The British Pharmaceutical Industry Since 1851

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Britain's pharmaceutical industry, like its petroleum industry, is one which possesses a national comparative advantage both technologically and in the balance of overseas trade; yet it is not easy to delineate. Until quite recently, some member companies also made ranges of different products such as foodstuffs, household goods and heavy chemicals. Moreover, many producers in the UK are subsidiaries of overseas pharmaceutical corporations. Even so, the companies involved do form a recognisable industry, competing among themselves in the field of high-technology health care.

The outlines of such an industry began to emerge in the 1930s but became far more distinct after 1948 when the National Health Service (NHS) was set up. Official policies of actively encouraging the technological leaders – foreign as well as British – at the expense of the less adventurous followers, through its pricing and clinical testing rules for prescription drugs, allowed those comparative advantages to be built up. Vigorous competition flourishes also in marketing and in distribution to retail chemists and to other outlets for both ethical drugs and 'over the counter' remedies.

This article outlines some of the principal changes that have taken place from 1851 onwards in the systems of manufacture and distribution of these medicines. It also addresses the question of how and why the transformation occurred from low- to high-

technology production, from small to large scale, and from dependence on imports of advanced drugs to a high degree of self-sufficiency at home.

THE INDUSTRY'S ORIGINS 1851-1914

While the term 'pharmaceuticals' was used as early as the 1880s to describe the core products treated here, successive UK Censuses of Production from 1907 to 1935 classified them as 'drugs, medicines and medicinal products'. Since the first post-war census of 1948, the adjective 'pharmaceutical' has been included in the sub-group of 'Order V. Chemicals and allied industries'. The earlier terminology indicates that during the pre-1939 era, firms making these products fell into three, sometimes overlapping, categories.

The first group, comprising makers of galenical or simple compounds of vegetable substances such as aloes or ginger, served the many people in Britain who sought to avoid having to visit doctors for their ills and instead preferred self-medication. In earlier centuries, 'wise women' had often provided alternative health care with herbal remedies. That important role was hijacked by men once doctors and apothecaries began to offer for general sale their own pills and concoctions.[1] Few of these patent or proprietary medicines were in fact patented, but the owners kept their formulae secret.

Among the earliest of such products were Dr Patrick Anderson's Scotch Pills from the 1630s onwards. The most widely known eighteenth-century nostrum was Dr Robert James's Fever Powders, containing antimony and vigorously marketed by the

London wholesale chemists and publishers Newbery & Co, of St. Paul's Churchyard. By contrast, Dr Samuel Solomon's restorative Balm of Gilead, made of brandy and herbs, enjoyed a few decades of considerable popularity. Then sales plummeted after his death in 1819, mainly because he had not employed a reliable wholesaler.

In 1851, UK patent medicine firms had a combined home turnover of about £250,000.[2] [3] The market leader was Thomas Holloway in London, who that year produced for domestic sale some £25,000 worth of pills and ointment. Claiming to spend £20,000 annually on advertising world-wide, he sold to all outlets with a medicine licence. He had decisively overtaken the pills of James Morison, which for a while in the 1830s achieved annual turnovers of £65,000 but which had been discredited following all too many fatalities attributed to excessive pill doses.

As Table 1 shows, demand thereafter grew spectacularly for these and less well-known patent remedies. As real wages began to rise above the subsistence level from the early 1860s onwards, ordinary people increasingly spent on nostrums for improving or maintaining good health. In 1884 there were estimated to be between 800 and 1,000 makers of 4-5,000 such medicines in Britain, about 19,000 people being employed in their manufacture and distribution.[4] Six years later, according to a separate estimate, no fewer than 2,060 million – mainly digestive – pills were being taken annually in the UK, or one a week for every man, woman and child.[5] Half came from patent medicine manufacturers. The firm of Thomas Beecham, then the acknowledged leader, made 250 million pills in 1890, rising to 308 million in 1915 and close on 500 million in the early

1920s. Many of these firms advertised extensively; Beecham in 1890 spent over £100,000 on all forms of publicity.

The other 50 per cent of pills were made by the second group, the wholesale drug firms. Their pills were generic products, using the formulae from the British Pharmacopoeia, published since 1863 under the auspices of the British Medical Association. These firms dealt in a range of raw drugs and preparations, and extracted alkaloids, such as morphia, from vegetable sources. About the only chemicals they processed were alcohol and acetic acid. A few of their products could act effectively against specific illnesses, as for example quinine – made from cinchona bark – did against malaria, but most were intended to clear the bloodstream or ease pain, and thereby help to build up the body's resistance to disease.

Some of these wholesalers were very old-established 'universal providers' for the medical profession, dealing even in surgical instruments. They included Allen & Hanburys, founded in 1715, Howards of Ilford which dated back to 1797, and Thomas Morson of London, T H Smith of Edinburgh and May & Baker of Battersea to 1821, 1827 and 1834 respectively. They bought their - often imported – ingredients at drug auctions, principally in London. Their laboratories were in the main concerned with drug testing, but they did carry out some limited research: Allen & Hanburys made repeated attempts to improve the process of extracting cod liver oil. May & Baker as early as the 1880s was assisted by a scientist of King's College, London, in the development of new products such as a cod liver oil and iron compound.

The third group of firms was dominated by Burroughs Wellcome, a London company established in 1880 by two American entrepreneurs, Silas Burroughs and (Sir) Henry Wellcome. In three respects Wellcome, in sole charge from 1895, operated on very different principles from his more traditionally-minded rivals. He introduced a high standard of quality control, more sophisticated sales techniques – being the first in Britain to arrange personal calls on doctors and to distribute free samples – and laboratories specifically for primary research. The Wellcome Physiological Laboratory of 1894 developed sera and vaccines, most notably against diphtheria, while its chemical research laboratory (1896) evolved a range of fine (refined or specialised) chemicals, including a drug to treat leprosy. In 1914 the newly-established Wellcome Bureau of Scientific Research began investigating cures for a range of tropical diseases.[6]

The British company Evans Sons Lescher & Webb (later Evans Medical Ltd), founded in 1902 by merging earlier Evans wholesale drug firms in Liverpool and London, about that date began to make biological medicines for humans and animals; these included sera and antitoxins for diphtheria, tetanus and meningitis. It worked closely with Liverpool University Medical School, with whom it jointly administered the Incorporated Liverpool Institute of Comparative Pathology. The company took over the Institute as a branch when the latter was faced with closure in 1911.

The Production Census of 1907 (see Table 1) found that the combined output of these three groups, in the ‘drugs and medicines’ category, accounted for only one-third of

Table 1: Pharmaceutical Production. UK 1851-1992

	Proprietary medicines (£mns)	Other (£mns)	Total Pharmaceutical (£mns)	Total UK Manufacturing Production (£mns)	Pharmaceutical/ Total UK Manufacture (%)
1851	0.2				
1875	0.6				
1900	1.5				
1907	1.5	3.4	4.9	1,428	0.34
1924	6.7	9.7	16.4	3,336	0.49
1935	7.9	11.8	19.7	3,034	0.65
1951	21.1	88.6	109.7	15,287	0.72
1963	na	na	234.9	27,826	0.84
1970	na	na	512.6	46,304	1.11
1981	na	na	2,618.1	163,937	1.60
1992	na	na	8,531.8	318,568	2.68

Source: Proprietary medicines 1851-1907. Based on patent medicine duty returns (Inland Revenue).
Pharmaceuticals 1907-70. Business Statistics Office, *Historical Record of the Census of Production 1907 to 1970* (H M Stationery Office, London, 1978).
1981-1992. Censuses of Production for those years (H M Stationery Office, London, 1983 and 1994 respectively.)

Note: na = not available.

one per cent of the UK's manufacturing production. Less than a third comprised proprietary medicines, the rest being fine chemicals and allied products. Most firms traded internationally; exports that year came to nearly 40 per cent of their total output, or almost £1.9 million out of £4.9 million. As retained imports were valued at less than £1.1 million, the industry was a net contributor to Britain's balance of trade.

However, many of these imports were of more advanced drugs, which came largely from Germany, then the world leader in this field. German scientists were carrying out fundamental research on a large scale, often in conjunction with university departments. The most celebrated scientist was Paul Ehrlich, who effectively combined physiological with synthetic chemistry to create a new science of chemotherapy: in those non-intrusive days defined as treating diseases with chemical substances that attacked the harmful parasites without adversely affecting the body as a whole. Ehrlich in 1909 discovered the synthetic anti-syphilitic drug *Salvarsan*, marketed by the German firm Hoechst. German firms exerted weight as dominant members of international cartels for a number of widely-used chemicals.

By 1914, the drugs and medicine industry in the UK also included a number of foreign-owned firms, including Hoechst UK Ltd. Although the Patent Act of 1907 gave foreigners protection only if they worked their patents in Britain, German pharmaceutical firms somewhat half-heartedly set up manufacturing branches, using obsolete plant brought over from home.[7] Likewise, the Swiss Hoffmann-La Roche made only slow and limited progress in Britain after arriving in 1909. US firms were then technologically

behind the Germans and came a poor third to Germany and Britain in world drug exports. The activities of the UK branches of Parke Davis (1902) and United Drug (1912) were on a relatively modest scale.

Most member firms sold in Britain to chemists and druggists, whose professionalisation was well under way by 1907. Legislation in 1852 had provided for registration of pharmaceutical chemists and an Act of 1868 for qualifying examinations to be set by the (Royal) Pharmaceutical Society of Great Britain, formed in 1841, and for the compilation of a register of chemists and druggists; in 1905 they totalled 15,000.[8] Their work was regulated by the Sale of Food and Drugs Acts of 1875 and 1899.

By the 1890s, a number of multiple chemists' chains had been established, such as Boots of Nottingham and Taylor's Drug Company of Leeds, later part of the Timothy Whites group which in 1968 merged with Boots, to offer cut-price medicines. Their rivals set up the Proprietary Articles Trade Association (PATA) in 1896 to combat price-cutting, and the controversy over prices rumbled on for decades. Many were also members of the London Wholesale Drug and Chemical Protection Society of 1867, subsequently the Drug Club (1891), governing relations with raw drug suppliers and brokers.

For deliveries to retailers, wholesalers used common carriers, sending small consignments through the royal mail; some undertook to fulfil orders on the day of receipt. Many wholesalers started as regional operators, but the leading London firms such as Barclay & Sons (1770) and Sangers (1803) began national distribution once

Britain had a comprehensive railway network. These and other large wholesalers such as Evans built up a considerable export trade, through the major ports, most notably London and Liverpool. Speedy responses to orders became increasingly demanded as the number of drugs, especially those required in emergencies, grew, and the telephone and overseas the cable proved useful here. All these interlocking production and distribution arrangements were to be seriously disrupted in 1914 by the arrival of what soon turned into a total war.

FIRST WORLD WAR AND INTER-WAR PERIOD 1914-39

The outbreak of war in 1914, while stimulating the demand for patent medicines – often used as placebos to ease stress – brought grave problems to the other sectors of the industry.[9] Heavy exporters, such as May & Baker of bismuth and mercury salts, found their trade decimated when the government, to safeguard home supplies, banned the export of many fine chemicals. London rapidly declined as the world centre of trade in raw drugs. Even more crippling were the shortages of many synthetic and other advanced pharmaceuticals after the cessation of imports from Germany.

An official Committee on the Supply of Drugs set about identifying those available from alternative sources, and the ones whose manufacture would have to be organised from scratch at home, most notably *Salvarsan* and the local anaesthetic *Novocain*. As Britain's technological leader, Burroughs Wellcome offered to the government its entire productive capacity; within a year it had developed a substitute for

Salvarsan, vital at a time when the numbers of civilians and soldiers infected with venereal disease were soaring. It also manufactured versions of aspirin and of *Urotropine*, used in typhoid cases. The Wellcome Physiological Laboratory made sera and vaccines for the army, while its scientific research bureau stepped up work on antidotes to tropical diseases. Its North American and Australian branches contributed much-needed supplies.

The Royal Society urgently enlisted the aid of university chemical laboratories, which embarked on the production of essential drugs such as *Novocain* and other anaesthetics. From 1917 onwards manufacture was transferred to commercial firms, including Boots and Parke Davis. By then the largest chain of retail chemists in Britain, Boots began to extend its manufacturing capacity from proprietary to pharmaceutical drugs, thanks to the single-minded efforts of the founder Jesse Boot. In 1915 he had set up a fine chemicals department, employing a research team poached from Burroughs Wellcome. Within three years Boots had launched products ranging from antiseptics and anaesthetics to aspirin and saccharin, as well as the tonic *Sanatogen*. Boots thus placed itself on a par with the longer-established manufacturers in the industry.

Evans' wartime activities, while not known in any detail, included a crash programme for drugs. By 1916 it had in operation a new and extensive chemical works, where in the following year it was making its own brand of *Salvarsan*. In 1914 May & Baker began production of the anti-malarial quinine, and shortly afterwards entered the field of synthetic organic arsenicals through an agreement with Poulenc Frères of Paris to

market the latter's *Salvarsan* equivalent. Two years later, having recruited a scientist formerly with Burroughs Wellcome, it started up production of this drug itself.

By the armistice of November 1918, these and other British firms could claim to have overcome, despite plentiful difficulties, the problem of replacing the range of German advanced drugs. However, although the demands of war had introduced many of them to novel techniques and had stimulated in-house research, most were reluctant to remain in these new areas as they feared the renewal of post-war competition from lower-cost German imports. In spite of the efforts made by the Drug Club, they failed to set up an industry-wide research association which would have undertaken collaborative work on common scientific issues. They thus lost out on funds from the Department of Scientific and Industrial Research, created in 1917 to promote applied research throughout industry.

The 1914-18 war and the UK's subsequent economic troubles did not lead to the creation of an industry dominated by a few giant companies. Instead, firms remained small and family-run. Those business leaders who might have effected large-scale mergers had their attention elsewhere. Jesse Boot had offered to sell his Boots firm to Selfridges & Co. Ltd., which had a pharmacy department, and did so in 1920 to the US-based United Drug Company, whose Rexall pharmacies were beginning to invade Britain. Henry Wellcome was heavily involved in an internal reorganisation; in 1924 his firm became part of the newly established Wellcome Foundation. May & Baker, by then claiming to be the UK pharmaceutical leader, was occupied in consolidating its links with

Poulenc Frères. The great national inter-war combines, such as ICI, Unilever and Associated Electrical Industries, each had workforces well in excess of the total number of those manufacturing drugs and medicines. Of the 200 firms in the latter industry in 1935, only 13 employed more than 500 people. The three leading companies accounted for only 18 per cent of total output.

However, individual firms were tending to build on their Research and Development (R & D) expertise they had acquired in the war. The Wellcome Foundation promoted further innovations in the field of vaccines and sera. Allen & Hanburys expanded its laboratory, and in 1923 began production of insulin jointly with the manufacturing side of British Drug Houses, founded in 1908 as a wholesaler for private chemists. Joseph Nathan & Co., then part of the food industry as maker of the Glaxo milk powder, in 1919 recruited the scientist (Sir) Harry Jephcott to run a small laboratory. He developed types of vitamins, both as additives to the milk products and as medicines in their own right. In 1935 he established Glaxo Laboratories Ltd., which soon began to manufacture liver extract for anaemia.

The most impressive pharmaceutical innovations between the wars came from May & Baker, using French know-how from Poulenc. In 1934 Rhone-Poulenc, as it had become, acquired control of May & Baker, but used its UK laboratories to develop the first sulphonamide drug, *M & B 693*, a pioneer in treating bacterial pneumonia. May & Baker tested this drug in the Middlesex Hospital's laboratory and also in that of the Pharmaceutical Society.[10] ICI initiated a programme of pharmaceutical research in 1936,

as part of a diversification plan out of dyestuffs into the discovery of new drugs. In 1944, it set up Imperial Chemical (Pharmaceuticals) Ltd., although for some years the latter's work was hampered by inadequate finance.

Meanwhile Beecham, the only UK patent medicine maker of note which transformed itself into a pharmaceutical giant, was taking the first steps in this lengthy transition process. After the ending of family control and its first registration as a limited company in 1924, its new entrepreneurs set up a laboratory and two years later launched the analgesic Beecham's powders. The chairman, Philip Hill, thereafter acquired a number of household goods and drugs firms, including those making veterinary medicines. As consultants he engaged scientists of the calibre of (Sir) Jack Drummond and Sir Charles Dodds. Having unsuccessfully bid for research-based companies such as May & Baker (1928) and Boots on its return to UK ownership (1933), in 1937 he endowed the Beecham laboratory in the Royal Northern Hospital, London, for product testing and R & D. In 1938 he purchased Macleans, of toothpaste and stomach powder fame, which had some valuable research facilities.

To allay fears of the UK industry that foreign competition would be damagingly revived after the war, in 1921 the government replaced wartime controls with a key industry duty on imports of synthetic and other fine chemicals; many overseas firms therefore opened branches in the UK. The Swiss CIBA had already established a laboratory here in 1919, and Sandoz came to Britain two years later. American arrivals included Wyeth (1926), Merck Sharp & Dohme (1927), W.R. Warner (1932) and Eli

Lilly (1934). Smith Kline & French entered via an agency agreement with the British A.J. White Ltd., in 1927, acquiring it in 1956. After the wartime expropriations, German firms were reluctant to set up branches again, and instead marketed their drugs through agents.

By 1939 Britain could be said to have a pharmaceutical industry, with member firms interacting with one another in a more structured way than in the past. Top managers regularly met on specialist committees of the Chamber of Commerce or in the former Drug Club, since 1930 the Wholesale Drug Trade Association. Even so, closer collaboration proved elusive. Two attempts after 1918 to form a joint research body failed as firms were reluctant to share their secrets. Instead, they competed in all aspects except price, most notably in intense publicity and maximising the range of products on offer. UK advertising outlay in 1935 on 'medical goods', including health salts and tonic wine, came to nearly £5.8 million, or 37 per cent of their manufacturers' net sales, exclusive of duty.[11] These arms-length attitudes came under pressure when war broke out again in 1939.

SECOND WORLD WAR AND ITS AFTERMATH 1939-1950s

Britain's pharmaceutical industry was not caught unprepared at the onset of the new war as it had been twenty-five years earlier. In 1938 the Medical Research Council had compiled a list of essential wartime medicines, such as pain-reducing analgesics and antipyretics to combat fevers. From 1941 onwards the Directorate of Medical Supplies in

the Ministry of Supply both oversaw the supply of drugs and arranged for the output in Britain of those most needed. Producers, who had already devoted scarce resources to analysing German drugs, were unhappy at being expected to bear the development costs of possible substitutes.

A synthetic drug to treat malaria being a very urgent requirement, early in 1940 *Mepacrine* was developed as identical with the German *Atebrin*. At the end of 1941, the Japanese conquests in the Far East deprived the allies of cinchona bark for quinine, and with official encouragement May & Baker, ICI and Boots collaborated to make improved anti-malarial drugs, notably ICI's *Paludrine*. Once the Far East became a major theatre of war after 1943, a vaccine against scrub or mite-borne typhus was evolved within six months.[12]

Two other pharmaceutical products received high priority. One was sulphonamide, of which companies at home tripled their output between 1942 and 1945. The other was penicillin.[13] In 1941 Britain's five leading pharmaceutical firms, namely Boots, British Drug Houses, Wellcome, Glaxo and May & Baker, jointly set up the Therapeutic Research Corporation (TRC), to co-ordinate and expand their research capabilities. ICI became a member in the following year. A major task of the TRC was to achieve the government target of meeting the armed forces' entire needs for penicillin, at a time when production still took the form of slow surface culture in pilot plants. At last, official subsidies became available. From December 1943 onwards, six new factories were built with £2 million of government money. As a result, whereas in 1944

penicillin supplies from the US exceeded British output tenfold, by the end of the war in 1945 production in the UK had overtaken US imports.

British scientists, companies and the government have been criticised for letting slip the opportunity to develop the far more efficient deep-fermentation process for penicillin. However, it was American enterprise and know-how that achieved the critical breakthrough, which allowed the drug to be mass produced; for a number of years British companies using the new process had to pay royalties to the US companies concerned. The fundamental truth was that for the beleaguered Britain, the paramount aim was 'to win no matter what the cost'.[14] As the historians of Glaxo put it,

> Critics under-estimate the desperate pressure [in the UK] for other drugs to be produced with the limited available facilities, and also neglect the difficulties of the war economy haunted by bombs, manpower shortages, lack of materials and accommodation.[15]

Instead, other wartime successes of the industry deserve attention. Glaxo, building on its expertise in vitamins, produced vast quantities of Vitamin B_2 to enrich imported white flour which lacked the vitamin but took up less shipping space than the whole-wheat variety. In 1914, all British insulin manufacturers combined to maximise insulin yields from the limited quantities of pancreas glands then available. Inter-firm collaboration and improvisation allowed output of pharmaceuticals to continue when plants were damaged by bombing. Raw material supplies, a constant worry for all firms, were allocated by a distribution system agreed between the industry and the Ministry of

Supply, and generally held to be both effective and fair. In 1940, on government prompting, a Pharmaceutical Export Group of 27 – later more than 100 – companies was established, to maintain the flow of exports: the annual value of these grew from £3.3 million in 1939 to £4.5 million on average over the next five years. The Finance Act of 1944 at last actively encouraged R & D by allowing such expenditure to be fully offset against tax.

As Table 1 makes clear, the pharmaceutical industry's output grew over five-fold in money terms between 1935 and 1951, or more than two and a half times allowing for inflation. Its stake in UK manufacturing production rose marginally from 0.65 to 0.72 per cent. The leading firms were beginning to pull ahead at the expense of a long 'tail' of lower-technology followers; the proportion of the industry's output from the three largest companies increased by 1951 from 18 to 27 per cent, with workforces averaging 4,400 as against 1,400 in 1935. While 192 of the total population of firms made pharmaceutical *preparations*, of which the top three firms made only 19 per cent, no more than 18 made the technologically more advanced pharmaceutical *chemicals*, the top three contributing 66 per cent of output.[16] To signify the industry's growing cohesion, in 1948 the Wholesale Drug Trade Association was re-named the Association of British Pharmaceutical Industry, and soon merged with the Pharmaceutical Export Group of 1940. In 1961 it became the Association of the British Pharmaceutical Industry.

In the 1950s Britain was probably second to the US in the size of its pharmaceutical workforce, but no data exist for Switzerland or West Germany. The UK

share of large plants, with over 1,000 employees, was 33 per cent of the total, compared with America's 44 per cent. It was during that decade, one of substantial US direct investment in European industry generally, that American companies became significant. The 25 firms between them contributed nearly a quarter of Britain's total pharmaceutical output, almost all antibiotics except penicillin, and a range of other ethical drugs and household products. They supplied nearly a third by value of the drugs purchased by the NHS.[17] There were also three Swiss-controlled firms and one (May & Baker) partly financed by French capital.

BEGINNINGS OF THE INDUSTRY'S TRANSFORMATION 1950s-1970

The rate of structural change in Britain's pharmaceutical industry accelerated markedly in the next few decades. A principal cause was the government's strategy for both pricing and drug safety, which astutely used market forces that induced firms to adopt more advanced technology.

As a single (monopsonistic) buyer of prescription drugs for the NHS, the Department of Health aimed to keep the cost to the taxpayer as low as possible, without thereby impeding the flow of new and improved drugs. Under the Voluntary (in 1978 renamed the Pharmaceutical) Price Regulation Scheme from 1957 onwards, it fixed drug prices at levels to allow manufacturers a reasonable return on investment.[18] Its formula encouraged expenditure on innovative R & D that promised to yield good returns, and large exporters received added incentives. It also penalised firms that were merely

followers. A number of the latter went under, but the foreign companies, which had previously become used to poaching for their overseas laboratories well-trained scientists coming out of UK universities, were pressured into carrying out more of their R & D in Britain.

Likewise, after a tragic mishap, the government strengthened procedures for the testing of drugs, in a way that benefited the more progressive firms. After the sedative *Thalidomide*, made by the Distillers Company Biochemical, was in 1962 found to be responsible for birth defects, a Committee on Safety of Drugs was set up, beginning work two years later. Its members were academic experts on behalf of the industry. In 1967 the Sainsbury committee on the relationship of the industry with the NHS recommended that quality control and testing should be undertaken by an independent official body; the Committee on Safety of Medicines took over in 1971.[19] Because these successive committees adopted the rigorous standards of the industry leaders, often with American regulations in mind, many surviving smaller firms either ceased to develop ethical drugs or were taken over by more powerful rivals.

In consequence, the number of new drugs launched in Britain fell sharply. However, the proportion of innovative drugs rose from 25 to 70 per cent, at the expense of local or derivative drugs. The former represented a higher percentage of the total flow than in either the United States or France. These deliberate official policies helped to transform the shape of the whole industry.

From 1957 onwards ICI's pharmaceutical division, having been given greater autonomy, stepped up its R & D effort, discovering the anaesthetic *Fluothane* and the anti-convulsant *Mysoline*. By that year, the three largest indigenous companies all had very gifted entrepreneurs who took full advantage of the opportunities created by government.

Sir Harry Jephcott, chairman of Glaxo from 1946 onwards, invested heavily in R & D, by 1955 achieving the synthesis of cortisone and launching a new generation of immunological drugs. He also built up overseas markets across the world except in the US and Japan where he was hampered by earlier agreements. Concerned as they were about the encroachment of foreign rivals, between 1958 and 1967 he and his successor acquired Allen & Hanburys, Evans Medical and British Drug Houses among others, so as to create a British giant capable in due course of challenging the world leaders.

The second entrepreneur was Sir Michael Perrin, a chemistry graduate who in 1953 became chairman of the Wellcome Foundation. Although Sir Henry Wellcome had in his later years promoted some useful innovations, a lack of day-to-day control had led to a period of drift, exacerbated after he died in 1936 by a cash shortage resulting from his substantial death duty bill. It was the largely autonomous American branch which until the 1950s kept the company afloat by earning nearly three-quarters of the profits and developing new products itself. Perrin now ploughed into R & D at home no less than 70 per cent of all Wellcome's profits up to 1970, and like Jephcott vigorously opened up markets overseas.

Unlike the other two men, Leslie Lazell of Beecham was not a trained scientist but an accountant, originally with the R & D minded Macleans. Philip Hill had died in 1944 after authorising the creation of a central laboratory, but his successor as chairman unwisely diversified into low-earning food companies. When Beecham's profits slumped, Lazell in 1951 was appointed chief executive. By skilful marketing, he built up the profits of household products such as Brylcreem and Lucozade so as to finance a massive R & D programme, costing £5 million a year by 1970. In 1954 he introduced a plan to make semi-synthetic penicillins; these came on stream from 1959 onwards, among the best known being *Penbritin*. He also invested heavily overseas, at first in the US and later in Europe.

Equally far-reaching developments were taking place in pharmaceutical wholesaling and distribution. Improved punch card systems helped to cope with the ever higher throughput and stocks arising from the rapidly expanding range of ethical drugs. Now that chemists were dispensing a greater volume of prescriptions, they demanded more frequent deliveries of medicines. A further impetus to reorganisation among distributors was provided by successive official steps to free up competition. In 1956 the government outlawed restrictive trade practices, and eight years later abolished individual resale price maintenance.

To protect their interests, regional trade associations amalgamated in 1966 to become the National Association of Pharmaceutical Distributors, from 1991 the British Association of Pharmaceutical Wholesalers. Not until 1970 did the Restrictive Practices

Court give a ruling that administered prices of medicines were legal. Glaxo's acquisitions since 1958 of Allen & Hanburys and other companies had brought extensive wholesaling interests into the group, and in 1966 these were hived off into the newly-established Vestric Ltd. The latter created a network to cover much of Great Britain, and set up custom-built warehouses as hubs of rationalised distribution areas.

MEETING GLOBAL CHALLENGES 1970-2000

During the final three decades of the twentieth century, Britain's pharmaceutical leaders increasingly looked overseas for their future growth. A basic problem for all of them was their small domestic market. As late as the 1990s, only $3\frac{1}{2}$ per cent of the world's pharmaceutical sales took place in Britain: a far lower percentage than the 33 per cent in the US, 17 per cent in Japan and 9 per cent in Germany. The UK leaders therefore had to compete with their overseas rivals globally, despite the latters' advantages through larger markets and greater financial power. In 1982, no UK leader was anywhere near the top of the world pharmaceutical sales league. Glaxo was 18th and ICI, Wellcome and Beecham 23rd to 25th respectively; Boots was only 42nd.[20]

Glaxo responded to this problem by selling off the 30 per cent of its assets unconnected with ethical medicines. It was greatly assisted by having, from 1981 onwards, as its best-selling drug *Zantac*, an anti-ulcerant which contributed two-fifths of its turnover, and by ranking fifth in the world market for antibiotics. In 1978 it was at

last able to invest directly in the US. By 1994 its US stake comprised 43 per cent of its turnover, as against 36 per cent from Britain and continental Europe.

Beecham, on the other hand, continued to rely on the 70 per cent of output in non-pharmaceutical products to help finance R & D and further expansion. Its attempt in 1972 to acquire Glaxo, which attracted a counter-bid by Boots, foundered after the UK Monopolies and Mergers Commission rejected its argument that only a company with substantial assets could compete in R & D with overseas rivals. The Commission's view was that British companies suffered no handicap from their relatively small size, since research teams of any reasonable scale could throw up worthwhile ideas.[21] Beecham's subsequent policy of further diversification only led to unsatisfactory results. After a radical change in direction, in 1989 it amalgamated with the American company Smith Kline Beckman, partly to spread the escalating costs of R & D. Moreover, marketing costs could be shared, as the SmithKline Beecham combine would become the world's second largest supplier of over-the-counter proprietary medicines.

As for ICI, whereas in the late 1980s pharmaceuticals represented only 10 per cent of the group's total turnover, the success of its anti-hypertension drug *Tenormin* made the pharmaceutical division into ICI's highest profit earner. In 1993 the ICI bioscience group, consisting of the pharmaceutical, agrochemical and specialities division was split off into Zeneca plc. Four years later, Zeneca merged with Astra of Sweden which made the popular anti-ulcer drug *Prilosec*.

Wellcome, while still relying on its US subsidiary for much of its profits, in 1981 launched in Britain its anti-viral *Zovirax,* the most successful drug in its history. Then in 1986 Wellcome plc was floated in London, the previous foundation thus becoming a commercial organisation. However, it relied heavily on *Zovirax* and on *Retrovir*, a treatment for HIV and AIDS, and a sequence of disappointing clinical trials failed to turn up satisfactory replacement drugs. In 1995 Glaxo made a successful hostile bid for the company, making the merged Glaxo Wellcome into the world pharmaceutical leader in terms of sales, just ahead of the American Merck. Also that year Rhone-Poulenc took over Fisons, which had already disposed of most R & D operations to overseas buyers, and Boots sold its prescription drug-making interests to BASF of Germany. In one year, therefore, the six top British companies were reduced to three.

In 1998 SmithKline Beecham, then ninth in the world pharmaceutical league, opened merger talks with American Home Products, manufacturer of some useful brand-name drugs. However, these were overtaken by a proposal to merge SmithKline Beecham with Glaxo Wellcome. Huge economies were forecast, both in R & D and in marketing, for example as Glaxo Wellcome's anti-ulcer *Zantac* could be sold jointly with SmithKline Beecham's *Tagamet*. Because important management questions proved impossible to resolve, this most ambitious of all the industry's merger proposals was called off.

For pharmaceutical distributors, the process of change was no less rapid. The Medicine Act of 1968 had required wholesalers to obtain licences, a move that

encouraged new entry by outsiders who could well have been less committed to the industry. Particularly affected were the 'comprehensive' wholesalers, standing ready to supply all the listed drugs, many of which were slow movers and therefore more expensive to stock. However, some firms responded positively by seeking greater efficiency. UniChem had been founded in 1938 as a supplier of independent pharmacies and had grown steadily ever since. In 1975 it was the first British wholesaler to introduce the computer system WOLF, or warehouse on-line facility.

When resale price maintenance at the wholesale level broke down in 1979, suppliers attempted to defend themselves through offering favourable terms to chemists who bought all their requirements from them. One casualty of this trend was Sangers, which sold virtually all the businesses it had acquired since 1803 and then closed. A major response, however, was increased merger activity. In 1985 Vestric was sold to AAH plc, originally an anthracite firm with a small health services division. The combine thus created was developed into the first truly national wholesaling organization. Ten years later, it was acquired by a German firm in the same line, Gehe AG. In 1997 UniChem merged with Alliance Santé to create Europe's second largest pharmaceutical distribution company, all customers of which would have access to French, Italian and Spanish, as well as British, drugs. If international amalgamations at the manufacturing level were becoming more common, distribution combines over frontiers were clearly expected to yield considerable economies of scale.

In the latest Census of Production report, that of 1992 (see Table 1), the total value of the pharmaceutical industry's output was seventeen times that of 1970. Its contribution to national manufacturing output had over those years more than doubled. Whereas the industry had spent only $2\frac{1}{2}$ million in 1949 and £22 million in 1970 on R & D, that expenditure rose in 1995 to £2,000 million, nearly a quarter of the country's total R & D outlay. Of the world's top twenty prescription drugs in 1995, five had been discovered and developed in British laboratories, as had ten of the top thirty-five drugs.[22]

The UK's revealed technical advantage in pharmaceuticals is measured by the national share of patenting in this sector relative to the national share of all non-US patents. If an industry is just pulling its weight technologically in an economy's overall industrial activities, the ratio will be one. The ratio for UK pharmaceuticals was 0.61 in 1890-6. It then declined to 0.31 in 1920-4 but recovered in 1940-59 to 0.62. Then in 1973-7 it rose to 1.15 and in 1987-90 was as high as 1.92, nearly double the 1.06 for Germany.[23]

As noteworthy was Britain's international trading advantage in pharmaceuticals. In the mid-1990s their exports were worth no less than £6,000 million, second in size only to North Sea Oil. The pharmaceutical trade surplus with the rest of the world was as high as £2,000 million. The industry employed nearly 75,000 people directly, and about a quarter of a million indirectly. A large proportion of this output, employment, R & D and overseas trade came from the subsidiaries of foreign companies, and the present survey should properly address the consequences for the industry and the British

economy of this overseas presence in the UK. However, the Association of the British Pharmaceutical Industry and the Office of Health Economics possess no data, and this information gap remains to be filled.

CONCLUSION

The pharmaceutical industry in Britain has thus progressed at a rate and in directions that could not have been foreseen in 1851. Substances of vegetable, or occasionally animal, origin have been very largely swept aside as its tools, in favour of synthetic drugs. Named 'magic bullets' by Paul Ehrlich, those have over the twentieth century improved out of all recognition in their capacity to target specific disorders, while causing as little harm as possible to the patient's system.

Yet by the millennium, the industry's capacity to deliver a succession of really novel 'blockbuster' drugs had tended to slow down. Recently, each of the top ten global firms had been introducing less than one such pioneering drug on average every two years. If more and ever larger-scale mergers did not always speed up this flow, an alternative course was that of outsourcing, or purchasing highly specialist know-how from outside. In the mid-1990s, such bought-in fruits of research made up nearly one-fifth of the industry's total R & D expenditure.

In the increasingly vital area of biotechnology, a number of smaller – mainly American – firms had sprung up since the 1980s, particularly concerned with isolating the molecules that could regulate the body's metabolism and eliminate harmful

organisms. SmithKline Beecham had been the first giant in the industry to grasp the value of such work, and linked up with the Human Genome Sciences Co. This 'genome' research, into the composition of people's genes, has gone hand-in-hand with 'combinatorial chemistry', to assemble in the most effective way groups of health-providing molecules. In 1994 Zeneca bought into certain disease management and technology firms. Glaxo, in the wake of its merger with Wellcome, followed suit by acquiring its own biotechnological subsidiary.[24]

The industry's overall task in the past, like that of the NHS since 1948, has perforce been very largely that of curing ills, at the expense of working towards forestalling them. An opportunity to develop the latter function is now given by predictive medicine, or using diagnostic methods to monitor and treat patients, especially those predisposed to certain diseases. When the chairman of Glaxo Wellcome mused on his company's future name being changed to 'Glaxcare', he was looking forward to a time when the industry might well become a true partner, rather than largely a handmaid, in the labour of delivering long-term health care to the nation and to the world.

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