Profitability and improved patient care—industry's viewpoint

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The word 'profit' in any form tends to induce an antipathetic emotional reaction that is particularly incompatible with another emotive term: 'patient care'. However, I hope to show that these two terms do have a beneficial and harmonious link in the case of the UK pharmaceutical industry.

Contributions by the pharmaceutical industry to patient care centre mainly on the provision of safe and effective drugs and medicines and information about them. It is generally agreed that drug therapy has revolutionized medicine in the past 30–40 years, but most of these changes are now taken for granted which forms a danger to their future continuation. Hence it is worth emphasising the contributions of medicines to such frontier subjects as organ transplantation, *in vitro* fertilization and treatment of virus disease and cancers.

I propose to make two simple hypotheses. First, that profit-centred, competitive, private enterprise is the only system yet devised in the world, capable of producing this flow of new medicines. Secondly, and as a consequence, reasonable profits are essential to make the system work. Hence, profit is not a dirty word and the only problem is to define 'reasonable' in an area where completely free competition, in classical terms, is not appropriate.

The first proposition is easily proved by it being self-evident that free enterprise industry of the type I have described is the only one that has succeeded anywhere in the world in producing new medicines. Academic contributions have often supplied important original knowledge from which a drug has emerged—or, on occasions, have supplied the drug itself—and will continue to do so. But the development of ideas and candidate drugs into complex formulations of safe, effective and high quality medicines, capable of regular and economical production requires integration of many highly specialized activities that only exist together in research-based, or innovative, pharmaceutical companies. These activities call for teams and departments of chemists, biochemists, pharmacologists, toxicologists, immunologists, microbiologists, pharmacists, geneticists, statisticians, clinicians,

registration and information officers, just to quote some of the complement of the research company. In addition the products must be marketed and distributed which needs another large range of specialists in the commercial, marketing and production fields. All of this has to be paid for and the only method available for this is by the price of the products—there are no subsidies or grants. It remains to show that these prices and profits are reasonable. I cannot prove this but can indicate some of the parameters involved.

The system is illustrated simply by Figure 1 which shows a dynamic cycle of: activities, involving costs, resulting in products which are sold (and services which are provided free) and a cash surplus. Most of this surplus is reinvested in the business and stimulates yet further activities; some is dissipated, either as tax or as interest to investors. The latter is not strictly lost to the enterprise as it boosts the confidence of shareholders and they are more likely to be forthcoming as and when fresh calls are made for new investments into the business. Incidentally, this dividend to shareholders is of the order of 2 or 3% p.a. on pharmaceutical company shares at market value. The investor is looking for growth in share value over the years, and hence, in his capital holding as the reason for this investment, rather than the much higher rate of annual return he would be able to gain from banks, building societies etc. Hence, a rise in share prices should be greeted as a good thing, because it both encourages investors and expands the business with more jobs, activities, products and profits. The remainder of the financial surplus is ploughed back into the business as investment and stimulates its various activities. For all but two or three world companies (and no UK ones) the shareholders are widely mixed representing pension funds, insurance companies, bankers, investment trusts, private persons. Marxist theory that the sweat of honest labourers produces goods whose added value goes into the pocket of the capitalist owner is as far removed from reality as it could be in respect of pharmaceutical companies. Professional managers run the companies and ensure that the dozens of

Figure 1 Innovative pharmaceutical industry.

Table 1 Pharmaceutical sales to the NHS (£m)

	<i>G.P.</i>	<i>Hospital</i>	<i>Total</i>	<i>% NHS costs</i>
1981	955	247	1202	8.9
1982	1114	284	1398	9.7
1983	1264	324	1588	10.2

special disciplines, as just described, are skillfully orchestrated in unison, and that a triple responsibility is fulfilled: to customers (patients), shareholders and staff.

The present climate is forcing us all to justify rigorously our share of a shrunken national economic resource so it is right that the industry should be examined to see if it is getting an appropriate share of the national cake. However, in this case it must be emphasized that the industry is also enlarging the cake—for everyone. Table 1 shows pharmaceutical sales to the NHS in £m at manufacturers prices (thus excluding oncosts from chemists and others) for 1981–83. Hospital costs of medicines are about one quarter of those from general practice because of both smaller volume of use and stringent cost-cutting, such as generic substitution, contract purchasing and limited lists of medicines. Thus, although the cost of medicines is about 10% of the NHS cost as a whole, in hospital expenditure, medicines represent only about 2% of the total spent—probably at an irreducible minimum—this is roughly equivalent to that spent on laundry services or engineering maintenance. Therefore hospital medicines provide only a minority of the income available for R & D and industry profits. The slight rise in the proportion of NHS costs spent on medicines is due to a ‘capping’ of NHS recent expenditure rather than an undue rise in drug costs; this figure has been 9–10% for many years’.

Table 2 shows the average number of NHS prescriptions supplied by FP10s per head of the UK

Table 2 Prescriptions—NHS

	<i>Per capita p.a.</i>	<i>Average cost per item (£)</i>	<i>Hospital in-patient weekly cost (£)</i>
1980	6.7	2.37	336
1981	6.6	2.79	433
1982	6.8	3.14	504

population and the average cost per item, or ‘net ingredient cost’. For comparison is shown the weekly cost of in-patient hospital care for the same years, but note that prescriptions are for an average duration of about 20 days, nearly three times the duration of hospital stay as costed. The relative costs of the two forms of treatment, although rarely are they strict alternatives, is more than 150 fold and an indication of the powerful cost-benefit ratio of medicines.

Table 3 shows the relative costs of various items of expenditure in the UK in 1980, where medicines cost about the same as newspapers at 5p per day per capita; about one tenth the expenditure on either clothing, or defence or alcohol or education. The UK spends less per capita on medicines than any other OECD country except Eire as a result of low numbers of items prescribed (a tribute to the medical profession) as well as to low cost of the items.

The fate of income derived from pharmaceutical sales to the NHS has been obtained from the pooled annual financial returns made by industry for 1982 under the pharmaceutical pricing regulation scheme. Production costs accounted for 40% of the income, research and development for 17%, profit 13% and administration and promotion each cost 12%. Minor items such as distribution accounted for the remaining 6%. Under new government restrictions the promotional allowance will be reduced to 10% for 1984

Table 3 National expenditure on various items in the UK per person per day in 1980

Item	Cost (pence)
NHS medicines	5
Newspapers	5
Tobacco	24
Defence	44
Education	47
Clothing	49
Alcohol	50
Housing	97
Food	114

and 9% for 1985. These profits of £160 m were distributed as follows. Dividends to shareholders and investors formed 10% to 15%, reinvestment 50% to 60% and the remainder went to taxation. Profits obtained from industry exports were larger and this trade contributed significantly to UK expenditure on R & D. Hence, sales of medicines to the NHS contribute only a proportion of the total industry research effort in the UK.

The benefits of the pharmaceutical industry to the nation are of two main kinds, medical and economic. The latter are described by Professor G. Teeling-Smith in his paper (Teeling-Smith, 1986). Medical benefits are summarized in Table 4. Space permits reference to a few of these only so I will mention those that are less well known or have been criticised such as promotion. To do this it will be helpful to illustrate the main steps involved in the development, and life, of a new medicine over 20 years or so and this is done in Figure 2. This figure shows an original idea (from somewhere within or outside the company) introduced into research which given time,

investment, skill and, often luck will result in a new product. Together with this 'hardware' a vital package of 'software' will be assembled of information on how the product should be used. Both of these must be presented to the medical profession widely, and speedily, that is by promotion. I hope that it would be generally agreed that any criticisms of promotion should be confined to its quality, and quantity, but not to its need which is vital to the dynamics of the life cycle, for promotion serves three important functions. First, it generates the financial returns needed to keep research and the whole enterprise thriving and Dr Cromie's paper (1986) shows why speed is important in doing this within the limited patent life available. Secondly, promotion of product benefits will stimulate competitor companies to look carefully at their own products and markets which may be threatened. This may spur ideas and activities within those other companies and their research may result in product improvements. Thirdly, promotion not only provides essential prescribing information for doctors but is a two-way process and the company will learn much about its new product from feedback from doctors via representatives. This information will help to give new guidance on how the medicine can be used to better effect and what refinements can be made to it. Also, important new therapeutic targets and ideas may be fed back to research which helps to design further new products, and hence to renew the cycle.

After expiry of their patent life, products will be available as 'generics' and now the whole basis of their promotion will be on price alone. Because of the low profitability of these products

Figure 2 The life-cycle of a medicine.

Table 4 Activities of innovative pharmaceutical industry

Products	innovative
	continuity
	service items
Research sponsorship	
Educational contributions	
Medical information	
Promotion	

there will be no surplus available to the manufacturers to provide the range of activities shown in Table 4. This is why the original product needs to bear a higher price to support those activities from the innovator who also needs brand name promotion of a high quality product to support sales after expiry of the unduly restricted patent life.

This dynamic cycle is totally dependent on product improvements however minor and in this way does not differ from any other high technology, research-based private enterprise industry. In these other industries, and in the philosophy of science generally, it is very well known that a succession of advances by small increments accumulate after a time into a large advance. We see this widely in television, computers, motor cars, aeroplanes etc, in each of which any single improvement could be called 'unnecessary', but the added effect of them on

the product over a number of years is dramatic. Clinical pharmacologists will be able to identify a number of drug groups that have followed a similar process such as the cephalosporins, adrenergic stimulants, topical steroids, oral contraceptives etc. Occasionally we have the large leap forwards, such as the H_2 receptor antagonists but as with science generally these cannot be expected too often. In addition, successions of similar drugs provide expansion of pharmacological and medical knowledge from the variations in their mode of action. For example, the range of β -adrenoceptor antagonists have focused attention on properties such as lipid solubility and penetrance into the brain, membrane stabilising effects, agonist effects etc., all of which advances scientific knowledge generally as well as refines therapeutic possibilities. Occasionally a major new property is discovered like inhibition of calcium mobility into cells which revolutionises pharmacology.

A yardstick of success in research is the rate of discoveries made and we have a good indication of this for pharmaceuticals from the number of new drugs, or new chemical entities, which are marketed each year after passing stringent tests for quality, safety and efficacy set by the regulatory system. These are shown in Figure 3 from data obtained by the Centre for Medicines Research (CMR) for the UK from 1960 to 1982, a total of 617 significantly new chemical entities

Figure 3 Number of NCEs introduced into the UK market.

Figure 4 Discrete single and combination medicines on the UK market in each therapeutic class (1984); (▨), number of single entities; (□), number of combinations.

Figure 5 R & D expenditure by the UK pharmaceutical industry in the UK (1982) by therapeutic class.

(Prentis & Walker, 1985). Since the introduction of regulatory procedures in the mid 1960s, the annual rate of entry of these products has been remarkably consistent at about 20 p.a. The therapeutic classes of drugs available in 1984 are shown in Figure 4. There is a broad range of medicines (both single entities and combinations) among 12 of the 16 therapeutic groups which does not support the criticism sometimes made that products are concentrated in a few areas only. The CMR is also collecting figures of how companies distribute their research expenditure and these preliminary results are shown in Figure 5 (Walker *et al.*, 1986). There is again a broad range of expenditure amongst 8 of the 12 groups shown especially the miscellaneous group, providing evidence that industry research is adventurous and is exploring wide fields. Over short periods it may seem that new products tend to

group in certain paths because they are well known and in demand, but this is in the nature of science generally where several centres pursue similar growing points.

Criticisms of the total number of medicines on the market have often been based on misleading, unrepresentative data for medicines may be counted in various ways. For example one drug, say salbutamol, may give rise to several discrete dosage forms, e.g. a pressurized aerosol, an insufflation powder, an oral formulation (tablet or liquid) or an injection, each with distinctive uses. In turn, each of these formulations may have a range of dosages and other pharmaceutical differences and each of these preparations requires a separate product licence. The CMR has analysed the present range of products in MIMS by these criteria and some of the results are shown in Table 5 (Prentis &

Table 5 Activities of innovative pharmaceutical industry

	<i>Number</i>
Product licences	15 500
Discrete single chemical entities	856
Discrete combination forms	590
Total	1446
Distinct dosage forms (single entities and combinations)	1670
Brand names	2123

Walker, 1985). The number of product licenses extant in April 1984 was about 15,500, but the number of discrete chemical entities, or drugs, is only 856 available as single entities and 590 as combinations, a total of 1446. Of these, 1670 medicines have been made available with distinct dosage forms as defined by separate routes of administration. The total number of brand names featured currently in MIMS is 2123 but if different versions or other minor variations of formulations are counted then a total of 4–5000 'products' might be achieved—the number often quoted as existing in the BNF or ABPI Data Sheet Compendium.

We should return to Table 4 and some of the activities of innovative companies. Apart from new products an important function of industry is to maintain continuity and quality of existing products, however much demand may fluctuate or whatever the technological problems or fortunes of their profit margins. This can, and is ensured by research-based companies even for so-called 'service items' which have very limited use and are often supplied free. Examples of these abound such as intra-theal products, drugs for rare diseases, diagnostic products and special formulations used infrequently.

Research expenditure in 1982 by the Medical Research Council was £100 m, compared with £75 m from Medical Charities and £420 m from industry. Part of this last expenditure was invested in extra-mural laboratory and clinical research and provides a useful help to the current budgets for departments of clinical pharmacological amongst others. The contributions from industry to medical education and scholarship are also well known. This has been called 'indirect promotion' by industry and a thoughtful paper discussed whether its present scale influenced doctors' judgements and opinions on medicines (O'Halloran & O'Malley, 1982). The conclusion was that it was probably not doing so.

Table 6 Medical information from companies

	<i>Number</i>
Companies surveyed	61
Staff graduates	177
others	143
Products	3048
Enquiries in 4 weeks (Pharmacists 40%, doctors 14%)	13 786

In a comparison paper I pointed out that this was only one of many pressures or temptations placed before doctors who should by their training and ethos be capable of recognising and resisting them (Snell, 1982). Direct promotion by companies is a further source of information and education. Promotion is controlled by quantity as previously noted and also by quality in several ways. All promotion must be in accord with the official data sheet which the DHSS has an opportunity to modify. There are also governmental regulations covering advertising and a very stringent Code of Practice administered by a committee containing an independent distinguished legal chairman and two independent doctors. This Code covers good taste as well as accuracy of presentation, and a scrutiny of journals is undertaken for infringements. Any doctor not wishing to receive industry promotion has only to notify the ABPI for all forms of mailings to him to cease and he does not have to receive representatives' calls. Nothing is perfect in this world and the industry welcomes constructive or well-founded criticisms from the medical profession. However, negative provocative articles, such as that by (Rawlins, 1984) readily gain public attention but may not significantly improve the situation.

Last year ABPI surveyed 61 companies for data on their information units and some of these results appear in Table 6 (Williams *et al.*, 1984). These departments are usually part of the company medical department; other specialized information units service laboratory research division. The 61 companies employed a total of 320 staff for these information units over one half of whom were graduates. Their services covered 3048 individual company products and in a 4 week period 13,786 external enquiries were assessed at a rate of over half a million.

This is a formidable service, given free, mainly to hospital pharmacists, but only by research-based companies. These units do not answer enquiries from the lay public for it is industry's policy to direct all such enquiries to patients' medical practitioners.

However, companies do provide some written information for patients and I believe this trend will increase. A few products include a package insert written for patients with information about the product; even more contain instructional messages on how to administer the medicine. Also, over a hundred booklets have been prepared by companies for patients to be distributed as appropriate by their doctors with general

information about management of their illness (Sloan, 1984).

I hope I have been able to show that the pharmaceutical industry provides, at reasonable cost, a wide range of products and services that make a considerable contribution to patient care that this is based entirely on profitability and a competitive private enterprise system which is in the patients' and the nation's best interest.

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