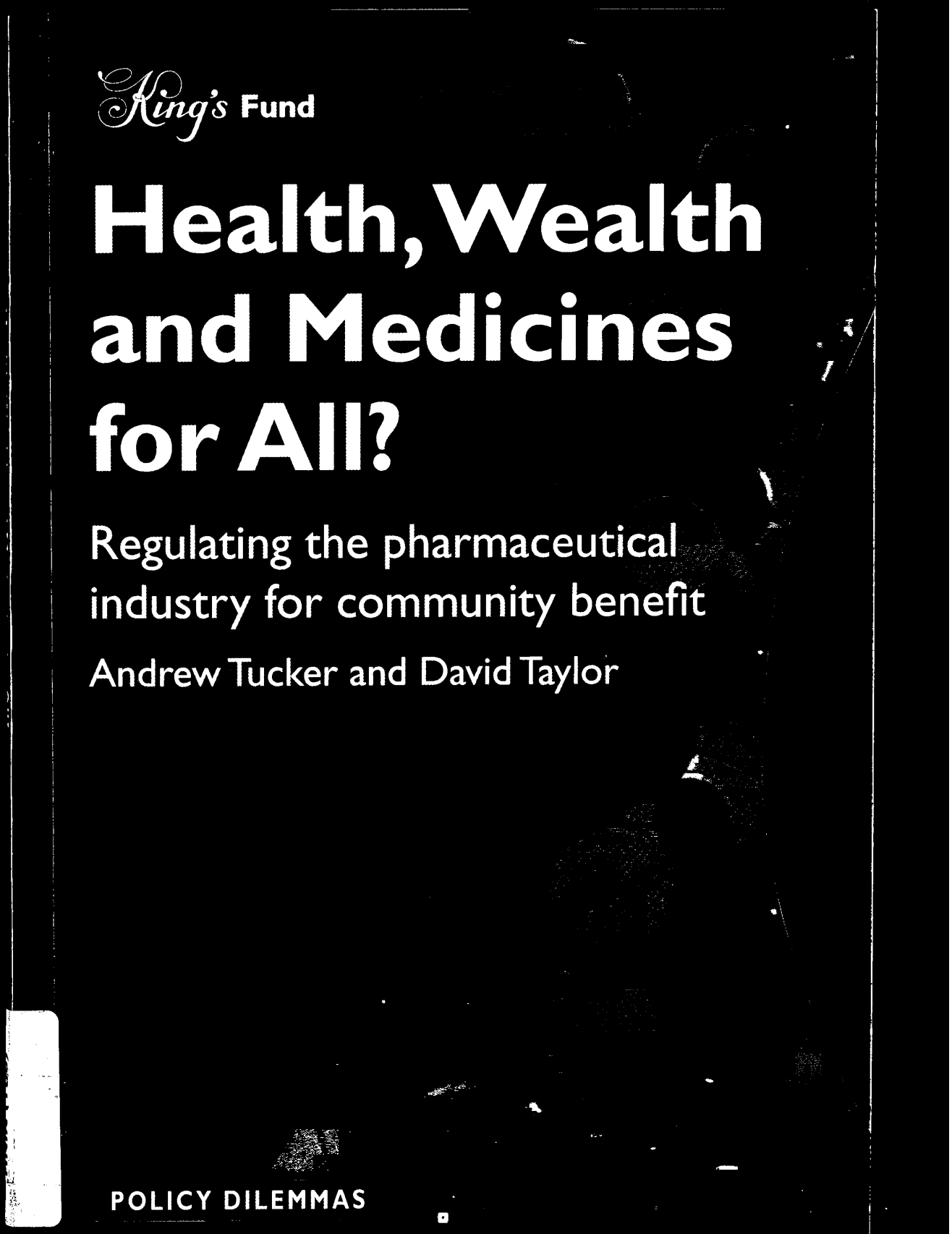
King's Fund

Health, Wealth and Medicines for All?

Regulating the pharmaceutical industry for community benefit

Andrew Tucker and David Taylor



POLICY DILEMMAS

Health, Wealth and Medicines for All?

Regulating the pharmaceutical industry for community benefit

Health, Wealth and Medicines for All?

Regulating the pharmaceutical industry for community benefit

Andrew Tucker and David Taylor

King's Fund

Published by
King's Fund Publishing
11–13 Cavendish Square
London W1G 0AN

First published 2000

ISBN 1 85717 431 3

A CIP catalogue record for this book is available from the British Library

Available from:
King's Fund Bookshop
11–13 Cavendish Square
London
W1G 0AN
Tel: 020 7307 2591
Fax: 020 7307 2801

Printed and bound in Great Britain

Any views expressed in this book are those of the authors and not necessarily those of the King's Fund.

Contents

Chapter 1

Introduction

From the Middle Ages onwards the production and supply of medicines across Europe has been subject to a growing network of statutory control. This was initially because of the toxicity of pharmaceuticals, and the desire of communities and their leaders to minimise poisoning risks by trying to ensure appropriate preparation and administration. More recent motives for regulatory intervention in the pharmaceutical sector include limiting health care costs, and the intention of government and other agencies to promote better standards of clinical care.

The pharmaceutical sector today is subject to a web of regulations designed to promote and protect the public's interests in the production and supply of medicines, along with those of professional, industrial and other stakeholders. One of the latest additions to the panoply of official bodies involved in the regulatory process is the National Institute of Clinical Excellence (NICE), set up in 1999 to provide recommendations on the clinical and cost-effective use of medicines within the NHS in England and Wales.

Pharmaceutical regulations take the form of both supply-side and demand-side measures. A key UK example of the former is the Pharmaceutical Price Regulation Scheme (PPRS), the terms of which are negotiated between the Department of Health and the Association of the British Pharmaceutical Industry. Since the 1950s it has served to limit pharmaceutical company costs and returns in relation to the supply of NHS medicines. Examples of demand-side regulation include the introduction of cash-limited prescribing budgets in primary and secondary care, prescription charges, and the 'blacklisting' from GP supply to NHS patients of some products.

Issues relating to medicine provision are often highly contentious. For example, the early decision of NICE against routine NHS use of the influenza treatment Relenza in the winter of 1999/2000 was criticised by some commentators, and supported by others. Fears that less advantaged people will not be able to obtain adequate access to treatments for conditions such as cancer have frequently been reported. Pharmaceutical prices and profits are also a matter of recurrent public concern, as are problems associated with side effects of medicines. Public, professional and political concerns about the prices and addictive potential of benzodiazepine tranquillisers had an important impact on attitudes towards the pharmaceutical sector during the 1970s and 1980s.

This book reviews medicines and allied regulation in the UK, and the growing influence of European Union law on national provisions. Comparisons with countries such as the USA are also made. The text is divided into:

- an overview of the evolution of the UK pharmaceutical market, and its control
- a more detailed description of the Pharmaceutical Price Regulation Scheme and other supply-side interventions, such as the regulation of pharmaceutical promotion
- a section on NHS 'demand-side' developments relevant to medicine spending and use, such as the formation of primary care trusts (in England) and NICE
- a concluding analysis relating to the future of medicines regulation in the UK and the European Union, where a major review of the medicines licensing process is due to take place in 2001. Areas where further research and analysis is needed to support policy decisions are identified.

Changing relationships between the professions and government are a key driver of new approaches to controlling the supply and use of

pharmaceuticals. Others include economic globalisation, consumerism in health care, and technological changes. As well as computerisation and increasing use of the Internet, these last now encompass the development of genomics-based diagnostics and treatments. Such factors will (alongside developments in areas such as e-commerce) fundamentally alter the nature of the pharmaceutical products and services available in the next century, and the challenges faced by regulators. They should also open up new opportunities for public benefit and increased human well-being, which, ultimately, is the purpose of all regulatory interventions.

Against this background a key objective of this book is to identify and discuss issues relating to the public's sometimes conflicting interests in the efficient, low-cost provision of old and new medicines, and in supporting the existence of a strong, profitable and innovative pharmaceutical industry in this country and abroad. The national policy dilemmas associated with the tensions between these goals are explored, as is the role of pharmaceutical sector regulation in the wider context of world-wide health and wealth improvement.

Chapter 2

The evolution of pharmaceutical regulation

Modern approaches to the control of the pharmaceutical industry and the licensing of medicines stem mainly from reactions to the Thalidomide tragedy, which occurred at the start of the 1960s (see Box 1). But the roots of pharmaceutical sector regulation stretch back far further. One of the earliest known written codes of medicine quality control in Britain was the Ordinances of Guild of Pepperers of Soper Lane in 1316.[1] This set out the terms for distributing imported drugs and spices. It prohibited apothecaries (and others) from mixing wares of different origins, and banned the adulteration of goods and the falsification of their weight by wetting.

Over subsequent centuries the apothecaries developed a strong trade guild. Its members both compounded medicines and supplied them directly to the public. This was in marked contrast to the situation in the rest of Western Europe, where a stricter division between medical practitioner and pharmacist roles has existed ever since Arabian approaches to medicine were introduced in the early Middle Ages.

In today's terms the British apothecaries acted as both community pharmacists and general medical practitioners. It was not until the mid-19th century that they split: one half joined with the surgeons and physicians (whose London Royal College was established in 1518 by Henry VIII) to form the unified medical profession; the other half linked with the chemists and druggists, to form the pharmaceutical profession.

The foundation of the Pharmaceutical Society in 1841 was an important step in this second process. From then through to the

Box 1: The Thalidomide tragedy

Thalidomide went on sale in Europe in 1956. It rapidly achieved high-volume sales as a sleeping aid and as a treatment for vomiting in early pregnancy. Its popularity was based on its prompt action, lack of hangover effects and apparent safety.

In 1961, a sudden rise in the incidence of unusual malformations occurred in West German babies. Whereas no cases had been reported in the ten years between 1949 and 1959, there were 477 cases in 1961 alone. In the UK over 400 similar cases were reported in the period 1959–61. Thalidomide was identified as the cause. This notorious event (from which the US public was protected, apparently because of the Food and Drug Administration's more rigorous approach to medicine licensing) precipitated radical changes in public attitudes to medical innovation, and political policies on pharmaceutical sector regulation.

In the UK a joint sub-committee of the English and Scottish Standing Medical Advisory Committees met in 1962 under the chairmanship of Lord Cohen of Birkenhead. It made a series of recommendations, including a call for the immediate establishment of a Committee on Safety of Drugs. This came into operation in June 1963, charged with reviewing the evidence on new medicinal drugs and offering advice on their safety. The CSD was chaired by Sir Derrick Dunlop, and consisted of a panel of experts from various fields. Assessments of submissions were carried out by a secretariat composed of professionals such as pharmacists and medical officers. However, the Committee had no legal powers. It worked with the voluntary agreement of the Association of the British Pharmaceutical Industry and the Proprietary Association of Great Britain (see main text).

modern era, pharmacy has played a central part in regulating the distribution of medicinal drugs to the public. UK government policies in relation to the pharmaceutical profession have traditionally been aimed at achieving an acceptable practical solution to the challenge of controlling the sale of poisons[2] and providing checks on the medically controlled process of prescribing, albeit that today options for extending the direct role of pharmacists (and nurses) in medicines supply are receiving increased attention.

This outline history helps to explain some of the rivalries and tensions that even now exist between and within the main professional groups involved in providing medicines to the public. It also highlights some of the factors differentiating 'Anglo-Saxon' and mainland European health care traditions, and attitudes to regulation and competition in the pharmaceutical sector.

Secret remedies – calls for reform before the First World War

During the second half of the 19th century there was little public pressure for increased scrutiny of medicines' safety and efficacy, despite the fact that 'cures' for conditions like cancer were being advertised. This may have been because most drugs in use at that time were still traditional 'Galenicals' (after the physician Galen), rather than new products of the then emerging pharmaceutical industry (see Box 2). The first major investigation of an adverse reaction to a drug was led by a British Medical Association working group in 1880. It found that small doses of chloroform – which was becoming widely used as an anaesthetic in surgery and to ease childbirth – could cause cardiac arrest. They suggested the establishment of an independent body to assess drug safety. But the study had little impact on the public or politicians.

Two subsequent BMA publications, entitled *Secret Remedies* (1909) and *More Secret Remedies* (1912), focused on the formulation of popular 'patent' medicines which by then were becoming widely advertised and used. They showed that some products marketed as treatments for illnesses such as tuberculosis, cancer and depression contained no effective ingredients. This led to the establishment of a Parliamentary Select Committee on Patent Medicines.

The Select Committee reported in 1914. The legislation proposed was shelved because of the First World War. But the Proprietary Association of Great Britain (the PAGB, which continues to represent the interests of the over-the-counter medicines industry)

Box 2: Origins of the pharmaceutical industry

The pharmaceutical industry as it is currently understood came into being only in the last hundred or so years. Its story began with the consolidation of the industrial revolution, when people in the growing cities of northern Europe and America and were losing access to traditional remedies. This was also the period during which research scientists discovered that bacteria could be stained for observation and that different staining characteristics served as a convenient means of classifying these primitive life forms.

Concepts such as that of the 'magic bullet' – a chemical 'missile' that would lock on to infectious organisms but leave the cells of their human hosts undamaged – followed. The then powerful dyestuffs industry in and around Germany and the UK diversified, and formed a central component of the emergent pharmaceutical sector. As companies' production and brand advertising capabilities improved they began to replace pharmacists as the primary makers of medicines. By the time the NHS was created, the task of community pharmacists was already focused mainly on dispensing.

Since then advances in areas such as packaging and computer technology have helped to further extend the pharmaceutical industry's role. During the 1980s and 1990s drug companies showed growing interest in 'disease management', the basic concept of which involves combining the management of health care services with the provision of pharmaceutical products. This has proved more difficult to establish in practice than many of its early proponents anticipated. However, the idea that medicines alone cannot usually deliver optimal health is sound. They need to be used appropriately, in conjunction with other forms of preventive, curative and supportive care.

was formed in 1918. It was established to police a system of voluntary advertising control in recognition of the fact that, if manufacturers did not regulate themselves, the Government would legislate. Among the PAGB's first rulings were bans on the word 'cure' in advertising and on the promotion directly to the public of medicines seen as requiring medical supervision.

New legislation on pharmacy and the sale of poisons and dangerous drugs was enacted in the 1930s. It extended requirements for medical

prescription, and further empowered the Pharmaceutical Society of Great Britain to act as the profession's registration and policing body. However, the regulation of the British pharmaceutical sector as a whole evolved in a piecemeal way during the inter-war period. For example, the Venereal Disease Act 1917 and the Cancer Act 1939 ruled out all public advertisement and promotion of drugs for these afflictions, to protect sufferers from substandard treatment and fraudulent claims. But a fully comprehensive national strategy was not adopted.

The US Government, by contrast, faced with the problem of ineffective treatments and a tragedy involving deaths due to the use of ethylene glycol in a patent medicine, decided on radical action. At the end of the 1930s it set up the Food and Drug Agency (FDA) with a wide remit, including that of medicines licensing.

The formation of the NHS and the Therapeutic Substances Act 1954

When the NHS came into being in 1948 the antibiotic revolution was already underway. By the early 1950s it was apparent that many more pharmaceutical innovations would follow. Yet medicines regulation in the UK remained relatively rudimentary. For instance, the quality of biological products like vaccines and antitoxins was poorly assured. At that time lack of standardisation meant there was no accurate measure of their purity and potency.

The Therapeutic Substances Act 1954 sought to address this problem, and to regulate the labelling of all pharmaceutical products. It provided for the first (passive) UK medicines licensing system, with the Minister of Health acting as the licensing authority for England and Wales. Similar arrangements applied in Scotland and Northern Ireland.

The Therapeutic Substances Act also contained provisions relating to the competence and working conditions of pharmaceutical

company employees. The logic for this was based on an awareness that poor production standards could undermine other measures intended to ensure the safety of medicines. Records of sales had to be kept, and medicine containers were required to identify both the manufacturer and the batch number. Seen overall, this legislation marked a new stage in the regulation of safety standards in the UK pharmaceutical sector (see Figure 1). Nevertheless, the licensing and allied arrangements introduced at that time were not rigorous by today's standards. They left decisions on whether or not to expose the public to the risks of a new medicine in the hands of its producer, rather than those of the state.

At the same time the advent of the NHS had created a new, publicly funded, market for prescription medicines. General medical practitioners became a key target for the educational and marketing efforts of pharmaceutical companies. Concerns about the costs of the NHS had already led to the imposition of prescription, dental and ophthalmic charges in 1952, and in 1957 the first version of the then Voluntary Price Regulation Scheme for NHS medicines was established. This for a time appeared to allay political concerns about the regulation of the pharmaceutical sector, and public expenditure on medicines. But it proved a short-lived effect.

The Medicines Act 1968

The Labour administration that came into power in 1964 did so in the shadow of Thalidomide. Its policy objectives included the expansion of high-technology based British industries such as pharmaceuticals. Yet it also recognised the need to regulate the pharmaceutical sector in a manner robust enough to regain public confidence. Its concerns related in part to the perceived weakness of the Committee on Safety of Drugs (see Box 1) as an organisation relying on the voluntary co-operation of industry, and in part to rising NHS medicine costs. Harold Wilson's administration had acted quickly to remove prescription charges (Wilson had resigned from

1802	Medicine Act
1815	Apothecaries Act
1841	Pharmaceutical Society founded
1851	Arsenic Act
1852	Pharmacy Act
1858	Medical Act
1864	First *British Pharmacopoeia*
1868	Pharmacy Act
1908	Poisons and Pharmacy Act
1909	*Secret Remedies*
1911	National Insurance Act
1912	*More Secret Remedies*
1917	Venereal Disease Act
1918	Proprietary Association of Great Britain established
1933	Pharmacy and Poisons Act
1939	Cancer Act; Food and Drug Administration formed in the USA
1946	NHS Act
1948	NHS formed, free at the point of demand
1952	Charges for prescription, dental and ophthalmic services
1954	Therapeutic Substances Act
1957	First Voluntary Price Regulation Scheme
1958	First ABPI Code of Practice for pharmaceutical promotion
c.1960	Thalidomide tragedy
1963	Committee on Safety of Drugs established
1964	Macgregor Inquiry reports; prescription charges temporarily lifted
1967	Sainsbury Report into Relationship of the Pharmaceutical Industry with the NHS; strengthened VPRS
1968	Medicines Act
1973	Britain joins European Community
1976	First meeting of the EC Committee on Proprietary Medicinal Products
1978	First Pharmaceutical Price Regulation Scheme
1985	NHS limited medicines list introduced
1986	EC 'Biotech Directive'
1989	Medicines Control Agency established
1990	NHS reforms – GP fundholding and the internal market
1994	European Medicines Evaluation Agency established
1997	Blair administration elected; *New NHS* White Paper ends NHS internal market
1999	Health Act comes into force; PPRS renegotiated; National Institute for Clinical Excellence established

Figure 1: Developments in regulating the pharmaceutical industry

the Labour Government in 1952 over their introduction) but was then faced with rapidly increasing NHS prescription numbers.

The first of several inquiries set up by the new Government to report was that of Lord Macgregor in 1965. This committee proposed that some types of branded medicines be placed in special categories. Doctors prescribing them would have to justify their action. The Standing Joint Committee on the Classification of Proprietary Preparations (the Macgregor Committee) subsequently focused attention on the relative efficacy of medicines, and questioned the value of combination products.

The Sainsbury Report[3] (1967) posed a significantly greater challenge to the UK pharmaceutical industry. It argued for more rigorous scrutiny of company costs, profits and prices, and was critical of the influence of pharmaceutical promotion on the practice of medicine. It advocated a reduction in intellectual property (patent) protection for pharmaceuticals, and a ban on the registration of new brand names for medicines in the UK. Later in 1967 a strengthened version of the Voluntary Price Regulation Scheme was introduced. At about the same time a new White Paper (*Forthcoming Legislation on the Safety, Quality and Description of Drugs and Medicines*[4]) was published.

The Medicines Act 1968 and the regulatory changes that accompanied it did not incorporate all the more radical concepts discussed in the aftermath of Thalidomide. It has been subject to a number of criticisms, including the charge that the medicines licensing process it established is not sufficiently open to public scrutiny.[5, 6] Yet it placed responsibility for licensing medicines firmly within the remit of public servants. The 1968 Act's provisions (see Box 3) came into effect on 1 September 1971.

Developments since 1971

The pharmaceutical sector has often featured in public debate in the three decades since the start of the 1970s. But following the

Box 3: Key provisions of the Medicines Act 1968

The Medicines Act required the formation of:

- **The Medicines Commission.** This is the key advisory body to ministers on broad aspects of policy regarding medicines. Additional powers and functions relate to tasks such as the production of the *British Pharmacopoeia* and other information about medicines.
- **Additional independent advisory committees.** Formed under section 4 of the Act, these include the Committee on the Safety of Medicines (CSM), the Committee on Review of Medicines (CRM), the Committee on Dental and Surgical Materials (CDSM), the *British Pharmacopoeia* Commission (BPC) and the Veterinary Products Committee (VPC).
- **A strengthened licensing system based on three categories – POM (prescription-only medicines), P (pharmacy medicines) and GSL (general sales list medicines).** The licensing authority has to be satisfied that there is evidence of the medicine's safety, quality and efficacy. Questions of cost and comparative efficacy (unrelated to safety) were ruled out as considerations for refusing a licence. Previous British legislation permitted any medicine to be sold via any type of outlet unless it contained a substance in Part I of the Poisons List or Part II of the Therapeutic Substances Act. The new Act ruled that all medicines except those on the General Sales List should be sold only from registered pharmacies.

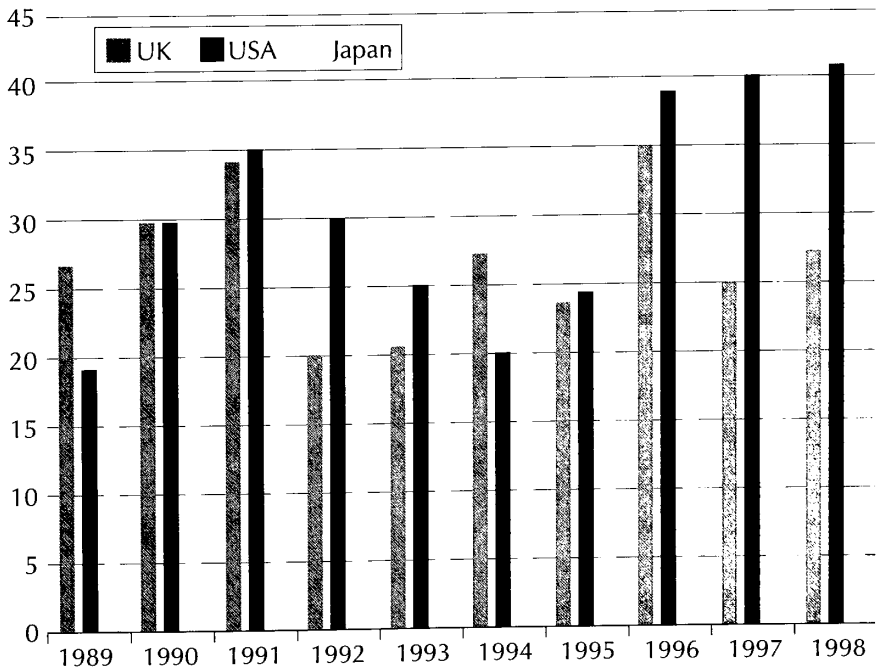
The Medicines Act, which since 1968 has been amended through numerous Statutory Instruments, also contained provisions for the regulation of the marketing of medicines, over and above those already applying to such activity in all sectors. Claims made must be consistent with the terms of the product licence. The Medicines Act also requires licence holders to produce standardised product data sheets setting out information such as the approved indications, contra-indications and adverse effects.

Medicines Act, concerns about risks to public interests have in general been less marked than was the case in the decade immediately after the Thalidomide tragedy. This moderated social and political environment, coupled with continuing discovery and innovation in the biological sciences, has permitted the continued

growth and success of the pharmaceutical industry in this country and abroad, based on its continued ability to discover and market new effective, medicines (see Figure 2).

However, pharmaceutical regulation has been far from static. Examples of relevant developments include:

- **The continuing evolution of the VPRS and the NHS.** The VPRS was renamed the Pharmaceutical Price Regulation Scheme in the late 1970s. This followed a high-profile conflict over the pricing of the tranquillisers Valium and Librium, which tested the strength of the UK Government's resolve to limit medicine costs. Since then the Scheme has undergone further important changes. The wider NHS has also moved through various approaches to resource allocation and cost control during successive political administrations.



Source: CMR International.

Figure 2: Number of new medical entities launched in the UK, USA and Japan, 1989–99

- **Good manufacturing and research practice.** Following the Therapeutic Substances Act 1954, UK licensing authorities have granted manufacturing licences according to standards set out in the *Guide to Good Manufacturing Practice*, also known as 'The Orange Guide'. (Although issuing manufacturing licences remains a national function, it is now governed by standards set in EU Directive 356/91.) British and other companies seeking to sell products in the USA must also comply with FDA requirements in this field, and those relating to clinical practice in the context of trials. The Medicines Act embodied a requirement for Clinical Trial Certificates, later superseded by an exemption (CTX) system. New European legislation on clinical trials has recently been agreed.

- **Patent life extension.** Despite the concerns expressed in the 1967 Sainsbury Report on the costs of medicines to the NHS, pharmaceuticals have been granted increased 'on the market' patent terms to compensate for extended product development periods. This regulatory trend, initiated in the USA, exemplifies interventions designed to protect public interests in maintaining economic incentives for investing in therapeutic innovation, rather than containing health care costs.

- **'Blacklisting'.** In the mid-1980s the Government took its first action to prevent general medical practitioners from prescribing selected medicines (including the brands of Valium and Librium) to NHS patients. These restrictions, which were vigorously challenged by the industry, in the main apply in areas regarded as clinically less important. GPs cannot prescribe affected products, covered under Schedule 10 of the GMS Regulations, in any circumstances, except to patients requesting a private prescription. Schedule 11 medicines can be prescribed at NHS cost for some specified indications, but not for others.

- **The formation of the Medicines Control Agency.** Following the 1989 Evans/Cunliffe Report, the Medicines Division of the

Department of Health was reconstituted as a more independent organisation, the Medicines Control Agency (MCA). It is self-funded, mainly from fees levied on pharmaceutical companies. The UK MCA has approaching 500 staff, working in areas ranging from processing licensing applications to the preparation of the *British Pharmacopoeia* (see appendix) and the UK contribution to the *European Pharmacopoeia*.

- **Pharmaceutical industry consolidation.** During the 1990s increasing research costs and the changing nature of pharmaceutical markets have encouraged mergers and acquisitions. These have had a major impact on the UK industry.

- **The establishment of the European Medicines Evaluation Agency.** This body, established in London in 1994, has played a key role in developing functions such as improved adverse drug reaction reporting (also referred to as 'pharmacovigilence') across the EU.

The European Union and European law

In part reflecting the transnationalisation of the drug industry, medicines regulation has become an increasingly global process, which in the EU has to be conducted within a framework set down in Brussels. Even before the UK joined the then European Community in 1973, efforts were made to marry Westminster's legislation with that of Britain's continental neighbours. For instance, although it was little noticed at the time, the Medicines Act 1968 was broadly consistent with European Community Directive 65/65.

Since the mid-1970s British regulatory initiatives and processes have been obliged to take into account the broader context of EU law. Illustrations of key European institutions and directives include:

- **The Committee on Proprietary Medicinal Products (CPMP).** This body held its first meeting in November 1976. It has

functions relating to the creation of a more co-ordinated and unified EU-wide medicines licensing system.

- **The 1986 'Biotech Directive'.** Council Directive 22/87 concerned the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology. It introduced two classes of 'hi-tech' medicinal product. The first is genetics-based (covering, for instance, therapeutic substances produced by recombinant DNA technology) and the second involves new molecular entities (NMEs) and/or novel non-genetic delivery systems or manufacturing processes. The Directive required that biotech products would have to be referred to the CPMP before any marketing authorisation could be granted. Others could be dealt with either via the centralised procedure, or via alternative procedures initiated at national level.

It would be beyond the scope of this book to describe comprehensively European legislation as it applies to the manufacture and sale of medicines. But two key points are worth emphasising:

- **Progress towards the harmonisation and integration of medicines regulation procedures and agencies has been slower than its advocates originally hoped.** Despite advances made in areas such as pharmacovigilance (see Box 4) and reviewing the value and safety of older products, significant tensions still exist between central EU bodies and regulatory bodies accountable to nation states. When disputes occur they threaten public interests in areas such as fairness and objectivity in the licensing of pharmaceuticals. The performance of the EMEA and progress within the European medicines licensing system as a whole is now due for review.

- **Conflicts between policies aimed at facilitating the free movement of goods within the European Community (in line**

with the Commission's long-term economic and political goals) and protecting the viability and effectiveness of national level health care provisions also remain apparent. This is most obvious in the context of the 'parallel importing' (see Box 4) of medicines between EU states with different pharmaceutical price controls and intellectual property traditions. BSE-related hazards have also highlighted such concerns. If public interests in better health are to be optimally protected, then greater consistency in the national and EU-level strategies underlying regulatory interventions will need to be achieved.

Box 4: Pharmacovigilance and parallel importing

The term 'pharmacovigilance' has been used to describe measures aimed at the earliest possible identification of unexpected medicine side effects. Relevant examples include those associated with Thalidomide at the start of the 1960s, the beta-blocker Eraldin in the 1970s, and the anti-rheumatic preparation Opren in the 1980s. Despite the good safety record of other medicines similar to these last two, Eraldin caused eye damage and Opren was associated with photosensitivity and potentially lethal toxicity in older users with impaired drug clearance capabilities. Pharmacovigilance systems may also detect problems such as the dependence syndromes associated with benzodiazepine tranquillisers, and perhaps other forms of psychotropic medication.

Further developing EU-wide structures for reporting adverse reactions to marketed drugs is part of the remit of the EMEA. The majority of serious adverse reactions are very rare events, which has meant that no pre-marketing trial regimen can ever guarantee to identify all possible side effects.

The UK 'yellow card' system relies on the voluntary submission by doctors and dentists of adverse drug reaction (ADR) reports. It was extended in November 1999 to involve community pharmacists. There are some 18,000 ADR reports annually, with about 440 reported deaths per year. Fatal reactions have accounted for a steady 4 per cent of total ADR reports over the last ten years.[7]

'Parallel importing' refers to the practice of purchasing a given product cheaply in one country and selling it more expensively in another.

Such commercial activities have been successfully defended in the EU Court of Justice, even in relation to patented products – see, for example, *Merck v. Primecrown*.[8] However, in the area of medicines supply the financial gains derived are mainly retained by the traders involved, and others in the supply chain. As far as the endpoint consumers of pharmaceuticals are concerned, savings are likely to be minimal, although in the UK NHS payments to pharmacists are adjusted by a claw-back mechanism based on the estimated average discounts they receive from buying cheaply.

The losses imposed by parallel importing on research-based pharmaceutical and other companies in the EU may damage employment and other social benefits. If, in time, parallel importing forces price harmonisation this could prove beneficial to the overall EU economy, although presently different EU states may have good reasons for setting higher or lower medicine prices. There are public interests involved in allowing new treatments for conditions like, say, HIV or cancer to be sold more cheaply in poorer parts of the EU than they are in richer areas.

Parallel importing conducted in an ethical manner should not present a threat to public health. But improperly supplied parallel imports could cause harm through, for example, inadequate patient information provision and lack of data on product origins in the event of medicine recalls. Pharmacovigilance systems might be impaired if it cannot easily be seen which production batch a defective treatment has come from. Options put forward by interests wishing to reduce parallel importing of medicinal products include a proposed exemption for patented pharmaceuticals from EU laws on freedom of goods movement, and higher pricing backed by country-specific rebates negotiated directly with manufacturers.[9]

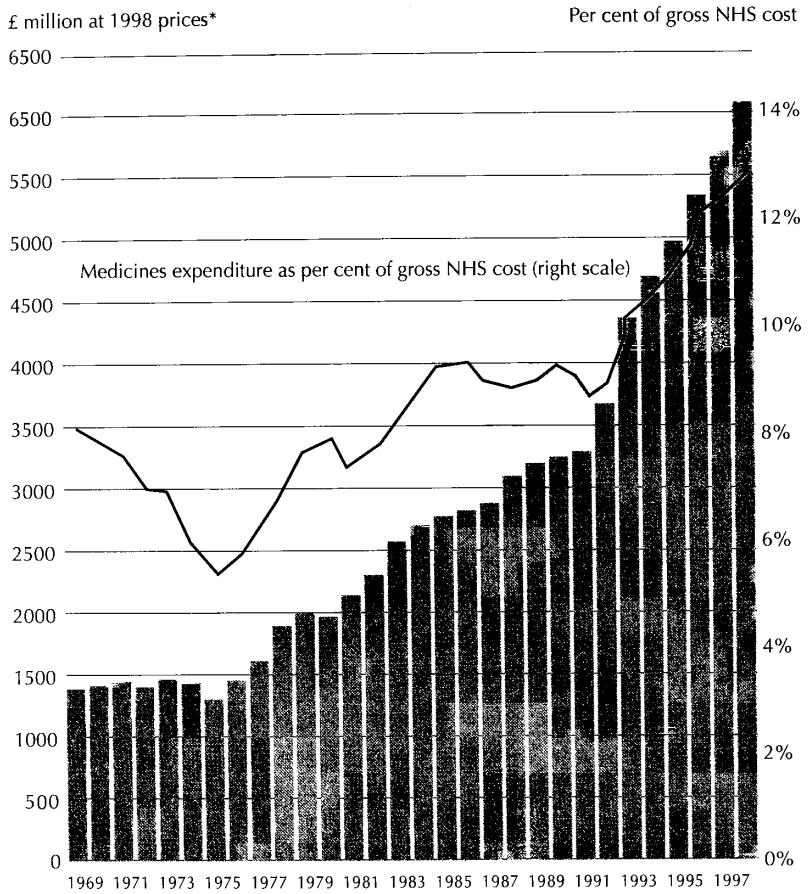
Chapter 3

Supply-side regulation – the PPRS and advertising controls

The activities of pharmaceutical companies and all other parties involved in the supply of medicines to the public are today subject to extensive monitoring and checking by a multiplicity of agencies. For example, pharmacists and dispensing doctors are subject to statutory, professional and NHS requirements. Pharmaceutical companies must comply with generic legislation covering areas such as employment, environmental protection and accounting practices, and specific legal and allied requirements applying uniquely to their industry. In this last context the two areas most commonly discussed (over and above the effectiveness and openness of licensing arrangements) in relation to the defence of public interests are medicine cost/price control and the regulation of advertising and other promotional activities.

Traditionally, pharmaceutical price and expenditure regulation has focused on supply-side measures designed to contain the costs of health care.[10] The PPRS model is an exceptional example of an approach that combines a substantial degree of freedom and flexibility for regulated companies in areas such as setting the market entry price of innovative products, with a reasonable level of overall cost control. Although, as Figure 3 shows, NHS medicines expenditure measured in manufacturers' prices rose from around 10 to about 13 per cent of total health service costs during the 1990s, UK per capita outlays on pharmaceuticals remain relatively modest in international terms (see Box 5).

At the same time Britain enjoys one of the world's largest pharmaceutical balance of trade surpluses. Part of the core policy dilemma affecting this regulatory field is that without such



Notes
All figures include medicines dispensed by chemists and dispensing doctors, and hospital purchases.
* As adjusted by the GDP deflator at factor cost.

Source: OHE. *OHE Compendium of Health Statistics*. 1999.

Figure 3: Total NHS expenditure on medicines (at manufacturers' prices),* UK, 1969–98

contributions to the national economy the funding of adequate public services could become increasingly problematic. The advantages that medicine cost reductions could bring to the health service have to be considered in relation to their possible knock-on effects in terms of capital investment, employment and the balance of pharmaceutical imports and exports.

Box 5: NHS medicines spending

The UK is second only to Switzerland in the world pharmaceutical exports league table, with a net balance of trade contribution of some £2500 million. Its domestic spending on pharmaceuticals is low compared to the levels of consumption recorded in North America and much of Europe. In per capita terms it is less than half that of France, Japan and the USA.

Spending on the NHS across the UK nations is now over £51 billion. Of this the highest proportion – two-thirds or more – goes on the wages and fees of staff such as doctors, nurses and managers. Health service outlays on medicines stand at about £6 billion.[11] In the last decade the number of prescription items per head of population rose from eight to ten. The English average is now nine items per person per year, while in Northern Ireland and Wales over 12 items per head are prescribed annually. The factors involved in such trends include:

- the introduction of new medicines, creating fresh treatment opportunities
- population ageing, leading to a greater proportion of people needing both short- and long-term medical care
- changes in treatment patterns, with less use of institutional care and in-patient therapy relative to interventions such as day surgery.

PPRS objectives

The PPRS has three main goals, agreed between the Department of Health and the Association of the British Pharmaceutical Industry. They are to:

- ensure the provision of safe and effective medicines to the NHS at reasonable prices
- promote a strong, profitable pharmaceutical industry, capable of delivering research-based innovations to meet public requirements for improved treatments
- encourage efficient, competitive medicines supply in this country and in the markets of other nations.

The original Voluntary Price Regulation Scheme, as it was called in 1957, pegged NHS medicine prices to those of exports. But since then the UK's approach to controlling medicine prices has gone through a series of incremental adaptations. The PPRS currently embodies an assessment of the capital value of assets employed in the production of branded medicines used by the NHS, together with a series of checks on factors such as production, research and marketing costs. Within this framework it determines the maximum level of profit that an efficient company can earn from sales of its products to the health service.

The transformation of the VPRS into the modern PPRS began in 1969, during Harold Wilson's first period in power. The term 'voluntary' was dropped from the title of the Scheme in 1978, although it remained a negotiated agreement rather than a statutory arrangement. (Government has, however, always had relevant reserve powers.) Subsequent versions of the PPRS introduced progressively more sophisticated ways of regulating promotional spending and other costs, including those incurred outside the UK in relation to the production of NHS medicines. In the early 1990s the Scheme was further modified to exclude the supply of non-branded medicines. This shift reflected NHS developments such as GP fundholding, and the view that where possible market competition should serve to set prices.

The most recent version of the PPRS was negotiated against the background of new legislation. The Health Act 1999 strengthened the Government's abilities to intervene – if and when necessary – independently of the PPRS to control pharmaceutical prices and profits. One important aspect of the new agreement introduced in October 1999 was a 4.5 per cent (£200 million plus per annum) reduction in NHS prescription medicines prices (and costs). It also included a variety of other changes intended to enhance the Scheme, and enable the UK to obtain optimal returns from its pharmaceutical sector.

The value of the savings to the health service of the 1999 changes introduced to the PPRS was to an extent obscured by unexpected rises in the costs of generic medicines, which are not subject to PPRS control. These accounted for an offsetting cost increase of about £200 million.[12] But action has now been taken to fix the maximum prices the NHS will pay for such products, and to prevent recurrences of the problems that emerged at around the time the latest version of the PPRS was announced.

Despite concerns about this and other issues (such as past delays experienced in companies providing required data, which the Health Act's provisions are in future designed to stop), both sides involved in its negotiation – the industry and the Department of Health – believe that the current PPRS will operate effectively in the pursuit of the overall national interest.[13, 14] It is not, for example, the case that less efficient concerns with less favoured products can simply put up prices in order to achieve their allowable profit ceilings. Apart from the restraints imposed by the PPRS itself, such companies would incur market disadvantages.

Mechanisms of the PPRS

The revised PPRS covers the supply of all branded, licensed NHS medicines. It will stay in force until 2004, unless a mid-term review is undertaken. This may be requested by either industry or the Government, after an initial two-and-a-half years. Companies do not now have to be members of the ABPI to be members of the Scheme. By the same token any company can elect not to be a member, or to be excluded from the PPRS because it has not complied with requirements. In such instances the new direct controls will apply.

For companies with NHS sales of £25 million or more the core reporting mechanism of the PPRS is known as the Annual Financial Return (AFR). Companies must submit their AFRs within set

periods after the ends of their financial years. They must be filled in according to defined rules, and provide information about overall company affairs and individual product sales. Additional aspects of how the PPRS works include:

- **Profit targets.** These impose ceilings on PPRS companies' profits. They are calculated at two different levels, depending on whether the figures are being used to check the acceptability of a company's overall earnings or if a price rise has been requested. In the latter case a tougher test is applied.

- **Price restraints.** No PPRS member can increase the price of any NHS medicine without prior approval from the Department of Health. If price rises are permitted then allowable profit ceilings are cut.

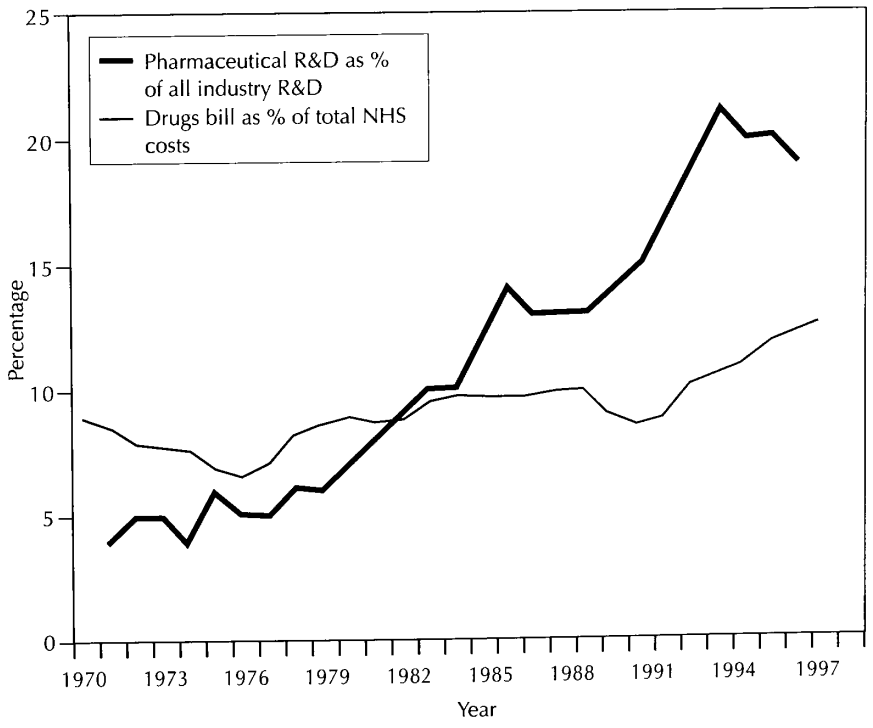
- **Tolerance margins.** Companies that through efficiency gains (as distinct from incorrect sales projections) exceed their forecast earnings can retain up to 40 per cent over their originally permitted return. This incentive should drive better performance and overall efficiency levels.

- **Research and development expenditures.** These are calculated within a range of 17–20 per cent of NHS sales. In addition, companies with successful innovations may be permitted up to 3 per cent more for additional R&D investment. Overall, the UK-based pharmaceutical industry's spending on research funded from both NHS and export sales has risen significantly as a proportion of all manufacturing industry funded R&D since the start of the 1970s (see Figure 4).

- **Sales promotion.** The formula used to determine permissible spending involves a basic allocation of 3–6 per cent of NHS sales, plus a fixed element (which favours smaller turnover companies) and variable inputs relating to the numbers of products with sales of £100,000 or more to the NHS.

- **Transfer pricing.** This term applies to the charge made within international companies when a component of a product is supplied across a national frontier, from one part of the organisation to another. Transfer prices are used in all industries, although because the pharmaceutical sector has led globalisation they are often associated with the movement of medicine ingredients between parent and subsidiary companies. The PPRS ensures that unapproved profits cannot be taken out of the country via such mechanisms.

- **'Sold on' products.** Large companies are often unable to obtain NHS price rises for older medicines, which may consequently become regarded as uneconomic. However, it has been judged



Source: CMR International and Office of National Statistics.

Figure 4: Trends in pharmaceutical R&D as percentage of total UK industry R&D and cost of drugs as percentage of total NHS costs, 1970–98

that – although sound business practice – it would be against the spirit of the Scheme for such products to be 'sold on' to smaller concerns which could charge more for them. The 1999 PPRS contains new regulations to control prices in such circumstances.

Medicine price controls in other European countries

In the rest of the EU many different methods are used to approve the prices of new and older medicines. Typically, dossiers on costs and product benefits have to be submitted to government-appointed committees, which consider whether a proposed price should or should not be approved. In some countries (such as Italy) price levels elsewhere in Europe are taken into account; in others (such as Germany) the price of similar 'reference' products available domestically is a critical issue.

In France, a government-appointed Transparency Commission decides whether a new medicine should be available to patients of the social insurance funds. It does so using seven criteria (such as the nature and severity of the disease, and the degree of innovation) to assess its medicinal benefit. Each product is scored at one of six levels on the Medical Benefit Assessment Scale (ASMP), ranging from 'major therapeutic improvement' to 'no improvement'. If inclusion is recommended, the Economic Committee then sets a price.

The latter operates within the 'Accord-Cadre' or Convention negotiated between the government and the French pharmaceutical industry. The objective of this is in part to reduce the unusually high volumes of medicine consumption recorded in France, by lowering promotional activity and encouraging more appropriate use of medicines. If sales exceed agreed targets, prices may be reduced. In 1996, the Juppe plans for welfare reform led to a global 'levy' on the industry equivalent to 2 per cent of sales as its contribution to health care savings.

Other recent developments in the EU include:

- attempts by **German** regulators to extend controls on pharmaceutical spending by means of more restrictions on what products could or could not be supplied on a reimbursed basis. These failed because of legal challenges based on EU competition laws

- moves in the mid-1990s in **Italy** (where medicine prices tend to be low, but volume use is – as in France – high) to increase substantially patient co-payments. Medicines were classified into list A (life saving) with low flat rate co-payments, list B (products with demonstrable therapeutic advantages), with 50 per cent co-payment, and list C (comprising 'other products'), with full costs borne by patients

- a decision, in September 1999, in **Spain** by its Department of Health to introduce a scheme whereby pharmacists must substitute a generic drug for a branded product if the branded product exceeds a certain price. The aim was to further curb the proportion of overall Spanish health care resources spent on pharmaceuticals, which during most of the 1990s stood at over 20 per cent.

These illustrations underline the fact that as the EU develops, Member State action to limit pharmaceutical outlays is having to focus more on informing demand-side decisions and developing more active pharmaceutical market competition, rather than imposing new forms of local price control. The latter are not consistent with the key EU policy goal of achieving a fully integrated single market for all goods and services.

Britain is already relatively well advanced in this context through the NHS innovations outlined in the next section, and because the PPRS leaves innovators free to price new products at market determined levels. The only other major economy where this is currently the case is that of the USA. It is also of note that the latest PPRS agreement contains a commitment on the part of government to examine – with the pharmaceutical industry – the possibility for price deregulation on the pharmaceutical supply-side.

The regulation of advertising and other promotional activities

The regulation of promotion sits on the border between supply-side and demand-side interventions. Although medicine purchasers, prescribers and takers are ultimately responsible for their own actions, their demands and choices are influenced by information and advertising funded by producers.

Traditionally, the pharmaceutical industry world-wide has spent as much or more on promotion as it has on research – that is, up to a quarter of its gross turnover. The reasons for this high proportion relate to the complexities of the pharmaceutical market and medicines usage, and the fact that demand for many medicines has in the past been relatively price insensitive. This encouraged companies to compete via often costly promotional programmes, aimed at doctors and other audiences.

In the UK the PPRS restricts promotional spending within the NHS market, and imposes penalties on companies that exceed permitted limits. The published information available indicates that it currently represents some 7 per cent of NHS sales, that is about a third of the R&D outlays funded from NHS medicine sales. In cash terms such percentages imply that on NHS PPRS sales of, say, £5000 million a year there would be an allowable promotion spend of around £350 million and a research contribution of over £1000 million.

However, care should be taken in interpreting such figures. In the case of research and development, for example, actual total UK outlays by the pharmaceutical industry are in the order of £2500 million, which is about a quarter of all British industry's privately funded R&D outlays. Additional funds from sources such as foreign earnings can be channelled into the UK research effort without PPRS penalty.

In the over-the-counter section of the market (comprising both pharmacy only and general sales list products, and now worth in the

order of £1500 million a year[15] in the UK) promotional spending expressed as a proportion of turnover is significantly higher. Although there are substantial variations within different segments of the market, sources within the OTC medicines industry suggest that estimates of 20 per cent are realistic.

The Medicines Act (Advertising and Monitoring of Advertising) Amendment Regulations 1999 (SI 1999 No. 267) represent the latest secondary legislation designed to strengthen British provisions, and to further implement the key Council Directive (92/28) covering this area. They came into force in April 1999, and set out regulations that supplement the controls in the Medicines Act 1968 to ensure that medicinal products are promoted appropriately and in accordance with their marketing authorisation. This legislation provides for statutory penalties if advertising regulations have not been complied with.

However, despite interventions by bodies such as the Medicines Control Agency, direct legal action has been little used since the start of the 1970s. This is because the statutory regulation of medicines promotion has been supplemented by the ABPI and PAGB codes of advertising practice for prescription medicines and over-the-counter medicines respectively. Complaints about promotional practice violations are, in the first instance, normally referred to the appropriate industry-side self-regulatory body.

The ABPI Code of Practice for the Pharmaceutical Industry was first established in 1958. It is now administered via the UK Prescription Medicines Code of Practice Authority. The code covers prescription medicine promotion in any form, including journal and direct mail advertising, the activities of company representatives and the materials used by them, the supply of samples, the use of inducements, the provision of hospitality and the holding and sponsorship of meetings. It also applies to the provision of information to the general public.

The Proprietary Association of Great Britain's codes cover the promotion of OTC products direct to the general public, and marketing to health professionals and the pharmaceutical retail trade. They follow the Advertising Standards Association's requirements in demanding that medicines advertising should be honest, legal and truthful. The PAGB requires member companies not to bring the industry into disrepute by their advertising. (Two additional codes apply to pharmaceutical companies operating in Europe and elsewhere. They are produced by the European Federation of Pharmaceutical Industry Associations – EFPIA – and the International Federation of Pharmaceutical Manufacturers Associations – IFPMA.)

Systems of 'co-regulation', based on a pragmatic balance between statutory controls and self-regulation by trade bodies, have received considerable support in the UK. Recently, for example, the Government's Regulatory Impact Unit argued that co-regulation systems are convenient, responsive and cheap to operate.[16] Despite concerns in some quarters that co-regulation has in the past permitted a lax approach and too influential a role for commercial bodies in medical education and NHS drug selection, it may be argued that this is not the case today.

The issues of advertising to the public and patient-focused public relations campaigns is currently more controversial. In the USA the FDA regulations have allowed direct-to-consumer (DTC) advertising for prescription medicines for some years. DTC advertising of prescription products is not permitted in the Member States of the European Union. Throughout the latter, however, press stories about medicines and their role in health care are commonly reported. Public interest related points to consider in relation to this area include:

- **The extent to which DTC prescription medicine advertising informs and benefits patients.** Advocates of this approach argue that patient empowerment would be increased by access to

(appropriately regulated) advertising messages, and that if (in an increasingly rationed care environment) companies are permitted to promote treatments to clinicians they should also be allowed to do so openly to the endpoint users of their products. It is now regarded as anachronistic that as recently as the early 1960s product names were not written on medicine bottles because professionals believed that patients need not know what medicines they had been prescribed. Similar arguments could, it is suggested, be applied to EU restrictions on pharmaceutical advertising to the public today. Against this, commentators associated with organisations such as the Consumers Association and Social Audit have pointed to the possible dangers of DTC prescription medicines' advertising, which they fear might generate ill-founded demands for drugs as opposed to other forms of health improving intervention.

- **The case for further regulating 'PR'.** Public relations activities might serve as a substitute for DTC advertising in Europe. Despite relevant codes of practice and statutory provisions, some observers suggest that the origins of media stories about medicines and allied issues are not always transparent and that further regulation could prove to be in the public's interest.[17] Questions may also be raised about the mechanisms through which they are selected for coverage within news and other publishing organisations. One future regulatory strategy could combine greater pharmaceutical industry freedom to run overtly public advertising and allied programmes on public health issues and/or the value of specific branded medicines, with more controls on non-overt, indirect, promotional exercises.

- **The impact on European industry of continuing to restrict direct public information.** The gradual shift of the pharmaceutical industry's focus away from EU centres to what is perceived as a more favourable environment in the USA may already have imposed heavy, if difficult to quantify, future costs on this country. If EU nations wish to retain a relatively strong position in

medicines research and fields like clinical trial organisation and the development of new medicines, a positive acceptance of the value of more direct communication between medicine takers and producers could prove vital.

- **Developments in electronic communication and commerce.** Internet communications are revolutionising consumer access to all types of information about health-related problems and technologies. As a result, many of the assumptions underlying past restrictions on medicine advertising and other forms of promotional control can be fundamentally challenged. For example, it could be argued that at present restrictions on conventional direct advertising are increasing the skews in information and treatment expectation that exist between poorer and/or less educated and richer and/or more educated health service users.

The issues raised in this context are complex, and should not be prejudged. It would, for example, be wrong to overstate the probable long-term impact of techniques such as DTC advertising in Britain (see Box 6). However, it is likely that in increasingly consumer-led health care systems and processes, where it is becoming accepted that informed self-care and 'expert patient' input are necessary components of virtually all successful care, modifications to EU and UK policies relating to the regulation of prescription medicine advertising to the public will eventually be introduced. These may well be accompanied by other changes in provider-side controls on the pharmaceutical sector, such as licensing requirements and procedures. Further developments in demand-side regulatory strategies can also be expected.

Box 6: Evidence on self-care decision-making and the impact of DTC advertising

The available research suggests that most medicine users do not derive detailed information from advertisements. For example, a survey conducted for the PAGB in the late 1980s[18] found that only two messages – the trade name and the condition being treated – could be effectively delivered via this route. Patients want information about side effects and safety at the points of prescription and dispensing, and in concise product literature. Information detailing when and how to use pharmaceutical products is also best delivered on the label, at points of purchase/collection, and via other written materials.

Subsequent PAGB studies[19] have shown that personal experience is the most powerful factor in determining the choice of self-care medicines. About nine out of ten people self-medicate for ailments previously experienced and eight out of ten people use medicines they have previously taken. However, whether or not evidence relating to self-medication can be applied to patient behaviour in the context of advertised prescribed medicines is uncertain, as is the degree to which data derived in US economic and social settings is applicable to the UK.

There can be little doubt that in the USA DTC advertising has been associated with altered prescribing patterns. But the extent to which it has promoted desirable changes in areas such as the way in which and duration for which patients take their medicines, and endpoint health outcomes, is not yet clearly understood.

Chapter 4

Demand-side innovations

The increasing sophistication and cost of health services have, during the 1980s and 1990s, led to more emphasis on, and investment in, health care quality management. This world-wide trend has opened up new approaches to controlling the use of (and spending on) medicines, focused not on drug companies' activities but on patient, clinician and institutional behaviours. In Europe, developments in this direction have been reinforced by the emergence of the single market, and the pressures on national authorities to move away from their historic reliance on supply-side regulation to limit or subsidise pharmaceutical company earnings. Such developments can be seen as part of a gradual move towards a more 'perfect' market for medicines, albeit that the pharmaceutical sector may be judged to be in continuing need of supra-normal regulation because of public concerns about safety and access to clinically and economically effective treatments.

User-side focused strategies[20] for changing patient demand patterns include:

- cost-sharing measures (such as out-of-pocket for prescribed items)
- developing the provision of over-the-counter and other self-purchased medicines, and limiting mainstream health care provider or insurer funding for selected pharmaceutical products
- health education programmes. The Netherlands and the UK have made notable investments in this context in, for example, public advertising on antibiotic usage and the threat posed by drug-resistant bacteria.

Examples of interventions designed to influence the behaviour of doctors, nurses and pharmacists cover, first, measures to ensure that personal payment systems do not contain perverse incentives to over use or over spend on pharmaceuticals. Positive incentives for rational – or just low cost – prescribing and dispensing are of proven effectiveness. Relevant European illustrations range from capitation or salary payment systems for first contact doctors (in Spain, Ireland, Italy, The Netherlands, Finland, Sweden and the UK) to the payment of pharmacists in ways that encourage the use of less costly supplies, as in the UK and The Netherlands.

Budgetary restraints on pharmaceutical or wider service expenditures incurred at practice and similar levels constitute a second line of approach. Examples range from the 'silo' (that is, relatively rigidly segmented) budgets being used during the early-stage development of English primary care groups (PCGs) for the control of pharmaceutical costs, to the many alternative forms of target and fixed budgeting employed in other EU countries and bodies such as US managed-care organisations. In the context of PCGs and primary care trusts (PCTs), the core issue to be addressed is the extent to which the capacity to hold a unified budget for not only medicines but all other local-level health care inputs can in practice be used to promote welfare gains, without undermining other valued services and outputs.

Audit and education-based programmes represent a third set of techniques for encouraging the cost-effective prescribing and delivery of pharmaceuticals. Interventions in this category encompass guideline dissemination (for example, in France and the UK) and the provision of comparative data on prescribing patterns (Sweden, Finland and the UK). They also include prescribing audits and pharmacist-led or supported medication reviews (The Netherlands and the UK), encouraging or requiring generic prescribing or substitution (in, for instance, Spain, Denmark, Germany and the UK), and the introduction of prior approval systems (most notably in the USA). These last require doctors and other prescribers to obtain

active managerial or funding agency approval before using selected treatments.

Such provisions may be backed by broader interventions, such as regional or national cash limits on pharmaceutical spending and changes in professional and other regulations. Relevant developments in the latter context involve initiatives such as extending the roles of non-medical prescribers like nurse practitioners in supplying a limited range of relatively low-cost treatments.

Specific instances of demand-side innovations intended to regulate medicines use and/or promote better clinical standards within the NHS include:

- the promotion of a culture of evidence-based medicine (EBM), and the use of well-researched clinical guidelines and cost-utility and other forms of economic analysis

- the provision in England and Wales of detailed, high quality prescribing analysis and cost trend (PACT) data to prescribers and health service managers. This has been accompanied by the supply of similar information by the PPA's counterparts in Scotland and Northern Ireland

- hospital and other locally agreed formularies, and the employment by health authorities and other bodies of pharmaceutical advisers. Efforts to persuade prescribers to prescribe 'rationally' – or at least as directed – are increasingly supported by promotional and allied interventions (see Box 7). For instance, the Keele University IMPACT programme involves pharmacists in what can loosely be seen as a UK equivalent to US-style pharmacy benefit management

- the 1999 Crown Review of Prescribing, Supply and Administration of Drugs. This proposed a new distinction

between independent prescribers (mainly GPs) and dependent or supplementary prescribers (such as professional nurses and pharmacists caring for previously diagnosed patients). Although the main practical consequence of the Crown Review has so far been to make legitimate protocol-based nurse prescribing and medicines supply practices already widely found in NHS hospitals, the ideas it generated might in time lead to more significant changes in community pharmacy and nursing

- the computer-based clinical decision support programme Prodigy advises prescribers on lower-cost treatment options. It is backed by other software packages designed to facilitate prescribing audits. Although the extent to which this system will be used in practice and be of value awaits satisfactory demonstration, in policy terms it represents an important attempt to use new IT capabilities to enhance prescribing

- the GP fundholding experiment, and the introduction during the 1990s of other forms of prescribing incentive schemes. The latter, which remain in place in various forms, offer practices limited financial rewards for curbing medicines costs. GP fundholding was ended via the Health Act 1999. But the creation of bodies such as primary care trusts, with unified, cash-limited budgets, is creating new financial pressures on prescribers to economise

- generic prescribing targets. Over two-thirds of all NHS medicine prescriptions are now written generically, compared with about a fifth at the start of the 1980s

- the wider quality agenda embodied in England and Wales in the creation of the National Institute for Clinical Excellence and the Commission for Health Improvement. Developments such as the establishment of NHS Direct may also have significant long-term implications in fields such as repeat prescribing, as well as in 'routing' patients to appropriate NHS provisions.

Box 7: 'Academic detailing' for improved prescribing

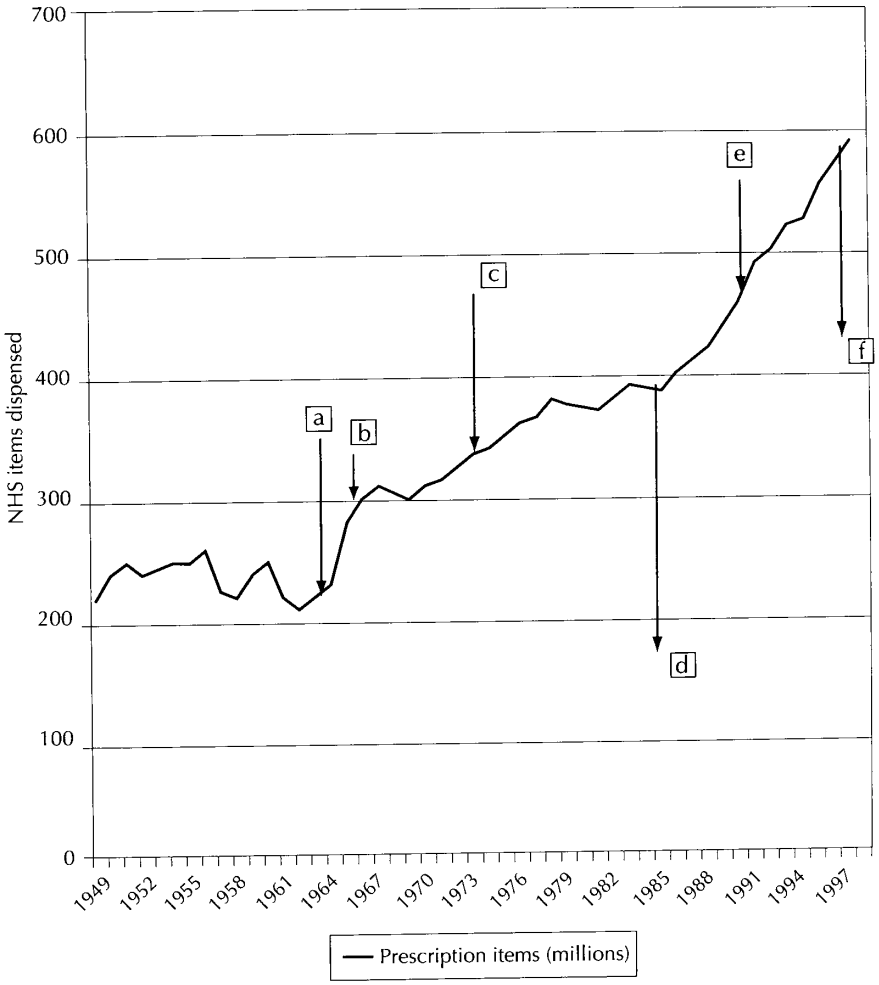
Avorn and Soumerai undertook pioneering work on this topic in the USA in the 1980s.[21] It has been replicated in the UK by a number of groups. In essence, academic detailing involves applying models of prescriber motivation and behaviour formulated in pharmaceutical company sales departments to the dissemination of cost reducing and treatment quality raising prescribing messages from other organisations. The most important techniques involve:

- conducting baseline knowledge and treatment preference assessment interviews
- focusing programmes on specific groups of prescribers, and the opinion leaders most likely to influence them
- defining clear educational and behavioural change objectives
- establishing credibility through respected organisational identities, referencing unbiased, high-status information sources and presenting all sides of complex and controversial issues
- stimulating active audience participation in educational interactions
- using concise graphics and other visual materials
- highlighting and repeating key messages
- positive reinforcement of desired behaviours via follow-up visits and reminder messages.

Cost-sharing

Patient charges for medicines are probably the most commonly used means of limiting demand for pharmaceuticals in the EU, where their legal standing has long been established.[22] In the UK there has been a long-running debate about the extent to which prescription charges can be considered consistent with the principles of the NHS and Aneurin Bevin's commitment to providing good quality care for all, free at the point of delivery.

With the exception of the period 1965–68 (see Figure 5), a flatrate charge has been payable via community pharmacists and dispensing



Notes
a. Prescription charges lifted
b. Prescription charges reintroduced with some exemptions
c. Exemptions extended to include under-16s and women over 60
d. Limited list introduced
e. PPRS imposes 2.5% reduction in prices
f. PPRS imposes 4.5% reduction in prices

Figure 5: NHS prescription charges and items dispensed by chemists and appliance contractors, UK, 1949–98

doctors since the early 1950s. This currently stands at £6.00 per family health service (FHS) prescription item. Its impact is limited in that about 80 per cent of all FHS medicines are supplied to people in

groups such as the elderly, who are exempt from payment (see Figure 6). Hospital supplied medicines are not subject to such charges. The revenue raised by prescription charges represents around £1.00 in every £7.00 spent on NHS community pharmaceutical services.

In addition, from 1984 onwards certain medicines have been restricted ('blacklisted') from NHS GP supply. The powers enabling this were originally contained in the NHS Act 1977, and are now executed via 'negative listing' under Schedules 10 and 11 of the General Medical Services (GMS) regulations. As noted earlier, blacklisted items – such as the anti-impotence product Viagra and the baldness treatment Propecia – can only be prescribed privately by GPs to their NHS – or other – patients. NHS savings have been made as a result of this policy.

The impact of cost-sharing on NHS patients has been the subject of a number of studies since the mid-1980s.[23, 24] Broadly, these indicate

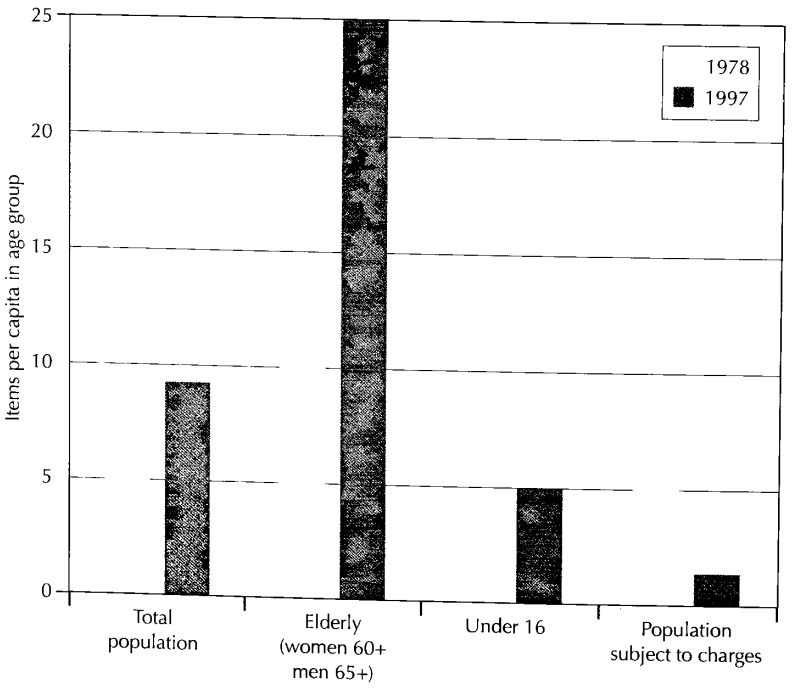


Figure 6: Per capita prescriptions items dispensed

that co-payments have generated modest reductions the NHS drugs bill. There is no substantive evidence of a negative impact on health status in the UK, albeit that there are extensive exemptions from charging in the NHS.

Where exemptions are not present the international evidence suggests that harmful co-payment related barriers to pharmaceutical care access can develop. These are most likely to affect poorer and otherwise less socially advantaged people, and might therefore undermine government policies on reducing health inequalities. Independent commentators have described the advocacy of increased reliance on user charges as 'misguided and cynical attempts to tax the ill and/or drive up the total cost of health care, while shifting some of the burden out of government budgets'.[25, 26]

Given the cost to the Exchequer of abandoning prescription charges (which raise approaching £500 million per annum) altogether, the most likely prospect is that NHS prescription charging policies will remain relatively static. Nevertheless, more innovations classified as 'lifestyle' medicines (and similar diagnostic or risk assessment products) may well be excluded from NHS supply. In wealthy and educated societies it seems inevitable that over time the private purchase of such goods will grow, and that members of the public able and willing to pay for them will demand increasingly easy, convenient access to them.

There is now good evidence that some products listed under Schedules 10 and 11 can deliver important public health benefits. Most importantly, the available data suggests that nicotine replacement therapy (NRT) medicines when appropriately used are among the most cost-effective of all pharmaceuticals.[27] This area is currently controversial, as a new form of smoking cessation product that requires medical supervision has now been marketed and changes in NHS NRT supply policy have been announced.

Informed patients, NHS Direct and the expanding roles of pharmacy and nursing

Although the evidence base is limited as far as health outcome improvements are concerned, increasing consumer involvement in health care decision-making at both the service development and the individual care levels is now generally accepted as a desirable goal. For example, the previous Governments' Patient Partnership Strategy[28] sought to augment NHS interaction with the public in the former context. Its approach has now been incorporated into the Department of Health's Policy Research Programme and the Standing Advisory Group on Consumer Involvement. The (English) Chief Medical Officer's current 'expert patient' initiative provides a relevant illustration of the present Government's concern to promote better personal care via individual patient empowerment.

Medical and other education courses today routinely include modules on topics such as consultation techniques. In part, these are aimed at promoting better understanding between prescribers and dispensers of medicines and their users. The Royal Pharmaceutical Society project on 'concordance' in medicines use[29] (that is, the establishment of shared understanding and goals between professionals and patients) identified the types of benefit that better information and support medicine takers could generate. Wasteful supply should be reduced and effective medicine use promoted by better two-way communication, and clearer recognition of the fact that the delivery of appropriate pharmaceutical care largely depends on informed self-care. This applies as much to prescription drug consumption as it does to areas of medication more traditionally seen as self-care.

NHS Direct and allied services currently being established (such as interactive Internet-based systems) should further help to empower NHS and private sector health care users to choose between types and levels of treatment, and deal with problems related to medicine taking. Ideally, NHS Direct will promote better co-ordinated care. It

ought to enable professionals of all types to spend more of their time with the people for whom their skills are most relevant.

However, medical and other observers who see the NHS Direct initiative and the introduction of new facilities (e.g. walk-in centres) as politically driven attempts to 're-brand' the NHS and increase its popularity with sections of the electorate with relatively limited care needs fear that in some instances they could fragment rather than improve service delivery. Work recently undertaken by the University of Sheffield's Medical Research Unit indicates that, in contrast to out-of-hours services provided by general practice co-operatives, there is no evidence that NHS Direct has so far had a significant impact on the overall demand for services such as A&E or ambulances, although it remains possible that it may be having an effect on the appropriateness of service use.[30]

NHS Direct may on occasions be able to promote desirable changes by competing with general practitioners and other NHS provider groups. But in the main it will need to complement and improve existing resources, rather than seeking to substitute for them. In this respect community pharmacy is well placed to work with NHS Direct and perhaps, in time, to become its high street 'front door'. People needing face-to-face help and advice for a wide range of lifestyle and self-limiting medical conditions could be referred to pharmacists, who may themselves come to use computer-based clinical decision support systems to underpin the quality of pharmacy-based consultations.

In the broader context of community pharmacists' and also nurses' roles in enhancing patient support and improving medicines use, additional opportunities for service innovations exist in relation to:

- **Prescribing costs and standards.** There is evidence from countries as diverse as Japan, The Netherlands and the USA that appropriate interventions from pharmacists can help to focus medical prescribing on optimally cost-effective therapeutic

options. Primary care pharmacists have already become closely involved in establishing and implementing PCG prescribing strategies, and the establishment of primary care trusts could generate further developments in the relationship between community pharmacy and general medical and nursing care. Recently proposed regulatory changes (announced for consultation by the Medicines Control Agency in MLX 260) will, for instance, allow bodies like PCTs to act as pharmaceutical wholesalers, as well as permitting community nurses and pharmacists to supply prescription-only medicines under the authority of locally agreed protocols, known as patient directives.

- **Repeat dispensing, and chronic disease management.** There is evidence (from, for example, New Zealand) that greater community pharmacist involvement in the management of repeat medication programmes reduces waste and increases treatment quality. This is consistent with UK hospital experience. Recent research has sought to validate this finding with respect to community pharmacy in Britain, and it appears that enhanced pharmacy control of repeat prescribing is likely to be introduced in this country, alongside developments like a greater number of nurse-led clinics offering more specialised support for people with chronic conditions needing long-term medical treatment.

- **NHS provision of treatments for minor illnesses.** Recent discussions on the strategic development of community pharmacy have covered options such as allowing pharmacists to supply OTC medicines at NHS expense to NHS patients exempt from prescription charges. This should improve the quality of service available, in part by reducing GP waiting times and workloads.

- **Emergency care.** Pharmacists should be able to contribute to public health through taking on an extended role in areas such as the supply of emergency contraception, the efficacy of which depends on early use after exposure to a risk of contraceptive failure or unprotected sexual intercourse. It seems probable that

(as is already the case in France) emergency hormonal contraception products will be reclassified as P medicines, as well as being available from pharmacists and nurses under patient directive arrangements.

From a public interest perspective options of this last sort raise questions about how decisions on changing the terms of medicines licenses are made, and whether or not more proactive public policies are required.

GP prescribing budgets

Financial incentives operating at both individual and practice level have been central to the development of NHS general medical practice, particularly since the 'Doctor's Charter' in the mid-1960s. The BMA has been a notably strong advocate of economic incentives for activities such as minor surgery in general practice. However, for the first four decades or so of the NHS's existence attempts to influence GP prescribing on the part of the state were limited to little more than the production and distribution of comparative cost information, coupled with weak advisory supervision via bodies like the Family Practitioner Committees. (The latter was disbanded at the start of the 1990s.) The reasons underlying this approach were:

- political concerns that the direct use of financial incentives to influence clinical activity could distort care patterns, and undermine public trust in the universal availability of health care through the NHS

- professional and pharmaceutical industry led resistance

- the fact that the family health services spending was open ended, to allow for variations in demand due to factors such as, say, influenza outbreaks. Even after hospital outlays became cash limited this arrangement persisted. It created divided incentives

for NHS management in relation to primary care pharmaceutical costs. Their growth was often underestimated at the beginning of financial years, because the Treasury would in any case have to meet them later. This relieved pressure on other parts of the NHS, at the cost of making GP prescribing expenditure appear to be 'spiralling out of control'. Drug industry promotion was routinely, if also somewhat cynically, blamed for this.

At the start of the 1990s two important sets of NHS reforms were introduced. The first, contained in the provisions of the NHS and Community Care Act 1990, led to the formation of the NHS 'internal market', GP fundholding and, eventually, unified district health authorities. The second was a 'new contract' for general practice, imposed by the Department of Health after repeated failures to achieve a negotiated agreement with the BMA.

The 1990 Contract contained a number of innovations, including item of service payments for conducting health promotion clinics (which caused such an increase in activity that it threatened a major GMS overspend, together with other perverse consequences) and relatively small lump sum payments for meeting immunisation and cervical cytology screening targets. Although some members of the medical profession denounced such payments as unethical, there can be little doubt that the latter have proved an effective way of influencing practice activity rates.

Independent GP fundholding was controversial, and has now been superseded by primary care groups and trusts in England and their equivalents elsewhere in the UK. Nevertheless, the fundholding scheme generated important insights into the dynamics of practice-level budget holding. A key aspect was that it pioneered the integration into a single budget of the funds available for a range of hospital and primary care activities, including medicines supply.

At the time that the original proposals for the creation of an internal NHS market were being developed, plans were also made for the

establishment of indicative prescribing budgets (IPBs) for all general practices. Although the IPB concept was not taken forward as initially intended in the early 1990s, economic incentives intended to moderate the prescribing of non-fundholding GPs were in time introduced. In the latter half of the 1990s health authorities were empowered to pay practices a fee of up to £3000 per GP for meeting agreed prescribing targets.

Large amounts of research have been undertaken in this field.[31, 32, 33] It confirms that GP fundholding and related schemes were effective in limiting prescribing cost increases, and generating real savings in medicine outlays. However, this conclusion needs to be treated with a degree of caution, not least because:

- **The effects on overall care quality and patient outcomes of incentivising prescribers and/or other professional groups to economise on treatment costs remain unknown.** As far as the NHS experiments undertaken in the 1990s go, there is little or no substantive evidence of harm stemming directly from pressure to cut primary care prescribing costs. But they presented prescribers with only modest and carefully planned financial incentives to modify patients' treatments. Stronger locally generated managerial and economic drivers incorporating more powerful incentives for budgetary restraint could in future have a more pronounced impact on the culture and outcomes of NHS care.

- **The savings generated as a result of the incentive schemes outlined above stemmed mainly from increases in generic medicine prescribing.** Economic incentives *per se* did not appear effective in promoting more complex changes in therapeutic strategy, which depend more on factors such as practice culture. Although there are national targets for further increasing generic prescribing, the extent to which it will further reduce UK prescribing costs is limited by the fact that almost all the pharmaceutical products that it is presently possible for the NHS

to supply in generic form are already being prescribed generically. The more expensive formulations in use are covered by patent protection, or are for other reasons available from only one source.

Taken together, these observations suggest that demand-side management of pharmaceutical use within the NHS will have to utilise techniques more complex than financial incentivisation alone to further enhance performance, let alone replace altogether the need for supply-side controls on the pricing and profitability of the pharmaceutical industry. This emphasises the importance of quality management techniques in modern health care.

The NHS quality agenda and NICE

The 'New NHS' strategy is aimed at:

- generating clear, evidence-based, service guidelines and standards
- promoting the local delivery of good care, with responsibility for all aspects of clinical and non-clinical service provision appropriately shared between trust board and health authority members and professional and managerial staff
- ensuring that service standards are being objectively monitored, and that potential or actual shortcomings in care or service management are corrected.

In England and Wales NICE's agenda is focused at the first of these levels. Clinical governance systems are aimed at ensuring the second. The work of the Commission for Health Improvement (CHI) lies at the heart of the third.

From the perspective of pharmaceutical sector regulation NICE represents the most radical component of these reformed arrangements, although the potential impact of stronger clinical governance and the CHI on prescribing and dispensing standards should not, of course, be ignored.

NICE is a special NHS authority responsible for:

- the appraisal of new and existing medicines and other health care technologies. It will make recommendations on the extent of desirable use of selected new and existing medicines, working to an agenda set by ministers

- the development of new clinical guidelines

- the promotion of clinical audit (including methodology development) and confidential inquiries.

Advocates of NICE hope it will improve the cost-effectiveness of NHS care and reduce inappropriate variations in clinical behaviour. But some observers in the pharmaceutical industry see its formation as an attempt to introduce an economic 'hurdle' – over and above existing tests of safety, efficacy and effectiveness – to surmount in the process by which medicines are accepted for use in the UK. They may believe that it will serve as a model for the future development of a similar body or bodies elsewhere in Europe. An 'EU NICE' might in part be designed to ensure that problems comparable to that of the 'postcode rationing' of medicines access within the NHS do not emerge as high-profile challenges for the Union as a whole.

The core of the charges against NICE is that by examining in a questionably transparent manner issues of affordability – and so implicitly, if not explicitly, setting rationing criteria – rather than looking purely at evidence of clinical and cost-effectiveness, it could impair clinical freedom, undermine public confidence and threaten patient well-being. In return it may generate only limited public spending reductions. Similar complaints greeted the formation of related organisations in Canada, Australia, Finland and The Netherlands. But it might be argued that the UK has much more to lose than countries such as Australia if global companies move research and other valued activities away to centres in the USA or, in time, locations in Asia and Latin America.

However, against such fears the logic underlying the case for collating economic and allied evidence relating to the value of medical innovations in a comprehensive, co-ordinated way, and for making findings based on the latter universally available in a credible, authoritative manner has a widespread appeal. It would be foolhardy for industry-related and allied professional interests not to recognise the strength of the political commitment to supporting NICE and allied concepts, not just in the UK but elsewhere in Europe.

The most viable way forward for all sides is therefore likely to be one that attempts to ensure that bodies such as the National Institute function as well as possible. This will require taking into open account the policy dilemmas and conflicts that inevitably underlie pharmaceutical sector regulation. Such an approach must be based on a common, informed awareness of the public's interests in not only improved efficiency of the use of scarce health care resources, but also in protecting Britain's position as a leading centre of clinical and pharmaceutical research. The public also has interests in retaining a positive trade balance in medicines, and in the discovery and safe supply of new means of preventing and/or treating more effectively presently incurable disorders.

Chapter 5

Conclusion – an agenda for R&D

The positive benefits that modern pharmaceuticals have contributed to the health and wealth of the UK, and the entire global community, are substantial. The existence of the modern pharmaceutical industry may in itself be taken to represent a major achievement, for not only this country but for the whole of humanity.

However, the gains that medicines research, production and marketing have bought have not been without cost, both financially and in public health terms. Problems since Thalidomide have ranged from the medical misuse of tranquillisers and arguably other psychotropic medicines[34] to increasing rates of antibiotic resistance.[35] The fact that pharmaceuticals remains one of the world's most profitable manufacturing sectors is seen by some commentators as evidence of inadequate medicine cost and/or spending controls. Others cite issues such as animal experimentation, environmental pollution, the quality of promotional claims made in both the professional and public media, and the role of pharmaceutical companies in the poorer countries of Africa, Asia and Latin America as potential or actual threats to community well-being.

Responding to such concerns in ways that will protect public interests requires enhanced communication, and more complete information exchanges. A key challenge for the 21st century is to establish more constructive relationships between pharmaceutical companies, governments and their agencies, the health care professions and consumer and other groups involved in pharmaceutical sector policy formation and regulation.

Robust approaches to protecting populations from inadequately tested technical innovations are of course vital, as are checks on the actions of all groups with the power to influence significantly the health of individuals and populations. But a shift away from blame and suspicion towards more effective co-operation between the pharmaceutical industry and other agencies involved in the pharmaceutical supply process would be desirable, in as much as it should promote more effective joint efforts to improve public health. The ultimate purpose of all regulatory interventions is to foster greater human well-being, in part through enabling optimal balances between competing – and often contradictory – policy goals to evolve with a minimum of friction.

The route towards this goal is likely to involve generating better mutual understanding and more informed trust between all actors in the pharmaceutical sector, including medicine consumers as well as their makers and prescribers. It will also require systematic analysis of the options available for further improving the overall working of the pharmaceutical market place. Topics requiring research and policy analysis include:

Medicine price deregulation. To what extent will innovations within the NHS make the PPRS unnecessary?

The 1999 PPRS agreement includes a commitment to examine this question. Notwithstanding barriers to change – such as the reluctance of politicians and the public to risk lifting supply-side statutory controls in an area where rapid technical innovation is likely to generate unpredictable new costs, but where denying universal access to innovations may be unacceptable – it demands close attention. This is so because of the requirements of the European single market. In time, the combined effects of bodies like NICE, the introduction of new forms of clinical governance and the emergence of PCTs (which have the potential to develop local medicines purchasing and supply mechanisms) could mean that central governments will take a less proactive role in setting the prices and/or the profits made on prescription medicines.

More competition between the providers of alternative treatments could in appropriate circumstances generate significant benefits for both the public and surviving companies. Nevertheless, experiments in deregulation also carry risks. If – as to an extent appears to have been the case with generic medicine supply in the NHS – competition fails to deliver expected gains, the final result could be a pattern of regulation more restrictive than the current PPRS. To the degree that the latter currently serves to prevent the abusive use of NHS monopsony purchasing powers, its elimination might harm public interests in a strong pharmaceutical industry.

Consumer empowerment: informed self-care, and more self-purchasing?

Different sections of the population are likely to benefit from different approaches to medicines supply. Younger, better-off groups may be prepared and able to pay out-of-pocket or through private insurance for access to the best possible treatments and/or preventive interventions. Other sections of the population are less able to pay, and may also be less able or willing to manage their own care. They have a greater need for 'voice' within the NHS and other systems.

Effective regulation demands strategies that are practically viable, and will not be circumvented by significant numbers of individuals. The interests of those most in need have to be defended in ways that engender majority acceptance. Understanding the beliefs, expectations, preferences and actual behaviours of all classes of medicine takers is a vital prerequisite for the effective delivery of care, and the prevention of drug-related harm. In future there may have to be new arrangements (perhaps based on self-held medical records) to allow easier self-purchased access to pharmaceutical products that should not be on unregulated public supply. How best this might be achieved is a significant issue for further investigation. So also is the issue of consumer charging for prescribed NHS medicines, and the degree to which it can promote increased efficiency or distort medicines use in ways that harm public health.

Regulating advertising and promotion in the 21st century. Is direct-to-consumer advertising of prescription medicines inevitable, and can Internet activities be effectively regulated?

The case for overt, but well-regulated, DTC prescription medicines advertising is stronger than is sometimes recognised in countries with paternalistic social traditions. The realities of modern medicines marketing and the impact of technologies such as the Internet suggest that there is a growing need for regulatory reform in this context. The assurance of information accuracy and integrity in all forms of medical media coverage (including the conventional press) deserves close attention. So too do issues such as the impact of e-commerce (plus possible changes in the legal position on retail price maintenance for medicines) on the viability of community pharmacy and other forms of retail service for less advantaged sections of the population. Given that the determinants of health extend well beyond the provision of health care, this is a matter of considerable importance.

The medicines licensing system: time for reform?

Following from the above, there is also a case for revising the arrangements embodied in the Medicines Act 1968 as they apply not only to the advertising of POM medicines but also to their licensing. Any such change would require reform at an EU rather than a national level, and consideration of this question is therefore timely in the light of the review of the medicines licensing process in Europe due to take place in 2001. Relevant questions for analysis range from the definition and ongoing viability of the current prescription medicine, pharmacy-only and general sales licensing categories to the use of electronic media to conduct medical consultations and issue prescriptions, and the regulation of home delivery services for medicines.

The mechanisms triggering changes in licensing status once a medicinal product is on the market may require examination from a

public interest perspective, alongside concerns about freedom of access to information supplied during licensing applications. The complex and costly nationally-based structures currently existing alongside (and influencing the working of) the EMEA also need examination, as do the ways in which UK-based commercial, professional, political and consumer movement interests work together to serve the public via bodies such as the Medicines Commission and other expert advisory bodies.

Professional roles and changing patterns of authority

New prescribing and dispensing arrangements (such as nurse practitioner-led facilities) could in some contexts create increased efficiency and improve the quality of pharmaceutical care. But extending prescribing and medicines supply rights to new professional groups might also fragment care, and impair its value to service users. Further analyses of how to incorporate quality management techniques into the fabric of professionally-led care, as distinct from merely imposing more control and inspection on highly educated workforces, ought to help new patterns of medicines regulation and use to emerge in ways that minimise unintended consequences and optimise the achievement of desired outcomes.

Strategies for pharmacy and disease management

The pharmaceutical profession evolved throughout the 20th century as its historic role in medicines fabrication and packaging was taken by the modern pharmaceutical industry. Further patient and consumer needs focused progress will be required in the 21st century. Pharmacists will have to work more closely with each other, with patients and with other primary and secondary care professionals to ensure the safe and effective use of new diagnostic technologies, and more sophisticated pharmaceutical treatments. The latter are likely to be increasingly tailored to individual patient needs.

Pharmacists will also require extended communication skills to enhance the quality of self-care, and enable those consulting them to

understand and use all types of medicine effectively. More research into the development of optimal pharmacy practice is needed, alongside that on the nursing and other professions. Pharmaceutical companies may also be able to extend their services in support of their products' use. The development of stronger private/public partnerships offers a further area for study.

The limits of economic evaluation

Through bodies such as NICE, economic evaluations are playing a significant role in determining health and medicines policy. It is in principle in the public's interest to maximise the efficiency with which resources are used. However, as with some clinical evaluations, not all economic evaluations are of high enough quality from which to draw robust conclusions, and the approaches used and assumptions made can on occasion be strongly questioned. For example, the interests of given individuals, families and patient groups can differ significantly from those of the community as whole, unless the importance of issues such as, say, social exclusion and the transmission of economic disadvantage across generations are taken fully into account. Research on the conduct and use of economic evaluations is therefore needed if their role in the regulation of the pharmaceutical sector is to be as relevant and worthwhile as possible. As a large employer of health economists, the pharmaceutical industry clearly has a role in developing robust evaluative methodologies as, along with others, it did and continues to do in clinical evaluation.

Intellectual property protection and global access to medicines. To what extent can and should national and regional regulatory regimens be integrated in the pursuit of world-wide health and welfare improvement?

Patents serve to protect innovators' financial returns and encourage investment in activities such as pharmaceutical research and the supply of effective medicines. Many valuable pharmaceutical

innovations have been delivered because of the existence of intellectual property protection. If – as is probable – research costs continue to rise there will be a case for extending provisions for the protection of biomedical discovery rights in the richer parts of the world, provided they do not inhibit non-commercial forms of scientific endeavour.

However, the supply of medicines to the world's poorest communities is not always well served by the economic incentives derived from patenting. This is not the 'fault' of the pharmaceutical industry, or even national level regulators. But it is an example of a problem of real importance to the future of humanity. (Some similar regulatory issues exist in areas such as atmospheric pollution.) Whether or not the world community can create a regulatory structure capable of ensuring a coherent global approach to world health is a question that goes well beyond the horizons of the UK pharmaceutical sector. But it is nevertheless one of vital interest to people in this country along with the rest of humanity, and one in which informed British leadership could prove valuable.

A better future?

Technologies such as genomics and computer science hold much promise for promoting further gains in human welfare. These stand to be in part derived from the better informed use of new and existing pharmaceuticals. Regulatory arrangements that permit valued activities and maximise freedom for individual and corporate enterprise wherever possible, yet prevent harm whenever necessary, are needed to foster such progress. This is the case not only in relation to medicines supply but in all fields of enterprise.

However, just as pharmaceuticals alone cannot guarantee health, regulation alone cannot ensure true excellence in any area of human activity. The primary objective of regulatory interventions is normally to moderate the risk of unwanted events, and to prevent or stop abuses. These are important ends. But their pursuit must not be

allowed to obscure other, on occasions even more vital, public goals. A tightly regulated system is no substitute for one that engenders innovation, empathy, self-motivated integrity and individual and collective goodwill.

These characteristics, and the values that underpin them, are vital ingredients in the political processes that generate good law and govern the effective implementation of agreed regulations. They are also central to the provision of health and social care that meets as closely as possible the requirements of the people receiving it.

If pharmaceutical manufacturers, purchasers, prescribers, dispensers and consumers wish to optimise medicines supply they need to work together to create balanced markets for such products, and effective systems for their delivery to all who require them. For these to function with a minimum of restrictive and counter-productive bureaucracy, all those involved also need to agree appropriate standards of behaviour and to the best of their ability live by them, despite conflicting personal and collective interests. In the final analysis, providing a framework for protecting the vulnerable and freeing individuals to resolve constructively the dilemmas inevitably associated with medicines research and provision is the fundamental social product of a good regulatory system.

Appendix

The *British Pharmacopoeia*

The apothecaries of Florence produced the first comprehensive, written codification on the production of medicinal drugs in 1498. This was Europe's earliest pharmacopoeia (from the Greek *pharmakon*, a drug, and *poiia*, making). Barcelona's *Concordia Pharmacolorum Barcinonesium* followed it in 1535. Others were published in Nuremberg in 1546 and in Mantua in 1559.

Britain lagged behind its European neighbours until the College of Physicians initiated the first discussions on the creation of a British formulary in 1585. The College eventually compiled and published the *Pharmacopoeia Londinensis* in 1618. A unified *British Pharmacopoeia* did not become available until 1864. The Medical Act 1858 (which established the unified profession) required the General Medical Council to compile a national pharmacopoeia. This superseded three rival ones produced in London, Edinburgh and Dublin.

Since 1971 the *British Pharmacopoeia* has been published by the Secretary of State for Health, acting on the recommendations of the Medicines Commission. The current document is more a guide to prescribing than to medicines production. This reflects the fact that making (and packaging) medicines is now largely undertaken by the pharmaceutical industry. The role of pharmacists has moved away from production to concentrate more on the processes of medicine selection and dispensing. This last includes ensuring that their endpoint users – patients – are adequately informed, and are helped to take pharmaceutical products in ways that help them to achieve the outcomes they most desire.

References

1. Griffin JP. The evolution of human medicines control from a national to an international perspective. *Adverse drug reaction toxicology review* 1998; 17(1): 19–50.

2. Holloway SWF. Professional business: the achievements of the Royal Pharmaceutical Society since 1841. *Pharmaceutical journal* 2000; 264(7077): 15–21.

3. HMSO. *Report of the Committee of Enquiry into relationship of the pharmaceutical industry with the National Health Service 1965–1967.* Cmnd.3410. London: HMSO, 1967.

4. HMSO. *Forthcoming Legislation on the Safety, Quality and Description of Drugs and Medicines.* Cmnd.3393. London: HMSO, 1967.

5. Collier J. Science, Politics and the Pharmaceutical Industry: Controversy and Bias in Drug Regulation. *BMJ* 1995; 311: 1101–02.

6. Abraham J, Sheppard J and Reed T. Rethinking transparency and accountability in medicines regulation in the United Kingdom. *BMJ* 1999; 318: 46–47.

7. European Agency for the Evaluation of Medicinal Products. *General report.* London: EMEA, 1998.

8. Joined cases C-267/95 and C-268/95. *Merck & Co. Inc and Others v. Primecrown Ltd and Others, Free Movement of Goods.* Brussels: European Union Court of Justice.

9. Rozek R and Rapp R. *Parallel trade in pharmaceuticals: the impact on welfare and innovation.* NERA working paper 16, 1992.

10. Taylor D and Maynard A. *Medicines, the NHS and Europe.* London: King's Fund Institute, 1990.

11. Office of Health Economics. *Compendium of health statistics*. 11th ed. London: OHE, 1999.

12. House of Commons Health Select Committee. *The cost and availability of generic drugs to the NHS*. London: HMSO, 1999.

13. Department of Health. *Pharmaceutical Price Regulation Scheme*. London: HMSO, 1999.

14. Association of British Pharmaceutical Industry. *Understanding the PPRS: the control of NHS medicine prices and costs*. London: ABPI, 1999.

15. Proprietary Association of Great Britain. *Market size statistics 1997/98*. London: PAGB, 1999.

16. Regulatory Impact Unit. *Self-regulation interim report*. London: Cabinet Office, 1999.

17. Mintzes B. *Blurring the boundaries: new trends in drug promotion*. Amsterdam: Health Action International, 1998.

18. Conducted by BMRB research agency for PAGB, 1987.

19. Conducted by BMRB research agency for PAGB, 1997.

20. Taylor D and Maynard A. *Medicines, the NHS and Europe*. London: King's Fund Institute, 1990.

21. Soumerai SB and Avorn J. Principles of educational outreach ('academic detailing') to improve clinical decision-making. *JAMA* 1990; 263(4): 549–56.

22. Mossialos E and Le Grand J. *Health care and cost containment in the European Union*. London: Ashgate, 1999.

23. Ryan M and Birch S. Charging for health care: evidence on the utilisation of NHS prescription drugs. *Social science and medicine* 1991; 33(6): 681–87.

24. Hughes D and McGuire A. Patient charges and utilisation of NHS prescription medicines: some estimates using a cointegration procedure. *Health economics* 1995; 4: 213–20.

25. Freemantle N and Bloor K. Lessons from international experience in controlling pharmaceutical expenditure I: influencing patients. *BMJ* 1996; 312: 1469–71.

26. Barer M, Evans RG and Stoddart GL. *Controlling health care costs by direct charges to patients: snare or delusion?* Toronto: Ontario Economic Council, 1979.

27. Stapleton JA, Lowin A and Russell MAH. Prescription of transdermal nicotine patches for smoking cessation in general practice: evaluation of cost-effectiveness. *Lancet* 1999; 354: 210–15.

28. NHS Executive. *Patient partnership: building a collaborative strategy*. Leeds: Department of Health, 1996.

29. Royal Pharmaceutical Society of Great Britain. *From compliance to concordance: towards shared goals in medicine taking*. London: RPSGB, 1997.

30. Munro J, Nichill J, O'Cathain A and Knowles E. *Evaluation of NHS Direct first wave sites*. Sheffield: University of Sheffield Medical Care Research Unit, 2000.

31. Baines DL, Tolley KH and Whynes DK. *Prescribing, budgets and fundholding in general practice*. London: OHE, 1997.

32. Gosden T and Torgerson DT. *The effect of fundholding on prescribing and referral costs: a review of the evidence*. Manchester: National Primary Care Research and Development Centre, 1997.

33. Bateman DN, Campbell M, Donaldson LJ, Roberts SJ and Smith JM. A prescribing incentive scheme for non-fundholding general practices: an observational study. *BMJ* 1996; 313: 535–38.

34. Medawar C. The antidepressant web: marketing depression and making medicines work. *International journal of risk and safety in medicine* 1998; 10: 75–126.

35. Amyes SGB. The rise in bacterial resistance. *BMJ* 2000; 320: 199–200.

Close regulation of the pharmaceutical industry has been seen as essential for the protection of the public for most of the last century. Yet the interest of government and the public in the low-cost provision of medicines can often conflict with the existence of a strong, profitable and innovative pharmaceutical industry.

Health, Wealth and Medicines for All? is part of the King's Fund Policy Dilemmas series. It explores the tensions between seemingly divergent goals, putting the role of pharmaceutical sector regulation into national and wider contexts. This wide-ranging book gives an overview of the evolution of the UK pharmaceutical market and its control; describes the Pharmaceutical Price Regulation Scheme and other supply- and demand-side interventions; and, in a concluding analysis, offers a number of suggestions for the future of medicines regulation and research.

In the fast-changing world of the 21st century, effective regulation must encourage innovation, self-motivated integrity and individual and collective goodwill. *Health, Wealth and Medicines for All?* indicates ways forward, and will be informative reading for policy-makers, pharmaceutical industrialists and members of the public, who ultimately use and pay for all medicines.

Andrew Tucker is Head of Communications at Pharmacy2U. He was previously Head of Policy at GJW Government Relations Ltd and worked for the Liberal Democrats as Senior Health Analyst. David Taylor has recently been appointed Professor of Pharmaceutical and Public Health Policy at the School of Pharmacy, University of London. His previous posts include Director of Health Affairs at GJW, Associate Director of Health Studies at the Audit Commission, and Director of Public and Economic Affairs at the Association of the British Pharmaceutical Industry.

ISBN 1-85717-431-3

9 781857 174311