a result we have had the galling experience of watching the mortality rate from myocardial infarction in the USA fall progressively from a level that was much higher than ours to one that is now less. The lesson I suspect is now beginning to be learnt and it will be disappointing indeed if a downward trend does not soon also begin to appear here.

Important though cancer and vascular disease are, the opportunities for reducing risk are not, of course, limited to them. The progressive improvement in health that has occurred in the last century has been brought about not only by the major advances that have eliminated so many infections and made most accidents a temporary nuisance instead of a threat to life and limb; but also by the prevention or cure of a mass of less common conditions – most notably by the relief of much mental disease and, in the last ten years, by the hydrogen ion antagonists that have transformed the life of people afflicted by duodenal ulcers. And, so long as we maintain conditions that encourage the

support of biological research, we can reasonably expect increasing knowledge to lead to similar reductions in risk in the future. One particularly promising field is the development of foetal screening to help avoid the birth of children with gross physical malformations or biochemical defects that lead to rapid physical or mental deterioration. Signs of similar advances in the control of the common cold, arthritis, persisting mental disease and senile mental deterioration are less evident – but if one peers hard enough they can, I think, just be discerned.

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ADDING LIFE TO YEARS

John Butterfield

Society is now confronted by a twofold health target. The first objective is to reduce the number of people who die prematurely. The second is to minimise the morbidity and disablement experienced by individuals, especially during the latter part of their lifetime. In shorthand, the first requires the addition of years to life while the second demands that we endeavour to add life to years.

Returning to the first of these two objectives, it is clear that much has already been achieved. However, premature mortality remains a significant problem. Data for England and Wales reveal that there were 577,890 deaths in 1981 and that more than 130,000 of these (that is, 23 per cent) involved persons who had yet to celebrate their 65th birthday – a milestone still 5 and 11 years below contemporary average life expectancies for males and females respectively.

A more detailed examination of these data shows that a significant proportion of premature mortality can be attributed to just a limited number of causes. Thus in 1981 coronary heart disease, malignant neoplasms and injuries and poisonings accounted for 70 per cent of male and female deaths below the age of 65 years.

In each of these instances, there is persuasive evidence that 'environmental' factors underlie causation. Tobacco and inappropriate diet, for example, are prominent in the aetiology of cancer. These two factors, in conjunction with raised blood pressure and a group of other influences including inadequate physical exercise and stressful lifestyles, are also implicated in the genesis and subsequent evolution of the arterial lesions found in coronary heart disease. And focusing on accidental fatalities, the motor vehicle remains an irritatingly unnecessary cause of death: in 1981 motor vehicle traffic accidents led to a total of more than 4,000 deaths in England and Wales.

Against this background, few could dispute the importance of behaviour as a causal element in contemporary morbidity and

mortality. And, having established this, it is clear that more appropriate patterns of behaviour could yield substantial health benefits. The evidence suggests that more widespread participation in exercise activities would go some way to reducing the toll currently exerted by coronary heart disease. And an earlier contributor to this session, Sir Richard Doll, has made clear in his studies of doctors' smoking patterns not only that the habit is associated with an increased risk of death but that stopping smoking – even after many years – is positively advantageous. I believe that his studies in this area may be seen collectively as yielding the most important and dramatic foundations for effective prevention of disease this century.

At the same time, however, it would clearly be highly inappropriate to dismiss as insignificant the potential contribution that continued progress in the understanding of biochemical and other mechanisms could make in terms of morbidity and mortality reductions. I personally suspect that as knowledge of the factors which make cells go into mitosis, of the mechanisms underpinning oncogenes and of many other factors emerges from molecular biology laboratories, we will be provided with the basis for constructing a host of new and effective interventions. The possibilities for new vaccinations are exciting but there are still many unknowns relating, for example, to the 'geography' of the interaction between receptor and virus. There can be no doubt, if one listens to the molecular biologists talking to the oncologists, that a great mass of knowledge is emerging for exploration by the pharmaceutical industry which should open up wide possibilities for new therapeutic intervention.

Turning to the second objective identified at the outset of this paper, it is clear that we have also to be concerned with the quality of those lives for which therapies are either inadequate at the present or simply non-existent. Within the mental diseases a prominent illustration of the latter is provided by senile dementia. This process of irreversible and usually progressive destruction of the brain in old age affects 10 per cent of the population aged 65 years and over, that is, more than 700,000 people. Furthermore, demographic forecasts combined with age-specific prevalence rates indicate that the total burden of care the disorder already imposes on the health and social services as well as relatives will become more severe over the remaining years of the century. We are uncertain of the extent to which senile

dementia is determined by environmental influences, for example, tobacco and alcohol use, and genetic factors. And in Altzheimer's disease, the work of Martin Roth in Cambridge in collaboration with Nobel Laureate Arun Klug is unravelling the biochemical nature of the tangles in the neurones, which holds out hope for future progress in understanding the chemical pathology of that condition and so perhaps of therapy.

In the same broad disease grouping there remains considerable potential for therapeutic advance in schizophrenia. More people of working age who are in hospital or disabled in the community suffer from schizophrenin illness than any other potentially handicapping condition. In the UK something approaching 150,000 persons are affected at any one time. Depression, which will be responsible for the hospitalisation in Britain of between a million and a million and a half people in the present population at some stage during their lifetime, is another important target for therapeutic research in neurobiology.

Many other neurological illnesses are also awaiting improved means of therapeutic intervention. Although 85 per cent of patients with Parkinson's disease (which afflicts between 60,000 and 80,000 elderly people in the UK) initially respond well to treatment with levodopa, the high incidence of unpleasant side-effects coupled with the gradual reduction in the efficacy of this treatment with time underscores the need for continued research.

The need for a therapeutic advance is even more marked in the context of multiple sclerosis. This disorder inflicts varying degrees of disablement on some 50,000 individuals in Britain and with onset generally occurring in early and mid-adulthood it strikes at a time when family and other commitments are at a peak. Yet in spite of substantial growth in the volume of research endeavours directed at understanding multiple sclerosis, we remain uncertain of its cause, no curative treatment has been found and palliation poses major problems.

Focusing on diseases of the musculoskeletal system and connective tissue – which cause physical impairment for approximately 1.2 million adults living in the community – there is no doubt that non-steroidal anti-inflammatory medicines have made a major contribution in the provision of effective symptomatic relief, especially in osteoarthritis. But an extension of therapeutic intervention to earlier stages in the aetiological chain – to prevent or retard the underlying disease processes –

might be expected to have an even greater beneficial impact.

Equally, there is considerable scope for therapeutic progress in rheumatoid arthritis which accounts for 14 per cent of the severe handicaps experienced by adults of working age. Most of the 500,000 people who suffer the crippling effects of rheumatoid arthritis are, however, in their sixties or older. Consequently, this disease in many respects exemplifies the type of target that is increasingly shifting towards the centre of attention in medical research: in other words, disorders which are relatively insignificant as causes of mortality or economic burden (measured in terms of sickness absence from work and hospital costs) but which, given present therapeutic deficiencies, are responsible for considerable personal suffering and social costs.

I believe that we can and must make valuable progress against these and other diseases which impinge so deleteriously on the quality of life. My optimism for the future stems in part from the concern I see everywhere around me and the thrust of the research work going on. It is all leading to new approaches. In Cambridge, for example, we have introduced into our midst a small commercially driven pharmaceutical research group involved in developing new neuro-pharmacological products. We are also intending to bring into our environment a medicinal chemist with a high reputation of being able to synthesise products detectable by nuclear magnetic resonance (NMR). Applied to pharmaceutical products, such NMR marking could provide opportunities for three-dimensional studies aimed at locating where drugs get to and therefore presumably operate in the central nervous system. In order to ensure that we do not get into an anatomical muddle, we are fortunate in that one of Europe's leading neuro-anatomists has just taken up our Chair of Anatomy. Collaboration between research workers from such different disciplines as chemistry, physical chemistry, anatomy and pharmacology must enhance the probability of progress.

To be realistic, however, it has also to be recognised that there are 'external' barriers to future advance and these have to be overcome too. The clouds over the sunshine pharmaceutical industry arise because in many minds modern chemistry is equated with pollution and one even hears that some patients believe that the dose prescribed today is polluting their bodies tomorrow – a sad reflection of the lack of understanding of the risk/benefit issues that have to be worked out and accepted

publicly before any medicine is brought into use. Of course the same is true in those who oppose science as it is applied in many other areas. Unfortunately, there can be little doubt that these attitudes are aggravating the problem of national funding for research and new knowledge generally.

In addition to these difficulties, the problems of drug side-effects pose an additional major challenge to the reputation of the pharmaceutical industry. Of particular concern is the increasing incidence of such side-effects with an increasingly ageing population. Estimates suggest that approximately 25 per cent of the elderly experience undesirable sequelae from the medicines they use. And, of course, this is particularly worrying when elderly patients have multiple diseases and require a wider and wider range of pharmaceutical products for each one of them. The increased incidence of side-effects among the elderly deserves much more scrutiny. The research led by Dr R. Holliday in the genetic division at the National Institute of Medical Research (see page 46 of the *Annual Report* of the MRC, 1983/4) shows that it is entirely possible that error accumulation in protein synthesis leads to cell ageing – for example in fibroblasts, ageing is associated with increasing numbers of inaccurate DNA polymerase (that is, protein) molecules. Cell ageing can therefore be explained in part by such a feedback mechanism.

Drug side-effects among the elderly could also have a simpler explanation at the chromosome level. Jacobs showed years ago that if lymphocytes were cultured from older and older people, an increasing proportion of the cultured lymphocytes had errors of chromosome count: aneuploidy. Perhaps with increasing age there is increasing aneuploidy in the liver and kidney cells too. Whether it is at the DNA or chromosome level, it would appear that with age an increasing proportion of cells simply have not got the proper enzymatic equipment to deal with the metabolism of the drugs we are providing. I personally hope, therefore, that not only will we be screening for diseases but that we will also channel significant research into devising screening techniques, perhaps on urine samples, to determine whether or not the elderly metabolise adequately the drugs we prescribe.

Leaving aside these problems and returning to the health objectives now confronting society, it seems to me that the diseases from which man suffers may be very broadly characterised

as those arising from bad luck and those attributed to ignorance of risks or ignoring risks. Examples of the former bad luck diseases would include multiple sclerosis and rheumatoid arthritis, for which we do not know the explanation: there is no question of the patient being ignorant of present knowledge. In these instances progress must rest on successful research and its subsequent translation into effective prevention or therapy. Here a thriving and innovative pharmaceutical industry is clearly one of a number of essential prerequisites for success in the future.

On the other hand, ignorance diseases – ignorance of disease risks or even deliberately ignoring them – present an entirely different problem. In many respects the morbidity and mortality they generate are a function of wholly inappropriate behaviour patterns. I am not sure myself that continued smoking of cigarettes in spite of the overwhelming evidence indicting the habit as a cause of lung cancer and as a major contributor to heart disease provides any longer a really suitable example of an ignorance disease. One wonders if any smokers are still ignorant of the risks or whether their continued smoking is in defiance of us or represents a risk-taking behaviour. Either way, the solution may be more problematic than in the case of bad luck diseases. Perhaps we should consult the neurobiologists to see if they can find ways of making individuals more responsive to information concerning the now increasingly well-established deleterious consequences of certain lifestyle patterns. At the moment there is clearly a major challenge confronting the health educator. He has to become a health promoter and this effort must not be confined to pre-conceived groups, for example people who have low levels of intelligence. My own personal experience has taught me that without adequate clinical information, successful intelligent people may be vulnerable to ill health resulting from inappropriate, or to put it more bluntly, ignorant behaviour. We must remember that patients do not know as much as we do about the complications of their diseases unless we take time to teach them these things – which teaching I call 'secondary' health promotion.

So we are back to the concept of taking care of the whole patient. Perhaps, philosophically, we have not really advanced as far or as fast as we think. When the Regius Professorship of Physic was established by Henry VIII in Cambridge in 1540, the word Physic embraced all of natural philosophy in the care of patients. Now we are all specialists in so many different branches

of science. To improve the quality of life of our patients we have to be all-embracing again and draw upon the efforts of a wide range of professional groups. These now range from research chemists to advertising and packaging experts in the pharmaceutical industry, as well as us physicians.

Hippocrates recognised the problem. Most of us remember his famous aphorism 'Life is short, the art long, opportunity fleeting, experiment treacherous and judgement difficult.' But we should not neglect the rest of that great aphorism – 'the physician must be ready, not only to do his duty himself but also to secure the co-operation of the patient, of the attendants and of the externals'. For Hippocrates the externals were the relatives who brought the patients to his clinic at Kos. Today an equally wide range of people is needed in our efforts to improve the quality of life before death and includes, of course, those who have the courage to develop and supply new medicines.

Acknowlegement

I am grateful to Nicholas Wells for much help in the preparation of this paper.

DISCUSSION

Rosalinde Hurley

I want to emphasise some points, made by the speakers this morning, that seem to me to bear on the common theme of information and of health education in its broadest sense. Mr Taylor addressed the concern of society when he spoke of the consumerism movement as one that eventually went on to expressions of policy and preference from the original concept of fair trade and product information. As part of this movement, the public has a growing desire for information on medicines as well as a genuine and perfectly legitimate concern about safety, about compensation for injury, and about such matters as profits, prices, promotion and product duplication. Alluding to that section of society who are the 'opinion formers', he spoke of the evolution of special interest groups within the main lobby.

Part of the message from Mr Taylor, as I saw it, was that if we continually treat such groups with suspicion or hostility, we do so at our peril, for it is dangerous indeed to underestimate genuine concern; we must learn to respond in a positive manner. For this reason, it is desirable to enlarge the status and skills of Information Directors. Our response to the challenge of change, in evolutionary form, started as denial, went on to hostile discreditation of critics, moved to an epoch of legal manoeuvring and blocking and, finally, perhaps is entering that phase that will lead to the fostering and encouragement of the special skills of which he spoke.

Mr Maddox spoke of anti-science and of the rise of what I will loosely call 'environmentalism' after the late 1970s. The concept of pollution arose from the stimulus of certain powerful books and events, and reached expression for us who are concerned with drugs in terms of pollution of the individual, that is the hazards and the risks of drugs. It is accompanied by fear of the multinational corporations which are larger, conceptually, than national governments and are, thus, awesome and to some seemingly beyond the control of nationally organised societies. Notwithstanding, industry has, in my view, been quick to

recognise and accept certain needs, paramount amongst them the need for regulation in the use and control of drugs, which was effected with its voluntary participation long before we had statutory controls.

We are all concerned about long-term monitoring of drugs and Sir Richard Doll urged that we should adopt a less haphazard approach, with controlled trials conducted on a much larger scale, and with automatic systems of quantifying any unsuspected effects. It is important not only to achieve this, but to publicise our progress. There, the goodwill of the media is needed, for if they are not well informed by us, the singling out of particular events may cause alarm to the public and may distort the ambience in which reasoned scientific evaluation can proceed in an ordered fashion.

Sir John Butterfield introduced a hopeful theme, that of the possibility of great advances in the prevention of diseases such as neoplasms or myocardial infarction, which are dependent on health education as well as on specific therapeutic advance. He reminded us of the advances and expected advances in neurobiology that offer hope of great potential benefits in disorders such as senile dementia, schizophrenia, Parkinsonism and multiple sclerosis – diseases that detract so violently from the quality of life as opposed to life itself.

Thus, I discern in the morning's session a great trend towards the belief that in information and health education lies part of the way forward. In the general discussion that follows, perhaps we shall have more of its practicalities placed before us. It is a worthy aim, and we are indebted to Sir John for reminding us that Hippocrates himself enjoined us that in the practice of our art we should seek the co-operation of our patients, of the attendants and of the externals.

DISCUSSION

Nicholas Wells

The four papers we have heard this morning have made it clear that the issues embraced by the session's theme of balancing risks and benefits are both complex and wide ranging. Risks and benefits rarely take the form of easily identifiable and quantifiable entities which yield clear-cut answers as to the desirability or otherwise of specific projects. In the case of medical interventions, for example, the values attributed to each side of the risk/benefit equation may vary significantly not only between patients but also for the same patient at different points in time.

Furthermore, technological progress implies that established risk/benefit measures ought to be subject to continuing reassessment. In this context a noteworthy example may be drawn from a recent 'Editoral Retrospective' in the *New England Journal of Medicine* (Braunwald, 1983). The latter forecasts that coronary artery by-pass grafting may soon be performed less frequently in the United States. Part of the explanation for this prediction is that pharmaceutical advance since the mid-1970s has reduced the difference in benefit formerly associated with the two types of therapy.

It is also clear that risks and benefits as they relate to pharmaceuticals have been studied in a variety of different contexts. Comparisons have obviously been drawn between the risks and benefits associated with pharmaceuticals and those accompanying other interventions. And in the 1970s debate surrounded the extension of regulatory requirements in the field of new drug development. There was widespread concern that any benefits accruing in the form of enhanced safety – which were in themselves open to question – were being achieved at the expense of delayed or foregone therapeutic advance.

Risk/benefit evaluation as it relates to health care in general and pharmaceuticals in particular is therefore concerned with a multiplicity of issues. However, a key issue which I believe we need to address is the apparent shift of emphasis or awareness away from the benefits of medicines and the correspondingly greater concentration on their limitations and risks.

It seems to me that many factors underlie this development. One explanation is that the benefits generated by modern medicines are not as dramatically apparent as was the case during the era when anti-infective medication became available for widespread use. Thus today's anti-arthritic preparations, for example, do not lead to substantial reductions in mortality rates or hospital admissions. Instead, they improve social functioning and raise the quality of life. But these impacts are difficult to quantify and consequently remain less conspicuous.

Another probable factor is the contemporary emphasis on disease prevention and health promotion. There has been a growing awareness that the volume of premature mortality is excessive in many advanced nations – in England and Wales, for example, approaching one death in every four involves persons who have yet to celebrate their 65th birthday – and at the same time it is clear that a large proportion of these deaths stems from preventable causes like coronary heart disease and some of the cancers. Consequently, and quite rightly, considerable efforts have been made to channel appropriate advice to the public regarding key behavioural factors – such as smoking, exercise and diet. However, one of the spin-offs of these activities has been to camouflage the present and potential role of medicines in these and other areas.

The general anti-science, anti-medicine fashion described by John Maddox is another important factor. Several of the prestigious Rock Carling Monographs and authors such as Illich (1975) and Kennedy (1981) have led the way in suggesting that the benefits of medical intervention have been overstated. On the other side of the equation, there has been an increasing amount of attention given to drug side-effects, especially in the newspapers. The precise explanations for these developments are open to debate; some may consider that questions relating to side-effects, for example, have been raised to such prominence simply to provide another channel for attacking the pharmaceutical industry. What is clear, however, is that issues of equal importance in this context – such as the need for appropriate prescribing habits as well as for the development of techniques that might help to identify individuals who might be particularly susceptible to drug reactions – have received little attention.

Finally, it is relevant to recall that these factors have been operating against a backdrop of concern at the rising cost of

health care provision. Although pharmaceuticals represent only 10 per cent of NHS costs and just 1 per cent of total government spending, it is estimated that the drug bill will rise to £1.7 billion this year. And in the current economic and political environment, there is growing pressure to justify such levels of expenditure. However, whereas in the past it was a straightforward task to demonstrate the economic gains generated by chemotherapy, this is no longer the case and today's medicines are generally seen as adding to the cost of the nation's drug bill without any compensating financial benefits realised via substantial reductions in hospital stays or sickness absence from work.

If this analysis is correct, then there would now appear to be a clear need to make more explicit the benefits yielded by modern drugs. And in this respect is it encouraging that efforts are being channelled into the development of new measures, such as health profiles and health status indices which reflect the fact that today's drugs exert a considerably greater impact on the quality of life than on its quantity. But many questions have yet to be answered. Who, for example, has responsibility for generating this information? It has been suggested that pharmaceutical manufacturers might collect benefits data in conjunction with the other data requirements of the drug development process. This may not prove acceptable, however, if it meant that the development phase became longer or more costly than it already is. Furthermore, the success of a new drug depends ultimately upon its observed value in widespread clinical usage so that information on its social benefits generated during the pre-marketing phase of its life cycle may be judged superfluous. Yet if we extend Jennett's line of argument contained in his recent Rock Carling Monograph then in the future such data might play an important role in facilitating marketing approval in the first instance (Jennett, 1984).

Another priority would seem to be to increase public understanding of the concepts of risk and benefit as they relate to medicine usage. In the House of Commons in 1980 Sir George Young, then an Under Secretary of State at the DHSS, expressed the view that 'this House, the media, the pharmaceutical industry and the professions carry a serious responsibility to ensure that the public accepts that modern drugs inevitably have risks as well as benefits and that complete safety is attainable only at a cost which most of us would regard as unacceptable – that is, turning

our backs on progress' (Young, 1980).

However, I think that we have to be wary of oversimplification. For example, although press coverage of drug matters might be interpreted as indicating a high degree of dissatisfaction among the public with their medicines, a survey conducted at the start of the 1980s found that 80 per cent of respondents were generally confident about drug safety. Clearly this is a complex issue and it raises questions concerning the media's role in creating as well as reflecting opinion which in turn has important implications for attempts to raise the quality of understanding of pharmaceutical issues.

That said, however, it has to be recognised that a rapidly growing proportion of the public is now demanding more information about the drugs it is prescribed. In addition people are becoming increasingly interested in health matters and indeed responsive to the evidence and advice that is being put before them. Look, for example, at recent trends in cigarette consumption and participation in exercise activities. It is also clear that patient preferences are becoming increasingly relevant to treatment decisions. As a notable example, research by McNeil and her colleagues (1981) found that 20 per cent of a group of healthy volunteers would choose radiotherapy rather than surgery for laryngeal cancer even though the survival rate at three years for radiotherapy is approximately half that for surgery. Surgery severely impairs speech and these individuals judged quality of life to be more important than longer survival. Long-term consumption of pharmaceuticals for chronic disorders might be expected to raise issues of a related nature.

Obviously, there is no overall solution to these disparate issues and the varying requirements of different patient groups. In the context of pharmaceuticals, it has been argued that there is a clear need for a more professional approach to the public affairs function in the industry. In addition I would suggest that the developments I have described indicate a need for reliable information upon which effective prescribing and other decisions concerning therapy can be made. They also herald the forging of a more interactive dialogue between doctor and patient.

In closing my remarks I should like to draw attention to one final cost/benefit issue which threatens to render our bright and hopeful sunrise a pale and shadowy dawn. I am referring to the financing of research that provides the key to future therapeutic

advance. Major new medicines now emerge only after a costly and prolonged process – estimated at between £50 million and £100 million over a period of ten to twelve years. Consequently research is an investment requiring the long-term provision of sustained and adequate finance. Yet the Medical Research Council is now facing cuts in real terms, and as Professor Richard Batchelor has pointed out in a recent letter to *The Times*, this may especially jeopardise projects requiring prolonged support (Batchelor, 1984). And the pharmaceutical industry too is unlikely to be encouraged to enter new and risky areas of research if confidence and the financial wherewithal to invest are regularly threatened. I think it has to be made clear therefore that short-term benefits achieved in the form of expenditure savings have a very real long-term cost. And that cost is the likelihood of foregoing the objective of adding life to years; that is, the possibility of one day being able effectively to treat diseases such as senile dementia, rheumatoid arthritis, multiple sclerosis and many others for which relatively little can be done at the present time.

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GENERAL DISCUSSION

The speakers' papers and discussers' comments presented to the third session of the Symposium stimulated discussion over a broad range of topics. Professor Margot Jefferys (University of London) set this period of general comment in motion by raising three separate issues. First, in the context of John Maddox's paper, she considered that the strengthening of the women's movement since the 1960s ought to be clearly identified as a factor of considerable importance in changing attitudes. Second, Professor Jefferys was concerned at Sir John Butterfield's reference to 'ignorance diseases', considering this terminology inaccurate. She expressed the belief that ignorance of potential benefits does not explain why people fail to modify their lifestyles as might be deemed appropriate. Rather, such intransigence reflects the many factors which attract individuals to their current behaviour patterns. Consequently, she argued that health education aimed simply at increasing information levels will not resolve the problem of encouraging people to adopt healthier patterns of living. Consideration has to be given instead to issues relating to social structure, individuals' views of their life chances and their perception of the extent to which they are able to influence the latter.

Responding to Professor Jefferys' concern, Sir John Butterfield explained that he was not using the word 'ignorance' in a pejorative sense nor in relation to potential benefits. Instead he was referring to ignorance of risks and even to people taking no notice of the latter despite knowledge of their existence and significance. His objective was to convey his belief that greater understanding than currently exists about causes and the means of preventing complications of diseases could play a part in helping to reduce today's unnecessarily high morbidity and mortality levels. But he conceded that if a more appropriate substitute for the word 'ignorance' could be found he would be happy to accept it.

In a final comment, Professor Jefferys highlighted the need to take account of the views of a broad range of parties in discussions of health matters. Thus those with unorthodox

approaches to medicine and critics of current practice in relation, for example, to pharmaceutical supply could contribute valuably to the dialogue, a point echoed by Dame Elizabeth Ackroyd. Perhaps more importantly, both expressed a desire to see more account being taken of the wishes of the consumers of health care.

This last theme was further developed by Martin Buxton (Department of Economics, Brunel University). He suggested that work on risk/benefit assessment should focus on two principal areas. First there is the measurement of objective risks and benefits as they relate to drugs and other forms of medical intervention. Second, there are the public attitudes to and perceptions of these risks and benefits. From this standpoint, he argued that whilst clinical trials and other evaluations yield information of more or less sufficiency in the first area, very little is known about public attitudes to risk and the sorts of decisions people wish to make in the context of health care. He made a plea for greater research efforts in this area because it is becoming clear that doctors have very different attitudes to risk and the trade-offs between quantity and quality of life to those held by most patients. At the moment, however, doctors are making decisions for their patients and these may be made either without recognition of the possibility that their patients may have different desires or with an inaccurate perception of the latter.

The general question of how individuals might become better informed in health matters re-entered the discussion via a contribution from John Spink (The Wellcome Foundation). He was specifically concerned with the problem of transmitting to patients information about the medicines they are prescribed.

He pointed out that the current movement towards original pack dispensing will create greater opportunities for manufacturers to enhance patient understanding of their medicines. But the issue that this raises is how much information should be provided? The pharmaceutical industry is frequently accused of seeking to provide only the minimum necessary yet, paradoxically, it is in the manufacturers' best interest, from a product liability point of view, to move towards the other extreme. Yet Mr Spink expressed uncertainty that maximising available information would be helpful to the patient and may in fact cause unnecessary alarm. It may also run the risk of eroding the relationship of trust between doctor and patient. Consequently, careful thought has to

be given to the question of what constitutes the appropriate amount of information to be supplied to patients.

This last comment drew agreement from Professor Rosalinde Hurley, who also pointed out that in balancing risks and benefits a major problem stems from the absence of a straightforward numerical formula to guide the decision-making process. The complexities in conveying the meaning of risk/benefit data coupled with the well-known difficulties of satisfactorily wording a patient package insert make it clear that the provision of information about medicines is not the straightforward issue it may appear at first sight.

In the same broad area of discussion, Dr Frank Fish (School of Pharmacy, University of London) argued that pharmacists are important members of the health care team and that they have a valuable role to play in health education. The pharmacist is especially well placed to communicate information in a way that patients may understand and to reinforce advice already provided by the doctor. Responding to this comment, Dame Elizabeth Ackroyd suggested that if pharmacists are going to fulfil their potentially valuable role, they will have to make themselves more accessible to the public than is often the case at the present time.

A number of other topics were considered during the discussion period. Dr J. A. Bonaccorso (Merck Sharp & Dohme, Latin America) suggested, for example, that it was insufficiently recognised that adverse drug reactions may reflect inappropriate prescribing rather than shortcomings of the medicines employed. And Sir Dudley Smith (Member of Parliament) raised the issue of the ageing population, venturing the opinion that there is too little appreciation of the economic and social implications of the demographic trends forecast for the remaining years of the century. It was also his view that the public has a very poor image of the pharmaceutical industry and that the latter must counter this perception by becoming more effective at selling its cause.

The subject which attracted most attention, however, was that of medical research. David Crouch (Member of Parliament), in pointing out that the British pharmaceutical industry now spends around £500 million a year on R and D compared with £120 million by the Medical Research Council (MRC), expressed concern at any further widening of the gap arising out of continuing shortfalls in the latter's funding in real terms.

Responding to this point, Sir Richard Doll agreed that the time had now come to go on the offensive to restore appropriate funding levels for the MRC. However, he also commented that this had not been his view until recently. Retrenchment in the past had, he suggested, provided an opportunity for the MRC to rid itself of unproductive work and thus promote support for new projects of high quality. But this was no longer the case and the cessation of growth in MRC funding in real terms was causing serious concern, especially in view of the diminishing financial support for research available from the universities.

Sir John Butterfield commented that financial constraints had had a particularly severe impact in reducing the scope for replacing obsolete equipment. He also suggested that this effect, which is not confined to medicine but extends to many other branches of science, provided an explanation for the movement of some researchers away from the universities to the private sector, where work could be undertaken using modern equipment. John Maddox also endorsed the general consensus that research funding had become inadequate and expressed the opinion that this factor explained what he regarded as the declining quality of British research over the past decade. Finally, Dr Fish drew attention to his fear that as research funds become yet more scarce, there might be a tendency for currently neglected areas of research to lose out even more to those which appear more immediately 'attractive'. This development could significantly retard therapeutic progress if fields of investigation such as drug delivery systems, were further deprived of funds.

SESSION IV:

ECONOMIC ASPECTS

CHAIRMAN'S INTRODUCTION

Colin Cooke

I begin with an apology for my being here. This apology is because I am here only through the untimely death of John Vaizey, and I very much regret that I should appear here under that circumstance.

In this session we are coming back to what are called in the programme 'Economic Aspects'. In previous sessions we have been discussing aspects of the future of the sunrise industries, aspects of the international scene, and aspects of balancing patient care with the risks involved. I think that we now come to the economic meat of the matter: of how the pharmaceutical industry can satisfy the demands upon it set by the aspects which have been discussed in the earlier sessions.

One of the advantages of old age is that you can remember quite a long while ago. I was thinking particularly this morning, in the matter of patients, of the village I knew as a boy before the 1914-18 war, of the chemist in the neighbouring town with his beautiful, large coloured bottles and behind the counter his drawers and jars, labelled with curious and not understandable words, full of the things he sold and made up. I also remember the village doctor and the surgery attached to his house, with outside the surgery a porch in which the medicines he mixed were waiting to be collected, labelled the mixture for Mrs Smith and so on. That seemed then the extent of medicine, and I don't suppose that there were any serious economic problems about the production of the materials that the pharmacist needed or the delivery of those materials through wholesalers to the pharmacist and then through the doctor's prescriptions to the patients. In other words, it was a fairly simple economic system.

Just before the 1914-18 war we had the first Health Act. The panel system that came in then, which developed through the 1920s, produced a different slant on serving the patient. The patient now was on the panel of a doctor, and the doctor was prescribing and being reimbursed for that, although much of it went on in the same way because the same suppliers were

supplying the chemists and the level was that of straightforward materials going into the chemist's shop. There was nothing really startling either about the drugs; if the pink medicine didn't agree with you, the doctor would try another colour.

Then, of course, we have had the immense development since the last war in which the thread of the old panel system still continues to come through. If genes are inherited, I think the earlier devices of health care are also inherited by the later system and you have to look into it to see what they are. The resulting development of the industry, the practice of medicine, the habits of prescribing and the methods of getting the drugs to people are such that we now have an economic problem on two sides: one is the economics of the industry as an industry, and the other is the economics of the whole of health care. In the Office of Health Economics we have been endeavouring to make some reasonable sense of parts of these for quite a long time now, but it is not altogether an easy thing to do. The link between the two economics, the economics of industry (that is, the economics of the production of drugs, the distribution of drugs, and the use of drugs) and the economics of health care provision for people is, of course, a political link. This is, in the best Adam Smith terms, an exemplar of political economy. I hope that when we come through this final session we shall be getting nearer some idea of that political economy.

THE IMPORTANCE OF A MARKET ECONOMY

Ralph Harris

Whether by oversight or design the very mixed contributors to this conference do not include a single bishop. So to elevate the tone of our proceedings, if not to raise the temperature, I propose to open with a couple of quotations from the Bishop of Liverpool, which I think may help to focus the discussion. Both quotes are taken from his recent socialist testament *Bias to the Poor*, the first in his chapter entitled 'A Crisis for Capitalism'. On page 136 he complains of the free market that:

> it is not only the inefficient that go to the wall; so do efficient industries which happen to be operating in areas from which the market has shifted away.

The second quote comes in the final chapter entitled 'Can the Church Bear Good News to the Poor' where he writes on page 219:

> There is no more painful matter in Church Life than pastoral reorganisation which involves closing churches . . . Yet it is right to go through the painful processes of making some churches redundant in areas where the population has drastically reduced.

He goes on to explain:

> If we keep too many church buildings, we trap congregations into putting all their energies into maintaining the buildings and justifying their existence by running Church organisations to use them.

If we substitute 'coalmines' for 'church buildings', we have a pretty fair vindication for the National Coal Board's closure programme.

My reason for reading these passages is certainly not to mock one of the most attractive leaders of the Church to which I happen to belong. It is to emphasise what misconceived humbug is so much of the lofty moral criticism to which the market economy and its practitioners are so vulnerable – and to which it will remain vulnerable until there is a better understanding of the system by which we all (including our bishops) freely earn our living and live in comparative freedom.

Yet the bishops are at least as much in the market as the pharmaceutical industry. They have to close churches, not for the hell of it, but because resources are scarce. They have to weigh up their costs against the proceeds of selling old sites and investing in new buildings. They have to live within budgets, mostly derived from voluntary payments by customers who are free to choose rival brands or to buy quite different goods and services. They indulge in advertising, packaging, display, product differentiation and even – to judge from the somewhat heretical Bishop of Durham – product development, if not switch-selling. The fact that their leading product is intangible in no way distinguishes it from many subjective satisfactions offered by commercial producers.

Indeed, not only are the churches part of the market economy, their ability to compete for the public's money and allegiance rests on the same freedom that allows consumer choice in more humdrum goods and services. It is a truism that religious freedom is severely curtailed in the countries of Eastern Europe because they lack the dispersed initiative and private property rights that are the cornerstones of a market economy. Yet the priceless boon of freedom is now taken for granted by bishops, and the system which guarantees their freedom is given no moral credit.

The importance of these episcopal criticisms is that they typify so much hostility to the market – and its practitioners – as being unworthy, selfish, materialistic, money-grabbing, profit-seeking. As with so much of the outpourings of Social Audit, hostility springs from judging the great issue of private enterprise by reference to motives rather than results. Thus even our critics may acknowledge the powerful productive impulses of private enterprise; but like many even among capitalists they nourish doubts about reliance on self-interest as the ruling incentive to effort, economy and investment. Hence, for example, the emotional cry against making money out of ill health.

Intentions versus Results

The first answer to such criticism is that good intentions are no guarantee of good results. If we supposed politicians are motivated by their conception of the 'public interest', would we have to approve of the havoc they have unintentionally wrought through the debasement of our currency to less than one-twentieth of its pre-war value with the attendant inequity and impoverishment of millions living on savings or fixed incomes? And what about the evil consequences of other well-intended, compassionate policies like rent control that have destroyed millions of lettings and worsened the plight of the homeless? Mr Aneurin Bevan (or was it Professor Titmuss?) described the NHS as the 'most unsordid act in British history', but are all its practical consequences such an unmitigated blessing? 'Do-gooders' may mean well, but they often turn out to be do-badders. The proof of public puddings is in the eating, not in the good intentions of the amateur cooks, spiritual or political.

It is true that inventors and entrepreneurs may be driven on – against many discouragements – by material ambitions. But if they are successful, by far the larger part of the benefit is spread among millions of consumers in better or cheaper products and services. More prosaically, such firms as Marks and Spencer, Boots, ICI, Beecham do not aim directly at doing good, but at doing well, that is, making bigger profits. But so long as competition is not impeded, the law of the market is that they will continue to succeed only by doing better for their customers than alternative suppliers. Thus spake Adam Smith in *The Wealth of Nations* over two hundred years ago:

> It is not from the benevolence of the butcher, the brewer or the baker that we expect our dinner, but from their regard to their own interest.

Mixed Motives

The second answer to those who damn the market by harping on about self-interest and profit is that they are in truth damning – and often damning falsely – the mixed motives of ordinary people as producers, workers and consumers who operate in the market.

It is like the fat man in the restaurant who blames his own obesity on the waiter. In truth the market is neutral: it will supply what consumers want from prayer books and communion wine to pornography and hard liquor. It will offer whatever incentives are likely to move people to work, save, invest, innovate. It is true that differential monetary rewards are the most common forms of inducements to effort in modern economies. But few people are activated, like cash registers, exclusively by ready money.

In choosing a job, for instance, people will give differing weights to less tangible features like long-run prospects, job satisfaction, location, vocation, social esteem, comfort, challenge, length of holidays or amount of overtime. No one is obliged to work for highest pay. Likewise as consumers, people will not always choose the cheapest buy, or spend all their income indulging their appetites. Most people have mixed motives. Even the prototype economic man, who sells his labour in the highest market and always shops for bargains, may be redeemed by sharing his surplus income among charity, poorer members of his family, and what the bishops would approve as other good causes.

The merit of the market is that it harnesses individual effort to maximise present and future social output, not by the narrow incentive of self-interest, but by the widest opportunity for everyone to pursue his own self-chosen purposes.

If bishops and other critics of the market economy don't like the goals pursued by fallen man, they should redouble their effort to elevate our conduct by preaching, teaching and personal example. It is no remedy to extend the coercive power of government, for the simple reason that we will not thereby transform the conduct of politicians or voters. Instead we simply transfer the same self-seeking human nature to the political process where it can be so much more corrupting as well as damaging to freedom and economic advance.

Thus the Bishop capped his 'Crisis for Capitalism' with what he called 'a challenge to Socialism to produce the same energy, imagination, profitability and efficiency in a public enterprise as an entrepreneur brings to his own business'. He looked for 'More efficiency not go-slow protection of jobs'. Tell that to Mr Scargill, Mr Buckton and the other Luddites in the so-called 'public service'. Mr Chairman, tell it to the marines.

Role of Government

It would take a much longer discourse to elaborate the necessary functions of government. Markets cannot supply collective goods and services, like national defence, the framework and enforcement of law to uphold the security of person and property: all have to be collectively provided and financed through taxation. Likewise, governments have to supplement private charity in guaranteeing a minimum income for people unable to maintain themselves in the market. Where consumers cannot learn to choose by trial and error – because products like guns, poisons or impure foods may seriously threaten health or life – there is scope for governments to guide or limit choice by labelling, setting standards, regulating sales or even by outright prohibition.

Economists, even more than modern bishops, are renowned for their disagreements. As their number has increased a wag has said that if all economists were stretched end to end they would still reach no definite conclusion. Nevertheless, I would venture to affirm that an overwhelming consensus of the profession has always been in favour of general reliance on the market, with government intervention reserved for quite specific purposes. The extent of this broad agreement rests not on political ends but on technical means. Thus economists of differing party allegiance are certainly not agreed about the ideal income distribution. But whilst some would pitch the poverty line higher and push progressive taxation further than others, most would agree that topping up low incomes is more efficient than universal provision of essential goods and services at subsidised or zero prices. The technical reason is that efficient consumption will generally be maximised by the interplay of competitive supply and free consumer choice.

Economists have also shared wide agreement that imperfections in the practical operation of the market call for correction by government action. The post-war legislation on monopolies and restrictive practices was accepted with the same approach to unanimity as were policies to dismantle tariffs and other impediments to free international trade. The analysis of external or third-party costs and benefits, associated with the name of Professor Pigou, was also almost universally accepted, at least in theory: though there have been increasing doubts about corrective

action as we have learned that government failure can be more distortionary and incorrigible than market failure.

If we ignore the minority of socialist economists who explicitly subordinate economic efficiency to a larger measure of equality, the most significant conflicts of professional opinion have not been micro-market analysis of policy, but on macro-monetary-fiscal policy where the Keynesians after the war came to dominate the field. The recent retreat of the Keynesian consensus has reflected the empirical evidence around the world that discretionary monetary expansion has inflated prices rather than raised real output and employment.

Indeed, the mishandling of employment policy by successive governments in Britain and elsewhere has directed attention to a new critical application of economic analysis to the conduct of politicians. Granted that governments have good reasons to overrule the market in specific cases, why should we believe they will act like philosopher-kings concerned only to advance the true welfare of society? Should we not ponder the timeless warning of Adam Smith against what he called:

> that insidious and crafty animal, vulgarly called a statesman or politician, whose counsels are directed by the momentary fluctuations of affairs?

The Results of the Vote Motive

After all, what is the prime motivation of politicians except to secure or maintain themselves in power? Thus in their quest for votes, even the less 'insidious and crafty' will constantly be tempted to buy popularity by offering subsidies, protection or other privileges to sizeable lobbies like pensioners, farmers, trade unions, council house tenants, owner-occupiers. In social security, education, medical care, there is obvious scope for each party to bid for electoral advantage by promising more generous benefits and so-called 'free' services. Since spending is more popular than taxing, the natural tendency is for governments to run out of money long before they run out of promises. When we reflect on the economic analysis of bureaucracy, which exposes a powerful interest group in favour of almost indiscriminate enlargement of

government, we see why the balance of the mixed economy has shifted remorselessly from the private to the so-called 'public' sector.

I will touch on only five of the evil consequences of this vote motive which has caused governments to expand their operation at the expense of the market. The first is that taxes are raised to the point where they simultaneously diminish and distort incentives in the use of human and capital resources. The second is that government expenditure runs ahead of revenue, leaving a deficit to be financed by burdensome borrowing and higher interest rates. The third is that the soft option of gaining government support diminishes the incentive for self-help by individuals, enterprises and communities, and has weakened the rich harvest of spontaneous voluntary action inherited from the nineteenth century. In this way the safety net for the poor has become a hammock for many who could and should be self-supporting.

The fourth consequence of the pressure on governments to spend is that short-term expediency takes precedence over prudent concern for investment in the future. We see the results, not only in the famous collapsing sewers of Manchester, but nearer at home, in the pressure on pharmaceutical companies to reduce their prices at the risk of sacrificing research and future development. Finally, over-taxation has inflated the underground economy and weakened respect for law in general.

If there were time I would have a shot at arguing that the appalling levels of unemployment in Britain and similar European economies are chiefly due to self-inflicted restrictions and rigidities which a mixture of political idealism and electoral calculation has imposed on our muddled mixed economies. If taxes were lower, labour and other markets freer, and protectionism less, the recovery of output and employment would certainly be more visible in Britain, as we see from progress in the United States.

Alas, as Mrs Thatcher has painfully discovered, diagnosis is easier than prescription. Milton Friedman put his finger on the difficulty of extricating ourselves from overblown government:

> The problem is that it's easier to avoid an activity than to eliminate one already undertaken. Everytime a government undertakes any activity, it tends to create a class of people with strong vested interests in that activity's continuance.

> There are always many apparently worthy proposals, so that if even a small fraction are accepted, government tends to grow and grow.

NHS in the Dock

Take the example of the National Health Service which should be near the top of the list for reform by any radical government. The most fundamental, long-run case against a 'free' health service is not only that it has suppressed the development of voluntary insurance and hospitals. Even worse, the NHS will prevent medical care from becoming one of the major growth services – along with education, holidays, travel, home comforts, leisure and hobbies – as standards of living continue to rise. So long as finance is confined to what chancellors can extract through the Budget, politicians are guilty of capping expansion and curbing individual freedom/responsibility by pushing taxes higher than people like and at the same time holding medical care below what they would choose for themselves and their families.

So far from the government's pledge of level funding keeping the warring pressure groups at bay, ministers will be engaged in a ceaseless, wasting battle of all against all to resist additional expenditure, whilst trying to relieve suffering and to improve therapies, especially by new, expensive treatments. Thus the moral indictment of the NHS is that politicians decide who shall suffer, even who shall die, by allocating resources without reference to what people would be prepared to pay directly for themselves and their family. Among several revealing quotes from Labour spokesmen, Douglas (Lord) Houghton said:

> What is in doubt is whether we in Britain will ever give medicine the priority given to it in some other countries . . . so long as it is financed almost wholly out of taxation.

In similar vein Richard Crossman acknowledged that:

> People are prepared to subscribe more in a contribution for their own personal or family security than they ever would be willing to pay in taxation devoted to a wider variety of different purposes.

Why 'Free' Services?

The central justification of providing medical care without charge was voiced succinctly by Aneurin Bevan at the Labour Party Conference in 1945:

> If we were rich enough we would not want to have free medical services: we could pay the doctors.

In other words, because some couldn't afford to pay in 1945, all must have 'free' services forty years later and forever more. Here is the basic flaw of a universal solution to a selective need which will continue to restrict the health care of an increasingly prosperous society. To finance the 'free' NHS and other welfare services for everyone, taxation has to be piled so high that most families are already paying their own way for welfare. Indeed, because of the costly inefficiency inseparable from provision by a public monopoly, most people are now paying through the nose!

It is anathema for any competent economist that government should supply scarce resources without charge, except in what are technically defined as 'public goods' (like defence and police services) where separable individual benefit and payment are not appropriate. The superficial notion that use of all health services should be determined not by price, but by 'social demand', leads to the attitude 'If it's free, I'll have more!'

In the absence of payment, there is no way supply can take account of priorities that are indicated in normal markets by individual choice and willingness to pay. In the absence of charging, suppliers have no incentive to maintain pressure against waste and rising costs. In the absence of competition, suppliers (doctors, administrators, porters, abulance men, etc.) can put their own convenience before the interest of patients. In the absence of 'rationing by the purse', scarce resources are rationed instead by administrative discretion, leading to hospital waiting lists and queues at the doctor's surgery.

So far from resulting in 'equal access', the NHS gives priority to those with the most political pull or social push.

No Hiding Place

And so we could go on – as may be seen from some forty papers from the Institute of Economic Affairs on the economic shortcomings of universal state welfare services. The unambiguous verdict on the NHS is that it provides most people with a poor return for the high cost they pay via taxation, with all the added damage that high taxes impose on our economic performance. Above all, the NHS is a moral dog-in-the manger: it cannot raise enough in taxes to supply better medical care, yet it discourages or prevents the citizen's urge to spend more out of rising incomes. At the same time, its defenders boast of moral superiority for a system which attaches more importance to the claim that services are 'free' than to the fact that services may not be available when they are wanted.

There will be no relief from the pressure on politicians to spend more, so long as the illusion of 'free' provision persists. Without prices there can be no equilibrium. Nor is there any lasting solution by better management, as urged by Sainsbury's Mr Griffiths. He should be asked whether Sainsbury's could maintain daily pressure for efficiency if they gave away their groceries free and billed the Chancellor?

My conclusion is that the crippling, multiple deformities of the NHS will not respond to pills or political placebos. On my market analysis they call for fundamental, radical surgery. The broad aim must be to guarantee the present minimum service for the declining minority who cannot afford to pay, whilst encouraging the majority to pay and insure privately from incomes that are no longer shrunk by taxation to provide indiscriminate state services.

The general lesson is that all avoidable departures from the market economy lead to such insoluble dilemmas that they should be reversed as soon as possible, and further departures avoided in the future. For welfare I would argue that the market is no less indispensable than elsewhere in the economy. Instead of saying, 'The NHS is safe with us,' let the government acknowledge: 'The NHS – no more than the National Coal Board – is not safe with politicians.'

INTERNATIONAL INVESTMENT IN INNOVATION

Michael Burstall and John Dunning

To a quite unusual extent the pharmaceutical industry organises its activities along transnational lines. This is not merely true of production and marketing but also of research and development. Most large drug companies have research centres of one kind or another in a number of countries, and, to an increasing extent, the products currently arriving on the market have been developed as part of a world rather than a purely national programme.

How has this process of decentralisation come about? What forms has it taken? What have been the motives behind it? What costs and benefits has it entailed for the companies and countries involved? In attempting to answer these questions, this paper draws upon information collected in the course of an inquiry into the role of multinational companies in the pharmaceutical industry which we carried out for the OECD (Burstall *et al.*, 1981) and another more recent study undertaken by one of us (Burstall and Senior, 1985).

The Scale of International Investment in Pharmaceutical R and D

It is common for a major drug firm to conduct research in several countries. Table 1 shows the location of the research centres of the world's top 30 companies. It can be seen that, apart from the Japanese firms, whose international operations are generally very limited, these enterprises normally decentralise at least part of their R and D activities. This is perhaps the more striking in that the local testing of new drugs is not included in this list.

Merely to enumerate these laboratories, however, can be misleading. Their capabilities may vary greatly. At one extreme, they may be free-standing research complexes able to carry out all the stages of product innovation. At the other, they may be limited to specialised functions or development work for local markets. Our enquiries suggest very strongly that a firm will

Table 1: Location of R and D Facilities of the Top 30 Pharmaceutical Companies in 1982

Company	Country								
	France	Germany	Italy	UK	Switzerland	Other Europe	USA	Japan	Other
Bayer	×	×	×	×		×	×	×	×
Merck and Co.	×			×		×	×	×	×
American Home Products							×		×
Hoechst	×	×		×			×	×	×
Ciba-Geigy	×		×	×	×		×	×	
Pfizer	×	×		×			×	×	
Lilly				×			×		
Hoffman Laroche	×			×	×		×	×	×
Sandoz					×		×		×
Bristol-Meyers							×	×	
Smithkline Beckmann				×		×	×	×	×
Abbott			×				×		
Takeda								×	
Warner-Lambert		×		×			×		
Boehringer-Ingelheim	×	×	×				×	×	
Upjohn	×						×	×	
Johnson and Johnson						×	×		
Glaxo			×	×			×		×
Squibb		×		×			×		
Rhone-Poulenc	×			×					
American Cyanamid			×	×			×		
Schering-Plough	×				×		×		×
ICI	×			×			×		
Wellcome				×			×		
Beecham				×					
Dow			×				×		
Schering, AG		×						×	
Fujisawa								×	
Sankyo								×	
Shionogi								×	

Note: Not necessarily complete.
Source: Authors' estimates.

normally conduct the most sensitive and demanding types of work in centres located in its country of origin. Only a few of the top 30 companies have laboratories of the highest capacity situated elsewhere.

To put a figure on the foreign research effort of these firms is

difficult. Some more or less informed guesses are presented in Table 2. As a group the Swiss companies spend the highest proportion of their research funds abroad; in the late 1970s this approached 40 per cent of the total, most of which went to their laboratories in the USA.

American member firms of the Pharmaceutical Manufacturers Associations spent about 20 per cent of their combined 1980 R and D budget outside the USA, with about three-quarters going to Western Europe and most of the rest to Japan.

Companies based in the European Community show a more varied pattern. Taken together, British firms are now probably spending 15-20 per cent of their research funds abroad, a substantial proportion being in their US subsidiaries. The same is true of their German rivals. French and, still more, Italian companies, however, have a much less international approach to research, as do those of the smaller European countries. Japanese firms do almost all their research at home.

The position of the host nations also merits attention. In most countries – Switzerland is the most important exception – a significant part of pharmaceutical research spending originates with the local affiliates of foreign multinational companies. In Italy the proportion is more than 40 per cent, and in France and the UK about 30 per cent. Elsewhere it is lower but still appreciable: 20 per cent in Japan and the USA, and 10-15 per cent in Germany and the Netherlands. The balance between inward and outward investment is discussed later in the paper.

The extent to which R & D has been internationalised has increased during the past decade. The proportion of the research budget spent abroad by major American drug firms almost tripled between 1970 and 1980. Although there are no quantitative data for their European counterparts, there is little doubt that they too have done likewise. Research has followed the same path as production and marketing, though not to the same extent and at a later point in time.

Motives for International Investment in Research

A company may have foreign research facilities for a variety of reasons. Sometimes it took over laboratories when it bought a firm for other reasons. In certain cases the driving force was

Table 2: Estimated R and D Expenditure by Pharmaceutical Companies in Various Countries in 1982 ($ millions)

Country of Expenditure	Nationality of Company									
	Belgium	France	Germany	Italy	Nether-lands	UK	Switzer-land	USA	Japan	Total
Belgium	30	10						30		70
France		400	50			20	20	80		600
Germany	15		700					50		800
Italy		10	20	120		20	30	50		230
Netherlands					80			10		90
UK		20	20		10	400	20	120		600
Switzerland			10				450			475
USA		10	100		10	50	250	2,000		2,500
Japan			20				30	100	700	850
Total	45	450	950	120	100	500	800	2,500	700	6,300

Note: Because of problems of allocation, columns and rows do not total. In addition, these estimates are based on data from a variety of sources and involve a considerable element of guesswork.
Source: Authors' estimates.

circumstances that no longer exist: thus, the Swiss majors began their involvement with the USA as a hedge against a possible world war. Most frequently, the laboratories were set up *de novo*. In general, however, the decision to move abroad or to expand an existing laboratory was strongly influenced by certain common factors, some of which were internal to the firm and some of which resulted from action by the governments of host nations.

The most powerful of the former is the desire to exploit the scientific resources of another country – 'to tap into another scientific culture', as one Research Director has put it. In operational terms this means forming close relationships with local universities and other public research centres and using the special skills and insights of local scientists. This cannot be done at a distance or at second hand. It is best achieved by creating a local research centre of genuine innovative capacity, which can interact fruitfully with the national scientific community. Clearly this is an expensive course of action, and only a few countries justify the effort.

Commercial reasons often play a part in the decision to begin R and D abroad. A large national market may require particular products in particular forms. Generally it is best to develop them on the spot and in close association with the local production and sales personnel. There is an obvious analogy here with Vernon's idea of the product cycle. In addition, it is sometimes said that, other things being equal, doctors are more willing to prescribe drugs which have some local content. Such requirements can, however, be met by relatively simple facilities and represent a much lower level of commitment and expenditure on the part of the parent company than does a major centre. They are, of course, much more common.

Pressures from host governments are also important. Many national administrations are anxious to build up the national capacity for pharmaceutical innovation, in effect, as a form of import substitution. They use a variety of instruments for this purpose. In the UK, for example, the permitted rate of return on capital for drug companies depends, *inter alia*, on their research effort in the UK. Similarly, in France the prices allowed to firms depend on their activities there, and, once again, spending on R and D is taken into consideration. Measures of this kind are common in both the developed and the developing worlds, and

cannot but have an effect on policies of location.

Other forms of government action are less important. Controls over the introduction of new drugs vary considerably in severity from country to country. At the present time, however, a product has to sell world-wide to recover its development costs, and the incentive to shift research to permissive nations is reduced. Nevertheless, American companies have in recent years often chosen to introduce their latest drugs in Europe rather than in the more restrictive USA, and this has undoubtedly influenced their levels of spending abroad.

Although appreciable in their effects, tax concessions and subsidies do not seem to have played much part in decisions to move research to other countries.*

The Choice of Host Country

Companies do not, of course, consider the possibility of starting research abroad in the abstract: they usually have a host country or countries in mind. The choice between alternatives is necessarily complex. But it seems likely that local strength in science, a large local drug market and pressure from host governments would predispose a multinational company to favour particular countries. At the same time, the history of the company, its current strengths and weaknesses and, indeed, opportunitites of the moment also come into play. It is therefore interesting to see how thirty years of multinational activity in the field of research have worked out for the principal host countries.

Focusing first on the UK, Table 3 shows the presence of a very strong scientific community. The pricing system is generous as pricing systems go, and actively encourages foreign companies to expand their local activities. Controls over new drugs are strict but applied in a relatively flexible way. The national drug market is of moderate size. Britain is a favourite site for foreign multinational companies to conduct research, and several have built up centres of considerable size and innovative capacity. US

* For a recent study of the UK situation, see M. Brech and M. Sharp, 'The Pharmaceutical Industry' in *Policy towards Inward Investment* (Chatham House, London, 1984).

firms are particularly prominent, but German, Swiss and French companies are also active. The interviews we conducted during the course of our studies suggested that the quality of British science has been the main reason for this development.

France, on the other hand, seems, in certain respects, less well placed. French science does not command the same respect as that of the UK, French drug prices are low, and relations between government and industry are frigid. At the same time, the French pharmaceutical market is a large one and successive administrations have put considerable pressure on the multinational companies to maximise their local operations. As a result, investment in R and D by foreign firms is considerable. However, the bulk of these research centres are used for local product development or for specialised kinds of research, and few if any have a serious capacity for innovation.

Germany has attracted less inward investment than might have been expected. German science has an excellent reputation, the internal market is a large one, and the regulatory regime unusually benign. It is, however, an expensive place to do research, and the markedly non-interventionist attitude of the German government may have had an effect. The same is true of Switzerland, where the demand for drugs is in any case low. The foreign research centres in Belgium and Italy are largely due to the acquisition of innovative local firms by companies from elsewhere.

The USA is particularly well placed to attract foreign investment in research. It not only dominates the world of science, but also forms the largest national market in the world. Controls over the introduction of new drugs are extremely strict, but prices are uncontrolled. Apart from safety considerations, American governments leave the industry to its own devices. Many foreign companies have research establishments in the USA, several of them being of the greatest importance. The Swiss multinationals predominate, but more recently German and British firms have expanded their local activities.

Japan is a large, rapidly growing and more or less isolated drug market. Research carried out in Japan by companies from abroad has expanded considerably during the past decade. In part this has resulted from increased general investment in the Japanese pharmaceutical sector, but there is also considerable interest in Japanese expertise in such fields as anti-cancer drugs

Table 3: Host Country Characteristics, 1982

Country	Strength of Scientific Community	Commercial Characteristics: Size of Local Market	Commercial Characteristics: Price Level	Regulatory Regime: Controls over New Drugs	Regulatory Regime: Encouragement to Maximise Local Activities
Belgium	Medium	Small	Low	Moderate	Yes
France	Medium	Large	Low	Moderate	Yes
Germany	High	Large	High	Moderate	No
Italy	Medium	Medium	Low	Moderate to easy	?
Netherlands	Medium	Small	High	Moderate to severe	No
UK	High	Medium	Medium	Moderate to severe	Yes
USA	High	Very large	High	Severe	No
Japan	Medium	Very large	High	Severe	No
Third World Country	Low	Small	Variable	Easy	Often

Source: Authors' estimates.

and biotechnology.

It is also instructive to glance at countries which are unattractive as locations for research. Most Third World countries are in this position. They are generally weak in science – India is a partial exception – and often provide a hostile political climate. Their only interest is as sources of exotic compounds of animal or vegetable origin. Few foreign companies are keen to place research centres in these nations, and, where they have done so, it is often as a result of political pressure (Burstall, 1979).

The foregoing review suggests a number of general conclusions. First, from the standpoint of the multinational company, there is no single reason which explains why one country is chosen rather than another. A research centre in nation A may be there because local science is strong, one in nation B because of arm-twisting by the local government, and another in nation C because the multinational took over a local firm in order to penetrate the national market.

Second, it seems that different motives lead to different results. If the desire to exploit scientific resources is an important consideration, then laboratories with a capacity for innovative work may well emerge. If, however, political pressures or purely commercial motives are uppermost, then local R and D may be limited in scope. It is quite possible for the same volume of inward investment in research to produce widely divergent outcomes.

Gains and Losses

What have been the rewards and penalities of the internationalisation of pharmaceutical research? The estimates of the industry must necessarily differ from those of governments. In turn, a government's views will vary according to whether it is the donor or the recipient.

Taking first the industry's perspective, it is possible that a company might both gain and lose by spreading its R and D over several countries (Table 4). It could gain in terms of the efficiency with which it develops or modifies its products. It could lose by failing to realise economies of scale as fully as would otherwise be the case.

Table 4: Gain and Losses from the Internationalisation of R and D

Protagonist	Gains	Losses
Multinational company	Greater efficiency in product innovation and/or development. Improved access to local markets.	Reduced economies of scale.
Host nation	Improved employment. Access to high-tech knowledge and skills. Strengthen linked sectors.	Damage to indigenous companies. Dilution of control over local innovative capacity.
Donor nation	May strengthen overall position of indigenous companies.	Possible loss of employment. Reduction in local innovative capacity.

There is evidence of both positive and negative effects, but, on the whole, it seems probable that the former predominate. As far as innovative research is concerned, there are diseconomies as well as economies of scale, and for many companies the point of diminishing returns has already been reached in their original centre. When a new establishment is to be set up, there are good reasons, which have already been discussed, for placing it in a different culture. Those who have done so seem to be pleased with the outcome. Equally, product development for substantial markets requires some local input and therefore some local facilities.

The losses to a company come if and when it is obliged to expand its local R and D beyond the level that it considers to be appropriate. This may have happened on occasion – the definition of 'appropriate' is necessarily flexible – but that it has been a critical factor may be doubted. As yet the additional investment required by a local research centre has usually been fairly modest. In effect it is a condition of operating in an otherwise worth while market, and it is a price that companies seem willing to pay. Remarkably few of them have chosen to withdraw from a country when this particular pistol has been held at their heads.

A host nation faces a different set of advantages and disadvantages. By attracting foreign investment in research it gains in terms of employment and access to foreign know-how and specialised skills. The demands of the incomers may

stimulate the growth of related parts of the economy. Backward linkages to the universities and to the suppliers of specialised goods and services are especially important.

On the debit side, the position of indigenous companies may be adversely affected through increased competition for limited human resources. Local control over the national capacity for pharmaceutical innovation is diluted. This is particularly the case when an innovative local company is acquired by foreign interests, as has happened in Belgium and Italy. Even with goodwill on both sides, the interests of the company and the host nation may be in conflict.

Once again the balance appears to lie on the positive side. There is little evidence that the presence of foreign-owned research centres has weakened local industries. The British experience suggests that shortages of skilled personnel or specialised services have not been a limiting factor for either indigenous or foreign companies. Indeed, it is highly probable that demand has stimulated supply.

The issue of national control is more contentious. A substantial proportion of the innovative capacity of several European countries is in foreign hands. This is a legitimate cause for anxiety. It is, however, fair to say that this has not happened in the nations whose record of innovation is genuinely outstanding. Rather, they have attracted foreign investment while their own firms have continued to flourish and expand.

The reason for this state of affairs is simple. The major drug companies developed in nations where the social, economic and cultural infrastructure is favourable. A foreign multinational will look for the same underlying factors in selecting a host country. It is strength that attracts, not weakness.

If there are definite gains from being a recipient of inward research investment, the position of the countries whose firms provide the investment is less clear.

At first sight it might appear that they must lose. Work which is done abroad is not done at home. Employment suffers, and the national capacity for innovation is reduced. Much anxiety has been expressed about these possibilities, especially in the USA. A closer examination suggests, however, that there are advantages as well as disadvantages for the donor nation.

A country gains by having strong drug companies rather than weak ones. Under modern conditions they must operate on a

multinational basis. They will, however, place most of their really vital activities in their country of origin. These activities will grow in importance with the firms. Up to a point, therefore, a company will gain by expanding its foreign operations.

Do such arguments apply to R and D? Within limits, the answer is yes. Much development work has to be done near the market. If done at home it would be less effective and the company would suffer. The situation with regard to innovative research is less certain. Even here, however, a laboratory may well gain by exposure to different ideas and techniques.

Once again there is a parallel with the Vernon theory of the product cycle. Just as the manufacture of novel goods initially takes place at home, and is only later shifted abroad to exploit local advantages in production, so with R and D. Innovation is concentrated in the country of origin, while the work of adaptation to local markets takes place elsewhere. In both cases the object is to maximise the profits generated by the innovation.

A nation would unquestionably lose capacity if a major firm were to move all its research abroad. It is highly probable that it benefits when selected parts are transferred to other countries.

A Balance Sheet

Most of the great powers of the pharmaceutical world are both donors and recipients of research investment, and we should like to conclude by striking a trial balance, to show, in however tentative a way, who has won and who has lost, in this lengthy and complex process of exchange.

The UK and France have undoubtedly gained, although in different ways. In both countries the volume of research spending is higher than would otherwise have been the case. The UK has come off best, in that it has attracted considerable investment in basic and innovative work. That carried out in France is generally of a more downstream nature.

The United States has broken even. The development of foreign research facilities by American firms has been largely balanced by European investment in the USA. This appears to be true both in quantitative and in qualitative terms.

Switzerland has been a net loser in that Swiss companies have invested heavily abroad, especially in the USA, while few foreign

firms have done so in Switzerland. It seems probable, however, that the Swiss majors have been strengthened by their international research strategies.

Most other countries show small positive or negative balances. Relative to their size, Belgium and Italy show large positive balances, but this is due to the special factors discussed earlier.

This pattern is what might have been expected. A donor nation is one with large indigenous companies. It has such companies for the same reasons that make it attractive to foreign firms. Inward and outward flows of research funds are therefore linked.

Could this situation change? This seems improbable. For the past twenty years stability has been the central characteristic of the industry. There has been change, but of degree rather than kind. The factors that make a country a major donor or acceptor are of a fundamental nature and unlikely to change in the short run. We expect the process of internationalisation to continue, but along established lines and at a measured pace.

Should government worry? Perhaps not. Most countries break even in the trend to the internationalisation of R and D. Even where there are losses they may be made up by indirect benefits. The pharmaceutical industry operates on a world-wide basis and any calculus of national welfare must begin from this point.

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PHARMACEUTICAL PRICING AND PROFITS

Duncan Reekie

'Sunrise' is a word we have frequently heard in the last two days. It is a neat term and contrasts attractively with its alleged antonym: 'smokestack'. The 'smokestack' traditional industries are in decline, future economic well-being consequently depends on the new, growing, technology-intensive, 'sunrise' industries. There is much truth in this model but we are all too well aware that it is overly simplistic. The adjectives 'smokestack' and 'sunrise' themselves encourage a facile interpretation of the situation. I shall therefore discontinue using the adjective 'sunrise' and replace it in my analysis with another piece of possibly more appropriate jargon: 'quicksilver'.

A company in a 'quicksilver' industry has two unique characteristics. First, demand for its products can vanish overnight. Second, its cost structure is such that certain fixed costs form a very low proportion of total costs. Thus should a firm deem it appropriate it can rapidly, and at low cost, cease to supply a given geographic market by closure of its production facilities.

Supply and demand, of course, are never wholly independent. Alfred Marshall likened them to two blades of one pair of scissors. One never knows which blade is doing the cutting. But for the purposes of exposition I would like to look at each in turn. First, what lies behind the transience of pharmaceutical demand? Second, what is the reason for the transience of pharmaceutical supply? Finally, how are the two interconnected and what are the implications?

In a quicksilver industry transience of demand is not due to fashion or consumer whim. Rather it is the result of technological advance. Thus in pharmaceuticals we have the now well-known concept of innovative competition and the more recent phenomenon of generic rivalry.

The vigorous nature of innovative competition in the pharmaceutical market is indicated by the way that products and

companies displace each other rapidly. Only two of the leading ten products on the British pharmaceutical market in 1980 were placed in the top ten in 1965 (Table 1). Of the leading ten firms in 1965, only four remained in that group in 1980. The company placed third in 1965 had fallen to thirty-seventh place by 1980.

Table 1: Competition in the British Pharmaceutical Market

(A) Position of 1980 leading ten products in 1965
(B) Position of 1965's leading ten companies in 1980

(A) Products		(B) Companies	
1965	1980	1965	1980
—	1	1	2
—	2	2	13
—	3	3	37
10	4	4	12
—	5	5	11
—	6	6	7
4	7	7	24
—	8	8	15
—	9	9	6
—	10	10	4

Note: Ranking by sales value.
Source: British Pharmaceutical Index (Intercontinental Medical Statistics).

As new and improved products appear from the industry's R and D laboratories prescribers switch their demand patterns from less effective to more effective or safer medicines. The frequency with which innovation occurs results in firms being exposed to demand of a quicksilver nature, where product switching by consumers takes place more often and more universally than in more traditional markets.

This aspect of quicksilver demand is now well understood by many if not all students of the drug industry. In Britain it was first highlighted nearly twenty years ago by the pioneering work of Cooper (1966).

More recently, however, a second cause of dramatically shifting demand has become prominent. This is the phenomenon of generic competition. Generic competition in any industry is simply rivalry (using some mix of the marketing tools of price and promotion) for the consumer's purchase decision: the rivalry itself is between products with common structural characteristics which distinguish them from all other commodities or groupings.

Thus any two morning newspapers, any two 3-litre cars and any two ampicillins are rivals generically. Whether they are rivals economically is a moot point. Only the consumer can decide whether *The Times* is a satisfactory substitute for the *Sun* or a 3000 c.c. Datsun an acceptable alternative to a Mercedes; or a paediatric orange-flavoured Penbritin syrup can be displaced, with no protest from a sick child, by a 250 mg. dry ampicillin tablet broken in two by a parent and followed by a sugar lump.

No third party can tell in advance which newspaper, which motor car or which drug will best satisfy individual consumer requirements. After the event, however, a study of consumer behaviour can show that some consumers do prefer the *Sun*, not *The Times*, some do prefer Mercedes, not Datsun, and some doctors do prefer to prescribe or not to prescribe Penbritin syrup as against ampicillin tablets.

Generic rivalry as a cause of falling or disappearing company demand has, as noted above, only recently become prominent. The reason is that in a high-technology industry innovations are generally protected from such competition by the patent system. In the past, when patents expired products had already been superseded by superior innovations and so the scope for and hence potential damage from an imitation product was very limited. In recent years this has become less true.

The number of new products introduced by this industry, while still high, has fallen dramatically since the 1960s. Two main reasons are advanced for this. One is that there has been a depletion of research opportunities. Drug R and D is faced with diminishing returns since most of the 'easy' discoveries have now been made. Remaining unconquered disease areas pose relatively more difficult technological problems. Second, R and D costs, in both physical resources and in time, have increased due to increased regulation and stringent requirements for product registration. Which is the more important reason for a decline in innovation is open to debate. What is indisputable, however, is that there have been fewer innovations and an increased R and D time span.

The latter, given the nature of patenting systems, has resulted in shorter periods of unexpired patent protection being available to new products. (The recent increase in UK patent lives from 16 to 20 years has mitigated this effect but is not sufficient to have removed it.) The consequence is that pharmaceutical product life

cycles have typically become longer while patent protection disappears sooner. Thus innovative rivalry (the principal type of competition in the 1950s and 1960s) has been joined by generic competition in the 1970s and 1980s as a reason for the existence of quicksilver demand. This point is illustrated in Table 2, which shows that 40 per cent of the top 10 products, and over one-third of the top 50 had no patent protection in 1982. All of the relevant leading 10 products were subject to generic competition, as were most of the relevant leading 50.

Table 2: Leading Products in the UK Drug Industry, 1982

Products	Number of Products where Patent Protection has expired	Number of Products Subject to Generic Competition
Top 10	4	4
Top 30	11	10
Top 50	17	14
Top 131	38	23

Source: Reekie and Allen, 1985.

How do these phenomena of a slowing down in innovative competition, declines in effective patent lives and a rise in generic availability affect demand? Is the quicksilver element of transience abated in any way? The answer would appear to be no. Data on generic competition by definition are not available for the three decades for which we can construct tables such as Table 1. The serious nature of the phenomenon is only a few years old: since, say, the early to mid-1970s. This is a sufficient span, however, to enable us to examine a little of the past and project that past into the future.

One historic examination (Reekie and Allen, 1985) looked at the experience of the industry's leading firms between 1978 and 1982. The sample firms held approximately 90 per cent of all NHS sales in both years. However, those firms whose product range was not subject to generic competition were commercially successful while firms with products which were so subject performed negatively. Table 3 illustrates this in terms of market share changes between 1978 and 1982.

This study was repeated using products not firms and, using Markov chain analysis, the results were projected forward to

Table 3: Effects of Generic Competition on Market Share, 1978-82

	Firms Experiencing a Market Share:	
	Increase	Decrease
Firms subject to generic competition	4	9
Firms not subject to generic competition	18	5

Source: Reekie and Allen, 1985.

1986. This yields a statistical impression of what the economic consequences of generic competition would be over a nine-year period. Table 4 summarises the results of the exercise. For every 2.9 products which were 'successful' in 1978, only 1 of the 2.9 had managed to remain 'successful' by 1986 in the face of generic competition. The consequence of this was the 'less successful' products with generic competitors almost doubled in number in the same period (hence the ratio 0.54). Previously successful products lost market share and moved from the numerator of the bottom left-hand cell. Not unsurprisingly, products without generic competitors suffered much less extreme market share category changes and did so in the reverse direction.

Table 4: Actual Market Share Achievements (1978) and Projected Share Achievements (1986) of Products Subject to and Not Subject to Generic Competition

Market share of Therapeutic Class	Ratio of Number of Products in Class in 1978 to Number in 1986	
	With Generics	Without Generics
0-30% (Less successful products)	0.54	1.2
30-100% (Successful products)	2.9	0.76

Source: Reekie and Allen, 1985.

To summarise, pharmaceuticals is a quicksilver industry subject to ephemeral demand patterns due to rapid innovation and, more recently, to less rapid but still high, levels of innovation coupled with frequent and successful imitation from generic products.

Turning to the question of supply, my definition of a

quicksilver industry was one where not only could demand disappear in a short period but so too could supply. Multinational industries in general are frequently alleged to be footloose. One hears of electronics firms which close assembly plants in the UK to move to Singapore where labour is cheaper per unit of output. Such a tale is expanded a year or so later when it is heard that the firm has moved on to Taiwan and subsequently to the Philippines.

Pharmaceuticals, of course, is a multinational industry *par excellence* and it too can, in principle, choose to relocate facilities where certain key inputs are available more cheaply. The NEDO Report (1972) argued that the UK attracted pharmaceutical R and D from the US because of the lower cost per scientist compared to North America. However, a slow drift from one country to another is hardly supply transience.

The drug industry does, in principle, have the general multinational ability to relocate. Relocation could be a costly activity, however, if it involved closure and re-establishment elsewhere of R and D facilities. The human capital of a team of scientists would almost certainly be lost as such a group of specific individuals would not be prepared to switch their country of domicile in one block. However, where individual firms are mostly concerned with the low-variable-cost activities of processing fine chemicals, manufacturing the chemicals into dosage forms, and packaging and distribution, this is not so. Such firms (or the industry as a whole in countries with little R and D) are vulnerable to closure or contraction. Drugs are high-value, low-volume products. They can be cheaply exported from countries where the R and D input is made. Transport costs are trivial. Given the small fraction of total costs accounted for by manufacturing, firms may feel that closure of manufacturing plants can save them the large absolute sums of maintaining such facilities but will only impose the relatively small costs of increasing production runs in plants elsewhere. Nor is this discussion hypothetical. One company alone has closed its research operations in Australia and its manufacutring plant in Canada.

So supply and demand transience do exist. Pharmaceuticals is a quicksilver industry. What, if any, policy implications can or should be drawn from my analysis?

National governments are inextricably involved with pharma-

ceuticals as a consequence of various state medical reimbursement schemes on the one hand, and regulation of product development and marketing on the other. Simultaneously, most governments wish to maintain a commercially successful indigenous drug industry. How is this to be done while avoiding both unsafe products and excessive medical care costs? Are there lessons to be learnt from the industry's quicksilver nature?

Outsiders do not always appreciate the nature of the industry's pricing policies; nor the short-lived nature of product success and the high dependence firms have on a minimum number of products. There is now a significant amount of evidence to suggest that prices in the drug industry are to a greater or lesser degree determined by market forces (Reekie, 1977, 1978; Dao, 1984). This is not to say that they are the same as they would be if the hypothetical perfect textbook market of the theoretical economist existed. Few, if any, industries have prices determined that way. None the less, the notion of the industry acting in a monopolistic manner to exploit a market in an unfair way has now disappeared in most countries. Interestingly, it is possibly no coincidence that in those countries where this is least appreciated, disinvestment has occurred or is threatened, whilst in other countries where those lessons have been learnt the industry is strong and expanding.

Take, for example, the illustrations of Australia and South Africa on the one hand with that of the UK on the other. Look first at Australia and compare drug prices there with those ruling elsewhere. One recent international comparison of drug prices in Australia, the USA, Western Europe and the UK provided the results shown in Table 5. All products available in common in each of these countries were included in the study. American prices were twice as great as Australian, and European prices nearly half as high again as Australia on a per pack basis. The second column adjusts for the comparatively lower GDP per capita which (on average) holds in Western Europe and the UK. When this is done, prices by nation are remarkably similar except in Australia, where they are substantially lower.

The reason for the results shown in Table 5 is the official Australian Pharmaceutical Benefit Scheme (PBS) and the strictness of its operation. The monopsony power of the Commonwealth Department of Health through the PBS has resulted in prices (and presumably profits) being among the

Table 5: International Comparison of Drug Prices, 1982

	Prices in US Dollars (per standardised pack)	Prices in US Dollars (deflated by GDP per capita)
Australia	100	100
USA	210	171
Western Europe	141	173
UK	138	182

Source: Reekie, 1984.

lowest in global terms. In Australian manufacturing industry in general, profits in 1979, as a percentage of funds employed, were around 15 per cent while the Australian Pharmaceutical Manufacturers' Association estimated that the equivalent drug industry figure was around 2 per cent. In the UK the figures are comparable for manufacturing industry but drug industry returns are closer to 18 or 19 per cent (Reekie, 1980).

Multinational firms operating in Australia protest that Australian consumers are 'free-riding' by not paying their full or proportionate share of initial, high fixed research and development costs. The data presented above do not contradict this view. 'Free-riding', if it is occurring, does of course represent rational short-term behaviour by the Department of Health. What might the longer-term implications be for the Australian industry? Consistent with the underlying rationale of quicksilver or transient supply is the fact that in Australia, at least two firms have closed down their R and D operations and another firm (Merck), which closed its active substance manufacturing plant a year or so ago, has now been joined by Ciba-Geigy, which ceased manufacturing in late 1984.

In Australia the addition of a strong monopsony element to the already existing rigours of quicksilver demand has been sufficient to trigger off disinvestment.

In South Africa the reimbursement situation is a litle different. The industry receives 66 per cent of its revenue receipts from the private sector where patients either pay privately or are reimbursed through privately operating and funded medical aid schemes. Only 33 per cent of industry receipts arise from the state sector for community health care, the army or government sector medical aid plans. This picture would appear to provide

the industry with protection from government monopsony power and resulting market distortions. That it does not is clear if we look at volume rather than value share. By volume the government sector buys 85 per cent of the industry's output (paying 33 per cent of industry receipts) at prices possibly lower than those under the Australian PBS (*Financial Mail*, 1984b).

In addition to this exercise of monopsony power the South African government is now considering the introduction of a system of generic substitution whereby the pharmacist could overrule the doctor's prescription and substitute a cheaper generic drug. Companies such as Roche have been reported as closing down operation in Australia and Canada 'in nearly similar circumstances'. While others such as Janssen of Belgium are quoted as saying that 'the industry will have to have a closer look at South Africa as a viable market. Disinvestment is the last resort but we all know what happened in Canada' (*Financial Mail*, 1984a). In Canada two factors discouraged industry investment in innovation. One is the minimal patent protection granted to new products. Compulsory licences can and are obtained readily and the royalties paid are but little above short-run marginal cost. Second, most provincial health authorities will only reimburse pharmacists at the price of generics, hence compelling innovating firms to price at not dissimilar levels. In addition to the Roche closure, American Home Products (Ayerst) completely shut down its large manufacturing and R and D activities in Canada. Other firms have contracted.

Turning to Europe, the hostile attitude of the Greek government towards the industry has allegedly resulted in Merck, Smith Kline, US Schering and Boehringer Mannheim all closing their direct marketing operations and leaving promotion to third parties. At the least, doctors now learn less about available products and patients are affected accordingly.

However, it must be pointed out that in each of the documented cases of closure and contraction there are reasons other than price pressures or specific anti-drug-industry regulations. For example, it is claimed that the Roche Australian R and D using the Great Barrier Reef as a source of chemical entities proved fruitless. It is suggested that the French language issue in Quebec, which compelled some insurance firms to move their head offices to Ontario, was the underlying reason behind some drug company investments moving out of the Province

towards the USA. These are all plausible explanations. None the less, the question still remains, why have drug firms not closed or contracted operations on this scale in those countries where the regulatory environment has been more favourable?

In the UK there is a much greater understanding of the problems of a sunrise or quicksilver industry. To take but two examples of this, one distant and one very recent. In the area of antitrust or monopoly legislation there is the well-documented turn-round by a Labour government in the 1970s over the price levels of Librium and Valium (Reekie and Weber, 1979). The manufacturer was originally ordered to pay the UK government £12 million for overcharging and to reduce prices on the products by 60-75 per cent. The bulk of the £12 million was ultimately reimbursed by government and product prices were allowed to rise above their original levels. This was due to a belated realisation that in an innovative industry prices will inevitably be above, perhaps by apparently ludicrous multiples, the level of short-run marginal costs; and that 'fair' prices in such industries cannot be determined by simplistic price : cost comparisons.

More recently the UK government has shown appreciation of the fact that quicksilver demand already exists in the drug industry through innovative and generic competition. This was clearly shown by the rejection of the Greenfield Report's (1982) recommendations on generic substitution. If implemented, this would have resulted in the filling of all prescriptions by pharmacists with the cheapest approved generic equivalent of any given drug. (In practice doctors could, but probably would not, have exercised a right to overrule the pharmacist.)

Tables 3 and 4 have already shown that firms and products subject to generic competition are more vulnerable to market share losses than those not subject to such rivalry. The question is thus begged as to how serious a threat such competition is to a firm's commercial health. In other words, given the presence of Schumpeterian competition by innovation, is there or is there not a danger that the 'Perennial Gale of Creative Destruction' will blow too strongly if generic competition is mandatory rather than merely permitted? Table 6 provides a framework for answering this question. Firms in the industry are heavily dependent for their very existence on their leading few products. Company 1, the market leader, is less dependent than most. But even it receives over half its revenue from only three products. And it is

just such products which are most exposed to both generic and innovative competition (Tables 1 and 2).

Table 6: Product Concentration Ratios, 1982

Firms	Main 3 Products as per cent of Firm Sales	Firms	Main Product as per cent of Firm Sales
1	51.9	36	61.2
2	67.8	37	87.1
3	63.6	38	33.1
4	51.6	39	38.8
5	48.9	40	51.9
6	78.0	41	80.1
7	40.3	42	73.2
8	84.9 (top 2)	43	51.8
9	39.1	44	80.0
10	39.9	45	84.4
Total firm sales as per cent of NHS sales		46.8	4.2

Source: Reekie and Allen, 1985.

This paper has shown that the pharmaceutical industry is subject to quicksilver demand and has responded by displaying quicksilver supply characteristics in Greece, Australia and Canada, and could do so in South Africa. In recent years R and D resources have been gradually moving out of the USA (Lasagna and Wardell, 1975; Virts and Weston, 1980). To the extent that Canada and Australia have highly regarded, culturally similar (and English speaking) medical establishments, one would have thought these countrires would have been desirable locations for US companies. But, according to the OECD (1981) it is rather 'the United Kingdom, the Scandinavian countries and South Africa [which] are the chosen locations of choice' for this reallocation of international effort. Whether South Africa will remain attractive is a moot point. The UK, however, appears to have at least partially understood the implications of providing the appropriate environment for a quicksilver industry. The two examples which were cited in support of this assertion were of a negative nature, however; they involved removal of attack or threat of attack by legislation rather than positive encouragement. That experience suggests that a conference of this nature has a vital role to play in the continued education which is necessary if we are to gain the benefits of quicksilver demand and not suffer the costs of quicksilver supply.

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FACTORS IN PHARMACEUTICAL INVESTMENT

Clarke Wescoe

The subject to which I was asked to address myself reveals immediately and forthrightly the character of the pharmaceutical industry. Investment is the commitment of resources for the purpose of earning a financial return or in the expectation of gaining future benefits. It is a peculiarly capitalistic term, particularly a well-accepted and meaningful term in the free-enterprise system to which I am committed. The international pharmaceutical industry is unabashedly and unashamedly a 'for profit' endeavour.

Profit is not a dirty word, although there are some who insist upon giving it an obscene classification. Especially is that true of pharmaceutical profits, which are looked upon as taking advantage of the sick. The profits of brewers, of tobacco companies, of car manufacturers are not looked upon in that same way. It is a truism that every person is inclined to resent the funds paid out for necessary medicines, for that results in a decrease in discretionary spending. Because they generate profits, the transnational pharmaceutical companies experience increasingly virulent attacks from a variety of sources: governments who have taken upon themselves the cost of health care; critics who believe that these profits are denying, to some, access to needed medication.

Without profit, this sunrise industry cannot long survive. Upon its profits depend the prosecution of research, the building and equipping of new facilities, the employment of substantial numbers of workers of all degrees – from unskilled to the most highly skilled. In fact, its profits help to support, by way of the substantial taxes levied upon them, the very governments which seek, it seems, more and more to diminish them. Upon its profits after taxes – returned in part to its shareholders in the form of dividends (taxed once again) – depend the pensions of a great many individuals in the private and public sectors and the return on carefully accumulated 'savings' of a great many others.

Beyond all that, the dividends flowing from those profits help to support the programmes of some of the industry's most vociferous critics who are shareholders in one or more of the corporations that make up the industry.

The transnational pharmaceutical industry is not monolithic. It is, rather, perhaps the most highly competitive of all industries. It is, above all, research-intensive. In the United States today there is great concern that innovative research may be falling off, that the scientific and technical innovations that made the nation grow and prosper may decline to a point where continuing growth and prosperity may come to a shuddering halt. That should be a concern for all governments. The record would show that research and development brought prosperity to those countries which encouraged and fostered it. Extractive natural resources are finite in quantity. The natural resource that is infinite is the educated mind – and the educated mind set to innovation and the unravelling of mysteries that still confound us is the undeniable key to a more prosperous and meaningful future. The pharmaceutical industry believes that the future belongs to those who create and innovate. Further, it believes that creation and innovation will lead to better and more effective medicines and to attack on disease entities that thus far have defied us. The industry does not believe that we have made the ultimate discoveries, that our present armamentarium of medicines contains all that it ever shall. In that we believe with the American essayist, Emerson, who wrote: 'it's a mischievous notion that the world was finished a long time ago'. Generations of entrepreneurs have proved that notion wrong and so, also, have the laboratories of the pharmaceutical industry.

Research expenditures of the transnational pharmaceutical companies continue to grow. In fact, research spending in the pharmaceutical industry is increasing at a rate faster than that of the growth in sales. Research becomes ever more costly, both in terms of the sophisticated instrumentation required to carry it out and in terms of the human resources necessary for its successful conclusion. Increasingly more tests are required to prove safety – a misnomer in terms of medicine, for, by their very nature, medicines cannot be safe for everyone – and efficacy – a relative misnomer too, for not every medicine is efficacious to the same extent for every patient.

Despite its vagaries and the unpredictability of outcomes,

pharmaceutical research continues. It is a unique type of research, probably the only research effort in which the ultimate trials must be turned over to outside resources – the clinical investigator and the hospital. It is also probably the most frustrating type of research, for its ultimate subject is man, whose responses may be quite different from those that laboratory experiments might predict. Thousands of entities are investigated before one eventually becomes a medicine. Despite what its downplaying critics may say, research advances are primarily made in small steps, in what may seem to the uninitiated to be minor modifications. The grand breakthrough is a rarity; that will remain a truth, contrary to the propaganda of anti-industry critics who deride the small advances as being meaningless.

Pharmaceutical research, which may be looked upon as a national treasure because of its corporate laboratories and its corporate scientists, as well as its support of clinical facilities and clinical personnel, will continue. It will continue at its present rate, however, only so long as its output can lead to profit. It is paradoxical to consider that, with all it has to offer, the pharmaceutical industry is being squeezed in a world-wide process of economic politicization with one apparent view in mind: a determination to keep down its profit margins and, thus, to destroy its research effort.

The constant pressure on profit margins is not the only threat to research that is walking the world. There are others of just as great significance. The three most inimical to the future of the research-based industry are: the threat to nullify patent protection; the move to undermine the value of brand names; the pressure to restrict the promotion of new products.

It would seem unnecessary to defend the concept that a corporation, just as an individual, is entitled to the fruits of its labour. The expenditure of significant sums of money derived from profit can only be justified by the industry if it is granted the right, assumed acceptable to all other industry, to sell its discovery for a reasonable period without the incursions of pirates or the intrusion of competitors to whom compulsory licensing is forced. The necessarily lengthy period of investigation and testing has already decreased the effective life of many patents. Some governments, such as my own, have acknowledged the unfairness of that fact by enacting legislation to extend the useful life of a patent, at least by a part of the period for which its

use was denied by the required testing and by the governmental regulatory process. There is the diametrically opposite thrust of non-governmental entities, such as Health Action International, to deny the patent system's protection to any medicine.

In the United States, the trademark or brand name is still looked upon as a property right. That is not so in some other nations where action is taken to vitiate brand names. A brand name has specific meaning to professionals in medicine and to patients alike in that it assures the expected quality of product and the manufacturer's responsibility to the consumer.

The matter of promotion of medicines to the medical profession is poorly understood even in the developed nations of the world. Effective promotion and advertising are necessary to produce a market for a new medicine. It is fruitless to believe that all physicians will discover the advantages of new medicines by reading the scientific or clinical literature. Effective and ethical promotion of new medical products is a type of continuing education for the medical profession. Who, it must be asked, is more qualified to explain the advantages of a new medicine, complete with benefit/risk assessment, than the company which developed the product and has all the basic data at its disposal? In the interest of the patient, new medicines must be introduced to the medical profession and that is accomplished by promotion, to which term a pejorative meaning is assigned by industry critics and government officials alike. An effective medicine unused is an effective medicine lost; a new medicine delayed in use means patients underserved and, at worst, lives lost or, at least, quality of life curtailed. There is no reason in medicine to accept the poet's doleful lines that 'full many a rose is born to blush unseen'.

Pharmaceutical investment is also carefully considered in respect of the location of manufacturing facilities. The most reasonable place for manufacturing facilities is that in which raw materials are available, where sophisticated chemical syntheses can be carried out, and where a readily available workforce exists, capable of operating sophisticated equipment and willing to give a day's work for a day's pay. The necessity for quality in a pharmaceutical product dictates careful evaluation of all these factors. It just is not possible in many areas of the world to conduct sophisticated manufacturing, just as it is not possible in many areas to carry out sophisticated laboratory research. The

responsible corporation must weigh all the factors before investment is made. Some areas are especially well suited to final packaging, and so finishing plants, which lend themselves to economic development and the training of nationals in new skills, have been developed in those areas. Inadequacy of electrical power and lack of a skilled workforce both militate against the establishment of pharmaceutical facilities in many areas of the world. In this far-flung competitive world, it is not possible for every country to be a pharmaceutical producer from chemical synthesis to final packaged product and certainly not possible for every country to be a pharmaceutical exporter, no matter the desire of its government.

The pharmaceutical industry has made its investments after careful consideration of local conditions and physical practicalities. If it is to continue as a viable, innovating industry, it will have to make its future investments in similar fashion. Not every small and developing country will become the site of sophisticated research laboratories; similarly, not every small and developing country will house an integrated industry starting with chemical synthesis and ending with packaged product. Some developing nations, the larger ones, have the capacity to accomplish these ends and have built a productive structure. Among these are several Latin American countries and India. The transnational pharmaceutical industry will continue to work with them and assist them if it is guaranteed the opportunity to make a reasonable profit.

Medicines at reasonable prices are available now in all sectors of the globe. The critics in the industry decry the fact that in some areas of the world a substantial portion of the health budget is consumed in the purchase of these medications. Not one of these critics has spoken out against the pitiful amount provided for health budgets despite an ever-growing clamour to achieve the WHO goal of health for all by the year 2000. It is not the pharmaceutical industry that is impeding progress to that goal. Rather, it is government indifference to the provision of adequate health care, government failure to provide an adequate infrastructure to ensure that health care, that is impeding the progress. It is difficult for the industry's critics to speak about government failures, about the presence of corruption, about the construction of airports and hotels in capital cities, rather than the building of a health network to care for all the people. It is

much easier to find a scapegoat – and that scapegoat has become the industry.

The industry has been granted little credit for the attempts it has made to alleviate these conditions. Industry has provided training in quality control for citizens of the so-called Third World. Industry has, in several small and impoverished countries, provided assistance in developing training programmes in inventory control and in distribution. Industry has provided medicines at preferred prices for WHO programmes. Industry stands ready to do more if only the rhetoric can be dampened and the practicalities faced.

In response to continuing criticism of its marketing practices, the industry has developed a code of marketing practices, well publicised through the International Federation of Pharmaceutical Manufacturers Associations. It has invited its critics to bring forth their complaints; it has handled those complaints expeditiously and has publicised its actions. To this point, no government or government agency has brought forward a complaint. The industry, unlike its critics, believes that governments do have expertise upon which to base their decisions of the approval of medicines and their succeeding regulations.

Not willing to accept the fact that a workable code is in place and is effective, Health Action International has developed a code of its own which is now being discussed within various UN agencies. That code which, with tongue in cheek, HAI indicates will accomplish fairness for all, constitutes an ideological economic agenda. The HAI 'code' makes no attempt to pressure governments to achieve minimal health care. It is a document designed to exert 'control of trade' and to impose upon industry one control after another. Its preamble declares that the majority in rural areas and urban slums do not have reasonable access to drugs; it neglects to mention that this majority, characteristically, has no medical services at all of a primary nature.

It proclaims for all the right to medicines but is strangely silent on a right to medical attention. It would provide for the fixing of prices of medicines, and to fix the fees of pharmacists as well. In order to encourage the development of local industry, excise taxes would be levied upon imported products priced lower than the local product and, thus, raise the price of medicines for all. It proposes that there be no patents at all issued for pharmaceuticals or, failing that, a significant shortening of active patent life. It

provides for compulsory licensing. It provides for a limitation of the number of marketing employees. It would require pharmaceutical importers to pay a percentage of their turnover to governmentally controlled research and development. It would require that a new product be registered only if it has equal, or better, benefit/risk ratio, has equal, or better, pharmaceutical properties or if it can be marketed at a lower price than the prevailing medicines. The adoption of a 'code' like this by WHO for developing countries alike would effectively destroy your sunrise industry.

In addition to codes, industry critics continually urge the rational use of drugs. It is difficult, at best, to define the word 'rational', for it has different meanings to different individuals. Years ago I challenged a Commissioner of the US Food and Drug Administration on his use of the term 'rational' as if it were a concrete word. I told him that it was quite possible, in Nazi Germany, that some believed Hitler's policies to be 'rational', whereas I could not subscribe to that. He stopped using the term thereafter. If we are going to talk about the 'rational' use of drugs, we had best insist that there be a definition of terms that all can understand.

Finally, critics and governments alike are enamoured of so-called essential drug lists. Well-meaning people everywhere have always tried to simplify complex situations by attempting to ignore the very reasons for the complexity to exist. Not every medicine produces the same reaction in all patients; it is essential, therefore, that physicians, to provide adequate therapy, have available a variety of medicines. I once told a British Cabinet officer that his striving to create an 'essential' list was reminiscent of the fact that every medical student, at some time or another, tries to draw up a list of medications that will suffice for him in practice forever. Modern therapy cannot be based for all time upon tried and true, but outdated, medicines.

One always hopes that people of goodwill, committed to superior health care, can reach agreement on principles. Agreement in our days seems more and more difficult to reach. The industry, if it is to survive, will continue to seek reasonable agreements.

If the sunrise industry is to survive, it will have to be appreciated that the 'codes' and the 'essential' drug lists are a threat to the developed nations as well as to the developing ones.

Inimical to a system based on competition and innovation, they must be recognised as fundamentally contrary to the interests of the medical profession and to the welfare of the ultimate consumers of health care. I think it is still true that no government has discovered a new medicine in a nationalised industry; I think it just as true that no government ever will.

Several years ago, when the World Intellectual Property Organization was discussing a revision of the Treaty of Paris, it was solely the representative of the United States who stood firm against the vitiation of patent rights. Similarly, at the recent World Health Assembly it was solely the representative of the United States who argued against a WHO code for pharmaceuticals. My country believes that in research and innovation lies the key to a more prosperous future. Apparently, others do not.

That statement may be a misconception. If so, it is a misconception based upon actual occurrences. I find it difficult to believe that each of the 100 governments would have voted that an international conference on the rational use of medicines was a critical necessity. That 100 representatives so voted is, to me, a confirmation of the fact that governments appoint representatives and fail to discuss with them, before the fact, the crucial issues that might arise at any international meeting. Representatives, I believe, go to meetings as that most regrettable ornament, as unguided missiles. I have serious doubts that, at the recent World Health Assembly, the introduction of the resolution relating to a code was by deliberate government intent. In like fashion, I believe many votes were cast as individual decisions, based on personal ideologies, not as government affirmations. In ways such as this do groups of individuals perpetrate a mischief.

If sunrise industries are to be nurtured, governments will have to decide crucial issues. In the twilight, if not the dusk or gathering gloom, of my career there is little that I can do to persuade them. There must be others, hopefully among this audience, who can take up this challenge.

I was asked, as the last speaker, to attempt to bring this conference to a close on an optimistic note. That I propose to do because I am, by nature, an optimist. I believe that governments will incline to supporting their national treasures, their innovative industries, and that in the long run they will be temperate in their actions. As a result, the future of the research-based pharmaceutical industry will not be truncated.

DISCUSSION

Tony Culyer

Although it is true, as Lord Harris tells us, that economists often disagree, I doubt that they do so much more than other scientists. In the purely scientific area of economics, like the sort of measurement, description and theoretical explanation provided by Burstall and Dunning and by Sir Bruce Williams, disagreements can be resolved by improvements in data and repeated testing of hypotheses. There remains some room for judgement but, as in the case of previously contested views about, for example, the long-term stability of the aggregate demand for money (a crucial issue in the monetarist debate), a consensus can arise based upon the fruits of well-designed empirical studies and an agreed set of scientific criteria by which to judge them.

But that, in a sense, is the easy part. The harder part lies in tackling complex questions under conditions of monstrous ignorance – especially, and inevitably, ignorance about the future. Such are most of the questions that have concerned us over these two days. In such circumstances, the characteristic economist's response is not, as Harris says, to provide a multitude of answers to a particular question but rather to respond with a multitude of further questions.

That is how I propose to tackle my brief as discusser. I have questions, not answers. I want to play the role of taxonomiser rather than problem solver. In so doing I shall leave the specific questions of industrial economics to Professor Kaufer and concentrate on the question of health economics. I want especially to relate my comments to the image-projection of the pharmaceutical industry, a persistent theme throughout the conference and to issues concerning a more constructive and creative scientific role that I think the industry can and should be increasingly playing.

The opening discussion introduced a mischievous muddle into our proceedings. There seemed to be a consensus between speakers and discussers that there is no scarcity in regard to energy in particular and, presumably, in regard to everything else

as well. This muddles two quite separate issues. Of course there is universal scarcity. Were it not so we would have no poverty; no need for property, markets, prices; no worry about our research budgets; no need to choose. But we do have these things and we do have these problems. Our personal demands are rival (if I want more of one thing I must sacrifice some of something else) and so are our interpersonal demands (if I want more of at least one thing and no less of others, you must go without something).

The potential energy in our universe may be to all intents and purposes limitless, but usable energy is not. It can be had only at great cost – and only at rising marginal cost too. A major resource scarcity is that of time. None of us here has enough. Were this not scarce no one would worry about the very real problem of effective patent lives or, in some countries, the woeful absence of any kind of property right in ideas.

The crucial point that our earlier speakers were meaning to make was, I think, that there are always alternative means of accomplishing an end. Some may be more or less effective, and more or less costly. But there is always a trade-off between alternative means to an end. This unhappy necessity arises only because of scarcity and never in its absence. The idea of trade-off is the central theme of all my comments.

The point is worth emphasising because it is characteristic of much of the criticism of the pharmaceutical industry that trade-offs are not discussed. Issues are presented as all-or-none, on-or-off, this extreme or that. Unfortunately, this syndrome also characterises much that is supposed to be supportive of the industry and is well represented by the papers of Harris and Wescoe.

Price and profit controls are usually presented in public discussion with total abhorrence by the industry's friends. This misses the crucial fact (and I think it is a fact) that we confront a trade-off issue that needs careful elaboration and good judgement to resolve. Lower prices and profits mean, in the short term, either higher consumer benefits or lower public expenditure (or both) on drugs. In the short term, it is easy to show (see, for example, Culyer and Posnett, 1984) that company losses are, pound for pound, outweighed by these other gains (whether public or private). But if lower profits (and lower expected profits) can imply migration of a footloose industry as Reekie rightly reminds us is the case, and if they also imply less R and D,

as they surely do, the real cost of the general short-run gains just described is the future benefits lost as a result of fewer effective drugs. (Small countries can often free-ride on the backs of others and at least in part escape some of the costs of Draconian controls or absence of effective patent legislation. Unfortunately, there are few ways in which a company can 'punish' such free-riding and force such countries to face a more realistic trade-off from a world, rather than a single country's, perspective.)

It is not self-evident what the right balance is, let alone that it lies at any extreme. It is a trade-off that I doubt can ever be fully quantified. But the crucial elements in it can be identified and intelligent judgement exercised about where the best balance probably lies.

It is all very well to have robust and enthusiastic defences of the profit motive – one expects no less from able and successful managers – but I do not think that they contribute a great deal to the careful examination of an issue like price and profit regulation which clearly involves costs and benefits and which can be discussed intelligently only if the existence of a trade-off is recognised. I found the paper by Wescoe disappointing in not facing up to this intellectual challenge and was uncertain with regard to whom his comments were addressed. Was he trying to persuade others to think otherwise than they do? Or was he just rallying the troops?

In an entirely different way Harris too fails to spot a trade-off problem. First, we should be clear that the form of ownership and finance of health services has almost nothing at all to do with the total amount of private and public money spent on them. One thing, and one thing alone, explains how much a country spends on its health care and that is its per capita GNP (Newhouse, 1975; Maxwell, 1981).

Second, we should note that the NHS, private insurance based systems and social programmes like Medicare and Medicaid all have two basic features in common. One is that user prices at the point of consumption are always lower than the cost of the care received, so all systems (not just the NHS) have a built-in propensity to over-demand. In simple insurance systems this is reinforced by automatic financing of the over-demand, so there is over-supply too. (Coinsurance reduces this but at the cost of reducing the value of being insured – another trade-off I shall not pursue here.) The other shared feature is that all systems

confront a set of ultimate decision-makers (the doctors) who really commit the money and are in a position to demand technologies (both expensive and cheap) without really considering the balance of cost and benefit (there is a whole set of trade-offs here from which they are usually effectively insulated). In this they are aided and abetted by the industries producing the technologies and by the professional urge to have the latest and the best. In the USA especially this is further intensified (notably with diagnostic technologies) by the threat of malpractice suits.

The real issue then on which Harris ought to have focused our attention is not how to get the NHS finances more market-based, but how we are to set about appraising the value of the services that we deliver, or might deliver (this is an issue that starkly confronts every health care system in the world) where 'value' is measured in terms of the health and welfare of patients (actual and potential) rather than being defined in terms of biological or biochemical function. Then the question becomes, having identified what is effective, how to adapt the market and institutional mechanisms that exist so that what is effective is what is actually done. The market will not do this automatically. Nor will bureaucrats. Who will? And how? How will the trade-offs be revealed and how will the ideal trade-off (if such exists) be acted upon?

This brings me to my final point. I have little doubt that the buzz-word of the later 1980s and the 1990s is going to be 'cost-effectiveness'; not just cost-containment but genuine value for money (public or private). Although Wells touched on this in his discussion, as did Sir Richard Doll in his paper, it is an issue of such importance that it has to be raised again in the context of the general need for a trade-off approach.

Cost-effectiveness is written by some as two separate words and by others as a hyphenated word. Either way it has two components. I am not one of those who favours limited lists of 'essential drugs' and my real reason for this is that, provided we have good information on the cost-effectiveness of drugs and a well-informed medical profession appropriately monitored as regards its prescribing, it is altogether unnecessary (as well as having much potential for mischief).

By effectiveness we must not mean merely that a drug does what is claimed for it clinically when appropriately prescribed. We must mean what I shall call relative effectiveness. Returning

again to trade-off, we need to know the performance of an entity relative to a relevant range of alternatives, many of which need not be pharmaceutical at all. We need to know one thing's effectiveness relative to the other possibilities for action (or, come to that, inaction). What will it replace? What will it complement? What other new procedures will it make possible? What will be the marginal improvement in patient outcome?

Although my dictionary defines efficacy and effectiveness as synonymous, some clinical epidemiologists make a useful distinction between them, using efficacy to refer to the effectiveness of a drug under the ideal circumstances of a clinical trial and effectiveness to refer to its effectiveness under normal practice conditions. They are obviously not at all the same thing. It is a great pity that the overwhelming bulk of clinical trials are of the efficacy rather than the relative effectiveness type. Yet only the latter are really relevant if we are concerned with practical efficiency matters and value for money in health care. The former have an important role, *inter alia*, in determining optimal dosage and identifying unsuspected toxicity. But they are quite irrelevant regarding the cost-effective delivery of care and the revelation of important trade-offs.

Moreover it has to be said that very large numbers of trials (many of which have been supported by the industry) are extremely poorly designed and executed, with poor controls (sometimes none), small samples, contamination by placebo effects, and a large number of other design imperfections. Unfortunately, such poor work often gets past journal editors. If you doubt what I am saying, compare the 'gold standard' trial designs discussed by, for example, Russell (1984) or Drummond and his colleagues (1983) with a random sample of actual trials reported in the journals. Failure to follow the best feasible design and execution strategies leaves the industry wide open to the kind of criticism increasingly faced from Social Audit (Medawar and Freese, 1982) and other bodies. It is all so unnecessary – if only the industry (and the medical researchers it supports) followed the same high research standards in trials as in laboratories. Any standard lower than the highest is a standard the industry cannot afford. Quite apart from professional pride, the plain fact is that the opposition is becoming very sophisticated so that the highest standard is becoming a condition of survival.

The other word is, of course, cost. Recent years have seen a

flood of so-called cost-effectiveness studies, often in medical journals and not written by or with economists (and also I should add, often not in any way implicating the pharmaceutical industry) in which the cost concepts used and the cost measures adopted are simply inadequate: capital and current costs are not properly treated, non-market costs are ignored, naive accounting averages are used, public expenditures falling on or saved in other agencies or even other departments of the same organisation are often ignored and, following the absence of a relative effectiveness approach on the other side of the hyphen, relevant alternatives are not costed so that the real trade-offs are neither quantified nor even exposed in principle.

The principles of practical cost-effectiveness analysis are now well established (Drummond 1980, 1981; Culyer and Horisberger, 1983). Their application is also being encouraged by government, as witnessed, for example, by the Office of Technology Assessment in the United States. If I am right that this is to be the buzz-word of the immediate future I wonder how the industry is going to respond: defensively and only in response to government requirements and cajoling or adverse publicity; or positively and creatively by giving a lead and showing a concern for the highest possible standard of scientific work at every stage of the development and marketing process? The writing is, I think, on the wall. One or two companies are responding in a way I can only applaud. But what of the industry as a whole?

I have been critical both of some of the papers and of the industry. I hope this criticism will be seen as coming from a friend. It has not been my intention either to carp or to belittle achievement. I have long admired the speakers whom I have criticised and have immense respect for the industry and the quality of the people in it. My hope is that some home truths whispered by friends (and this Symposium has heard several from many) will find a way into the industry's thinking.

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DISCUSSION

Erich Kaufer

At the beginning of this conference Sir Bruce Williams stated that the prosperity of the sunrise industries depends upon the prosperity of the smokestack industries and vice versa. This is a point of fundamental importance and is central to the comments I wish to make.

In his opening lecture at the EARIE conference two months ago, Professor Scherer analysed the possible causes of the slump in world productivity growth. Since the first oil price shock the industrialised countries have gone through a productivity growth slump connected to two sharp recessions, one in 1974/5 and the other in 1981/2. What is less well known, however, is the fact that the growth rate in output per employee was already falling well before 1973.

Focusing on the experience of the United States, which is representative of that of Western Europe, available data show that for the period 1968-72, the US productivity growth rate declined by 0.45 per cent. Company-financed R and D expenditures had been growing at 6.4 per cent in real terms throughout the 1960s. But they peaked in 1969, fell for two years afterwards, that is, before the first oil price shock, and resumed their growth at a much lower pace until the end of the 1970s. Basic research by companies peaked in 1966 and then fell off by a quarter. It was not until 1979 that it attained its 1966 level again. The number of patents issued to US corporations had been growing at a rate of 4.3 per cent per annum all through the 1950s and 1960s. But again this growth rate peaked in 1971 and the number of patents declined by 27 per cent from 1971 to 1978.

It has been estimated that if output per hour of work in the US had continued to grow during the 1970s at its 1960 trend rate, private sector output in 1983 would have been 31 per cent higher than it actually was. While there can be no doubt that the two oil price shocks have contributed most to this loss, that is to the decline in productivity growth, it is also apparent that even before the oil price increase, forces were already operating which

would have reduced the productivity growth. Even if it is assumed that only 5 of the 31 per cent can be explained in this way, then it must still have had a substantial impact on the pharmaceutical industry. This is because if private sector output had been five per cent larger, health budgets would have been much less constrained and efforts to suppress profit margins by price controls and forced generic prescription would have been weaker.

But why did companies reduce their R and D expenditures in the late 1960s? Numerous hypotheses have been advanced but I find one in particular to be both plausible and intriguing. In the 1960s Japanese companies began an unexpectedly swift push first into the American and then into the European markets on a broad front. However, the Japanese trade pattern is different from that among the Western industrialised countries.

There are two very different patterns of specialisation in foreign trade. One is called inter-industrial specialisation or inter-trade and the other is referred to as intra-industrial specialisation or intra-trade. Inter-trade is characterised by the fact that a country loses almost all of its industries in which it has a comparative disadvantage in exchange for a gain of all those industries where it has a comparative advantage. Inter-trade poses severe adjustment problems because the location of whole industries is redistributed all over the world. Intra-trade consists of a specialisation between the same industries of different countries. Intra-trade is a product-based specialisation. Intra-trade is called 'trade without tears' because no country loses its industrial base.

In the past foreign trade among the Western industrialised countries predominantly developed along the lines of intra-trade. But that does not apply to the trade pattern with Japan. Japan's trade with the other industrialised countries is predominantly a pattern of inter-trade. That means Japan pushes her trade partners into a position where they are threatened with the loss of whole industries. This is trade with tears and with red ink!

Oligopoly models of R and D under rivalry predict that if a rival takes its competitors by surprise the latters' initial reaction will be to cut back on R and D expenditures. Though I do not know what went on in the minds of, say, US steel executives, it seems plausible to me that US and later European companies reacted to the Japanese threat by reducing their R and D expenditures which

in turn contributed to a productivity growth slump.

This scenario implies several lessons for sunrise industries. First, the prospects for sunrise industries are heavily dependent on the prospects for smokestack industries. The smaller the productivity growth in the latter, the smaller the demand potential for the former. But the pace of innovation is driven by the strength of the demand pull. A weaker demand pull on a sunrise industry implies a lower rate of innovation in that industry which then feeds back in the form of a lower productivity push for a smokestack industry. Japan has stronger smokestack industries than we have, and it has, therefore, better prospects for sunrise industries.

Second, on the basis of past experience, the pharmaceutical industry must be alert to the danger that Japan may try to repeat its inter-industrial pattern of trade in the context of pharmaceuticals. If the pharmaceutical industry wants to avoid the fate of other former sunrise industries, it should make an all-out effort to force Japan into a pattern of intra-industry trade in pharmaceuticals by heavy direct investment into Japan.

DETAILS OF SESSION CHAIRMEN, PRINCIPAL SPEAKERS AND DISCUSSERS

Dame Elizabeth Ackroyd DBE has been Chairman of the Patients Association since 1978. She is Vice-Chairman of both the Waltham Forest Community Health Council and the London Voluntary Service Council. Amongst many other commitments, she is a Member of the Bedford College Council and Governor of Birkbeck College.

Dr Michael Burstall is a lecturer at the University of Surrey where he heads the Industrial Chemistry Group. With John Dunning and Arthur Lake he worked on the study of multi-national drug companies published by the OECD in 1981. With Ian Senior he has just completed an investigation of competition and competitive strength in the European pharmaceutical industry for the European Commission.

Professor Sir John Butterfield OBE is Regius Professor of Physic and Vice-Chancellor of the University of Cambridge. Prior to this he served as Professor of Medicine at Guy's Hospital and was Vice-Chancellor of the University of Nottingham. He has served as a member of numerous committees and councils, including being the Chairman of the Medicines Commission from 1976 to 1981, a member of the Medical Research Council and Chairman and Vice-President of the British Diabetic Association. He has written extensively on the subject of diabetes, health care and education.

Dr Colin Cooke OBE JP was the former Chairman of the OHE Editorial Board and has been associated with the Office from its foundation. He was involved with the National Health Service from 1948 to 1976 with particular interest in the organisation of primary medical care and the development of local health centres. From 1944 to 1970 he was a Fellow and Senior Bursar of Magdalen College, Oxford, and has been Emeritus Fellow since 1970.

Professor Tony Culyer is Professor of Economics at the University of York. He has held visiting professorships at

Queen's University, Kingston, Canada, the Ontario Economics Council, Otago University and the Australian National University. His major research field has been in health economics, in which he has published over a hundred books and articles.

Mr Peter Cunliffe CBE has been the Chairman of the Pharmaceuticals Division of Imperial Chemical Industries since 1976. He is a member of the Executive Council of the European Federation of Pharmaceutical Industries' Associations and is a Vice-President of the International Federation of Pharmaceutical Manufacturers Associations. He was the President of the Association of the British Pharmaceutical Industry from 1981 to 1983.

Professor Sir Richard Doll OBE FRS has held posts as member and then Director of the Medical Research Council's Statistical Research Unit, Regius Professor of Medicine in the University of Oxford, and Warden of Green College, Oxford, and is now honorary consultant at the Imperial Cancer Research Fund's Cancer Epidemiology Unit. He has been a member of the Medical Research Council, the WHO Advisory Committee for Medical Research, the Scientific Council of the International Agency for Research on Cancer, the Adverse Reactions Sub-Committee of the Committee on the Safety of Medicnes, and the Royal Comission on Environmental Pollution.

Professor John Dunning is Professor of International Investment and Business Studies and Chairman of the Department of Economics at the University of Reading. Before joining the University in 1964, he was a professorial visitor at various universities in the Unites States and Canada. He has acted as a consultant to the British government, the United Nations and the Organization for Economic Co-operation and Development. He has published several books and many articles on multinational enterprise and international direct investment.

Tom Garvey is a director in the Directorate for Internal Market and Industrial Affairs of the Commission of the European Communities. His Directorate deals with pharmaceuticals and veterinary medicines. Other sectors for which he has responsibility include the removal of technical barriers; motor vehicles and agricultural machinery; electricity, mechanical engineering, metrology, standardisation; foodstuffs; chemicals, plastics and

rubber; and distributive trades.

Dr Maurice Goldsmith is Director of the Science Policy Foundation. He is also Director and Trustee of the Guinness Awards for Scientific Achievement, President of the Commonwealth Association of Science, Technology and Mathematics Educators and Chairman of the Committee of Commonwealth Professional Associations. Amongst other commitments which include being the Honorary Treasurer of the Confederation of International Science & Technology Organisations for Development, he is also Editor of *Science & Public Policy*, *Outlook on Science Policy* and *CHANGE*. He has edited several publications on science and technology.

Lord Harris of High Cross has been General Director of the Institute of Economic Affairs since 1957. Prior to this, he was a lecturer in political economy at St Andrew's University. He is President of the Mont Pelerin Society, a member of the Political Economy Club, a Council Member of the University of Buckingham and a Trustee of the Ross McWhirter and Wincott Foundations. He is the author of numerous publications which include studies of advertising, hire purchase, welfare, monetary policy and countless articles on the delusion of central economic planning.

Professor Rosalinde Hurley has been Chairman of the Medicines Commission since 1982. She is Professor of Microbiology at the Institute of Obstetrics and Gynaecology and Consultant Microbiologist at Queen Charlotte's Maternity Hospital. She has been President of the Section of Pathology of the Royal Society of Medicine and is an Honorary Secretary of the Society. She has recently become President of the Association of Clinical Pathologists. Apart from publishing several books, she has written widely in medical and scientific journals.

The Rt Hon Aubrey Jones is a Fellow Commoner at Churchill College, Cambridge, and President of the Oxford Energy Policy Club. From 1950 to 1965 he was the Conservative MP for Birmingham, Hall Green. For the next five years he chaired the National Board for Prices and Incomes. He has been the Vice-President of the Long-Range Planning Society since 1973. He has held several academic appointments at both Oxford and Cambridge Universities and was invited to be the Regent Lecturer at

the University of California and the Guest Scholar at the Brookings Institution in Washington, DC.

Professor Erich Kaufer is Professor of Economics at the University of Innsbruck. In 1965, having achieved his PhD in economics at Marburg University, he undertook post-graduate studies at Cornell University and the University of Michigan. From 1970 to 1977 he was Professor of Economics at the University of Saarland. His main field of research has been in industrial economics, public regulation and competition policy. He has been the author of many books and articles and is the expert for health economics at the Mainz Academy of Sciences.

Mr Michael Kenward is the Editor of *New Scientist*. In 1967 he joined the UK Atomic Energy Authority as an experimental physicist at its Culham Laboratory for fusion research. After two years he started working for *New Scientist* and over the years has written extensively about all aspects of energy technology. In 1976 Cambridge University Press published his book entitled *Potential Energy*.

Mr Peter Laister is the Chairman of THORN EMI, which he joined in 1979 after a career with the Esso Petroleum Company Ltd, the British Oxygen Company Ltd and Ellerman Lines Ltd. He is a Council Member of the Industrial Society, a member of the Industrial Development Advisory Board and is a Governor of BUPA. He is also Chairman of the British Foundation for Age Research and a Member of Council of University College, London.

Dr Sanjaya Lall is the Senior Research Officer at the Institute of Economics and Statistics and a Fellow of Green College, Oxford. He has worked at the World Bank and has acted as a consultant to the National Economic Development Office, the Institute for Research on Multinationals in Geneva and various other international organisations. He has published extensively on the subject of multinational corporations, transfer of technology and industrialisation in the Third World. He is deeply involved in the many debates surrounding the international pharmaceutical industry in the Third World.

Mr John Maddox is the Editor of *Nature*. He lectured in theoretical physics at the University of Manchester and was

science correspondent of the *Guardian*. He was the Director of the Nuffield Foundation and has been Managing Director of Macmillan Journals Ltd and Director of Macmillan & Company Ltd. Amongst other commitments, he has been a member of the Royal Commission on Environmental Pollution and the Genetic Manipulation Advisory Group. He writes and broadcasts extensively.

Professor Frank Münnich has been the Head of the Institute for Theoretical and Empirical Welfare Economics at Munich University since 1978, during which time he spent six months as a Visiting Fellow at several American universities. From 1960 to 1968 he was a research assistant at the Alfred Weber Institute for Social Sutdies at Heidelberg University. After two years in the United States, he returned to Germany as a Professor at the universities of Dortmund, Essen and Innsbruck. His current research interests include health economics, equilibrium theory under uncertainty and economic systems.

The Rt Hon Dr David Owen MP is the Leader of the Social Democratic Party and has been the Member of Parliament for Plymouth since 1966. Whilst serving in the Labour government, he became the Minister of State for Health and Social Services and subsequently the Secretary of State for Foreign and Commonwealth Affairs. In 1979 he was the Labour Opposition Spokesman on Energy. In 1981 he co-founded the SDP. He was the leader of the SDP Parliamentary Committee from 1981 to 1982; Deputy Leader of the Party 1982-3; and became Leader of the Party in June 1983. He has published books on health, defence and human rights and is a member of the Independent Commission on International Humanitarian Issues.

Professor Duncan Reekie is E. P. Bradlow Professor of Business Economics at the University of the Witwatersrand, Johannesburg. Formerly he was Reader in Business Economics at the University of Edinburgh. He has lectured widely in universities in New Zealand, Australia, Canada, the United States and Europe. He is a specialist in the economics of industrial organisation and has written several books on the pharmaceutical industry and on advertising.

Dr Balu Sankaran is Director of the Division of Diagnostic, Therapeutic and Rehabilitative Technology at the World Health

Organization. Prior to taking up this post in 1981 he was Director-General of Health Services in India. Following his post-graduate training in the United States and England, appointments at the All India Institute of Medical Studies and a two-year Rockefeller Foundation Fellowship at the University of Illinois, he was made Professor of Orthopaedic Surgery at the University of Delhi in 1967. In 1970 he became Director of India's Central Institute of Orthopaedics and Traumatology.

Lord Swann FRS is Chairman of The Technical Change Centre, a Wellcome Trustee and a director of two companies as well as being the Chancellor of the University of York. He was Chairman of the British Broadcasting Corporation from 1973 to 1980. Prior to this he was the Principal and Vice-Chancellor of the University of Edinburgh, having initially served as the Professor of Natural History and the Dean of the Faculty of Science. He has been a member of many learned scientific committees both in England and Scotland, including the Medical Research Council, the House of Lords Select Committee on Science & Technology and the Scientific Foundation Board of the Royal College of General Practitioners.

Mr David Taylor joined the Office of Health Economics in 1972 and became its Deputy Director in 1976. This year he was appointed Director of Economic Planning of the Association of the British Pharmaceutical Industry. During his time at OHE he researched and wrote over 40 of the Office's publications, and he has authored about 200 other published studies, articles and book chapters. He is currently a Visiting Senior Research Fellow at the University of York.

Professor George Teeling Smith OBE has been Director of the Office of Health Economics since its foundation in 1962. Prior to that he was Deputy Managing Director of the Winthrop company in Britain. He is Professor Associate in Health Economics at Brunel University.

Mr Nicholas Wells has been with the Office of Health Economics as an economist since 1974. He has written a large number of papers for the Office, covering a wide range of topics. He has a special interest in preventive medicine and the economics of pharmaceutical innovation. He also acts in an advisory capacity to several charities.

Dr Clarke Wescoe is the Chairman of the Board of Sterling Drug Inc. A graduate in medicine from Cornell University, he has served as Dean of the School of Medicine and Chancellor of the University of Kansas. He joined Sterling Drug Inc. in 1969 as an executive officer.

Sir Graham Wilkins is Honorary President of the Beecham Group, having retired from the chairmanship in July 1984. He joined the company in 1945 and his career has been divided between the Consumer Products and Ethical Pharmaceuticals side of the business. He is non-executive Deputy Chairman of THORN EMI and a non-executive director of Courtaulds and Hill Samuel Group. He has been a Vice-Chairman of the Proprietary Association of Great Britain, President of the Association of the British Pharmaceutical Industry, Chairman of the Medico-Pharmaceutical Forum and President of the European Federation of Pharmaceutical Industries Associations.

Professor Sir Bruce Williams KBE is the Director of The Technical Change Centre. From 1967 to 1981 he was the Vice-Chancellor of the University of Sydney. Prior to that he was the Professor of Political Economy at the University of Manchester. He has written extensively on technical change and economic growth.

Mr Ron Wing is President of the Association of the British Pharmaceutical Industry and Chairman of Sanofi UK Ltd. He has held senior marketing appointments with The Wellcome Foundation and the Boots Company Ltd. Subsequently, he was appointed Chairman of the Pharmaceutical Division of Reckitt & Colman Ltd. He is a member of the East Yorkshire District Health Authority and of the Council of the University of Hull.

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