

Annexe E

PPRS and industrial policy

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EXECUTIVE SUMMARY

Some types of investment in the pharmaceutical sector are footloose in the sense that they can be carried out anywhere in the world where a suitable environment exists, regardless of where final sales are made. These include R&D investments and some manufacturing investments. For a variety of reasons – such as the spillover effects R&D may have on other sectors and its consequent contribution to economic growth – many governments seek to encourage companies to locate these investments within their national boundaries, using a range of industrial policy instruments in an attempt to do so.

Some stakeholders regard the PPRS as an important component of the UK Government's industrial policy towards the pharmaceutical industry – that is, as a means of attracting and retaining pharmaceutical R&D investment within the UK. While major stakeholders disagree over whether this is one of the scheme's aims, it is important to assess whether the PPRS does serve this purpose.

Accordingly, this annexe:

- considers the possible rationale for Government attempts to attract pharmaceutical R&D investment in the UK
- shows that the UK has been relatively successful in attracting and retaining R&D investment in the pharmaceutical sector
- identifies the range of factors that drive the location of R&D investments and help to explain current successful UK performance, and
- draws some high level policy implications for meeting industrial policy aims in the future.

Of the various potential economic rationales for attracting R&D in the UK, the most plausible are those that are based on geographical spillovers – that is, benefits from R&D that accrue to other companies located near the investment in question. Other potential justifications are less compelling and, in some cases, are based on a conflation of the aim of attracting investment in the UK with that of supporting UK-owned firms, whether located in the UK or not.

A previous attempt to quantify these benefits – conducted for the Pharmaceutical Industry Competitiveness Taskforce (PICTF) in 2000 – suggested R&D spillovers and labour rents could reach up to £520 million. It also suggested that there is a potential terms of trade effect of between £1 billion and £2 billion, although this figure is a significant overestimate as it takes no account of offsetting effects – namely the fact that resources currently allocated to the pharmaceutical sector would be used elsewhere to produce exportable goods or to replace imported goods.

A major finding of this study is that, contrary to popular belief, the PPRS does **not** contain explicit incentives to locate R&D investments in the UK. Indeed, the R&D allowance under the scheme relates to R&D wherever in the world it is carried out. Theoretically, PPRS rules on transfer pricing could even produce a disincentive to invest in the UK. In practice, however, this effect is not currently likely to be a significant effect because the profit cap has not been binding for most firms. Further, there are strong reasons for believing that any pricing scheme that did

contain explicit incentives to locate in the UK would fall foul of EC rules relating to the free movement of goods and state aid.

Factors that are found to have an important effect on the location of R&D investment include:

- a highly skilled workforce with relevant scientific qualifications
- the presence of opinion leaders in the medical field
- access to high quality clinical trials infrastructure
- existing R&D activity, including public sector R&D, and
- historical and cultural factors.

Financial factors, such as labour costs, taxation rates and tax credits, also have an impact but are generally held by industry to be of secondary importance to the 'quality' of the investment environment (that is, to be determinative only when countries are equally attractive on quality grounds).

The revenues companies receive from the sales of products in a particular market are not a driver of footloose investment – only of market specific expenditure such as marketing – since companies are not required to invest in a particular country to receive revenues from selling a particular product. However, some companies have suggested that there is still an indirect link between price and the location of investment, since companies will use the threat of withdrawing investments as a means of persuading governments to maintain high prices. It is rational for companies to make such threats in an attempt to make features of the policy environment – such as pricing and reimbursement decisions – more favourable. It is not clear, however, that these threats are always credible, particularly if the country in question performs strongly in relation to the drivers identified above. We could find no clear relationship between price level and success in attracting R&D investment.

We therefore find that there is very little evidence to link the price of pharmaceuticals in the UK with the overall attractiveness of the UK as a pharmaceutical R&D investment location. Note, however, that this does not mean that we subscribe to the view that overall pharmaceutical prices should be pushed as low as possible. R&D investment in valuable drugs should be strongly rewarded to provide the right incentives for companies to continue investing in useful products in the future.

If the Government does want to attract investment into the UK the most effective means of doing so would be to invest in the explicit drivers identified above that have a direct effect on the attractiveness of the UK as a location for investment such as investing in the scientific skill base or improving the environment for clinical trials. Examples of initiatives that do this, such as the creation of the UK Clinical Research Collaboration, are to be welcomed.

In relation to pharmaceutical pricing policy, we conclude that any future reform of the PPRS must retain the current policy of not discriminating between firms on the basis of the location of their investments. Indeed, this policy should be made more explicit as several companies and public bodies we spoke to on our international case studies seemed to think that the scheme is currently used – explicitly or implicitly – to favour UK-based firms. Such perceptions are

unhelpful: for companies they risk undermining stability and transparency; and internationally, they may help to legitimise potential discriminatory behaviour by other players in the future.

Any reformed scheme would therefore need to be very explicit, in its objectives and in the rules guiding it, that UK-based firms will not be favoured. An additional – although longer-term – option for underpinning this transparency would be to give pricing responsibility to an independent, technocratic authority that is insulated from Government or Industry influence. Such an approach has been used with some success in other countries such as Sweden, although we recognise that it would probably require primary legislation to effect such a change in the UK.

Moves towards clarifying these issues would be consonant with the Health Select Committee's recommendations to remove industry sponsorship objectives from the Department of Health's pharmaceutical regulatory and policy functions.

1 INTRODUCTION

1.1 This annexe:

- considers the possible rationale for Government attempts to attract Research and Development (R&D) investment in the UK
- examines UK performance in attracting and retaining R&D investment in the pharmaceutical sector, and
- identifies the range of factors that help to explain this performance, considering in particular whether the pricing regime is one of them.

1.2 We find that the PPRS does not contain explicit incentives to locate R&D investments in the UK and conclude with a consideration of alternative policy mechanisms that could be used to meet industrial policy objectives.

1.3 It should be stressed that this annexe focuses exclusively on the industrial policy objectives of the PPRS – that is whether the scheme is necessary to attract and retain investment in the UK. This should not be confused with the question of whether the PPRS promotes efficient investment in new and useful drugs and affects access to drugs (availability and take up). These questions are addressed in Annexes A, B and D.

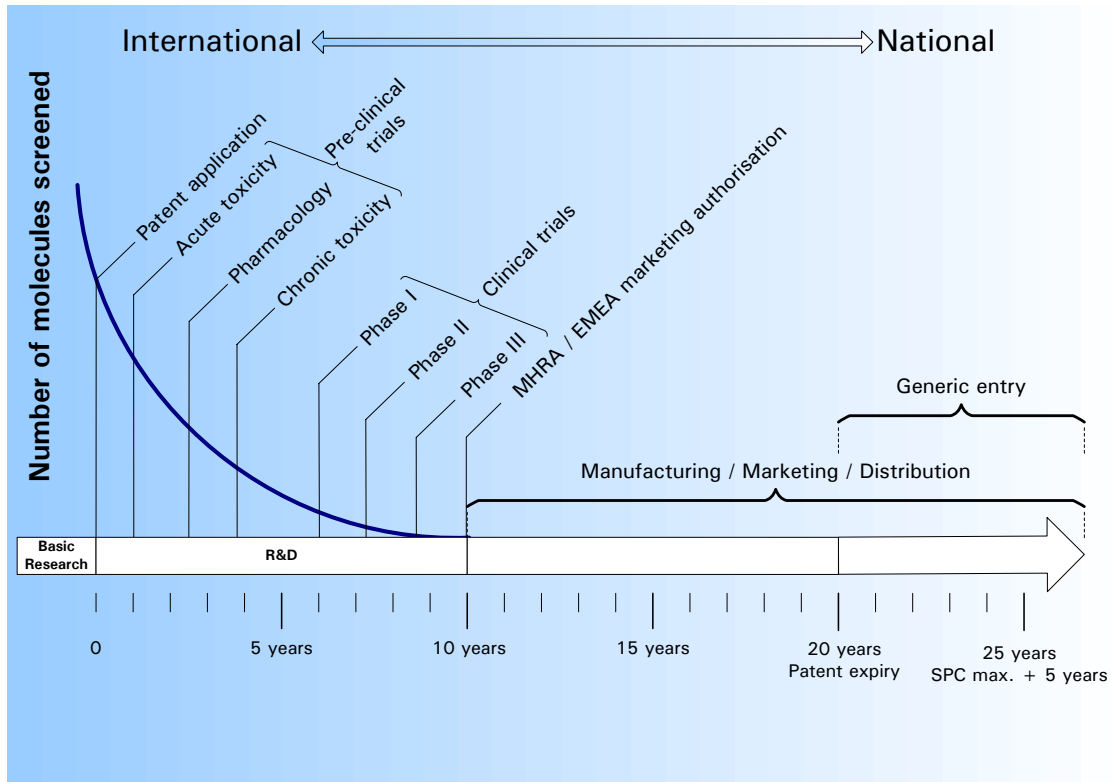
1.4 As context for the analysis that follows, the rest of this introduction considers two related questions: what is meant by industrial policy in the pharmaceutical sector and, in this context, how is the 'UK' pharmaceutical sector defined?

What is meant by industrial policy in the pharmaceutical sector?

1.5 The diagram below presents a schematic overview of the drug production process, from basic discovery to generic entry after patent expiry. Box 1.1 contains a brief description of the key stages.

1.6 It is possible in the diagram to distinguish between components of the production process that can be considered 'international' (namely can be located anywhere in the world for supply to any given country) and those that are 'national' (that is need to be located in the country in question). As the diagram moves from left to right and becomes lighter, so the activities become increasingly 'national' in scope.

Figure 1.1: Lifecycle of a drug



1.7 In broad terms, R&D and manufacturing can be considered international activities, whereas marketing and distribution are national activities. Danzon (1997)¹ give a more detailed breakdown of costs according to the following typology:

- joint global costs (R&D plus a component of manufacturing such as the fixed costs of so called primary production)
- costs that are incremental for operation in a particular country but joint across products (certain country head office costs, a proportion of sales force expense), and
- costs that are variable for particular products in a country (such as promotion, distribution and secondary production).

¹ Danzon, P. (1997), 'Price Discrimination for Pharmaceuticals: Welfare Effects in the US and the EU', International Journal of the Economics of Business, Vol. 4, No. 3, 1997;

Box 1.1: Stages in the lifecycle of a drug

1. Basic research is sometimes conducted within public sector institutions such as universities.
2. Pharmaceutical companies can acquire patent protection once basic research has led to the identification of promising New Molecular Entities (NMEs).
3. Pre-clinical trials precede any testing on humans, and involve rigorous testing of selected NMEs in laboratories and animals.
4. Clinical trials are carried out in humans. Three stages of trials are carried out before drugs receive marketing authorisation, namely:
 - Phase I trials in 20-100 healthy adults to test the drug's safety;
 - Phase II trials in 100-300 patient volunteers to determine the safety and efficacy of the drug;
 - Phase III trials on larger groups of patients (typically 1,000–3,000), to gain further data on safety and efficacy;
5. Marketing authorisation must then be obtained before drugs can be launched onto the market (see later);
6. After drugs reach the market, Phase IV pharmaco-vigilance trials begin. These seek to identify any adverse drug reactions and continue throughout a drug's lifetime.
7. Generic manufacturers are able to enter the market and sell generic copies of the drug after a drug's patent (and any supplementary protection certificate) has expired.

1.8 The industrial policy of the UK Government (and indeed other governments) focuses on attracting and retaining investment in the international (and therefore 'footloose') component of the supply chain. This was the explicit remit of the Pharmaceutical Industry Competitiveness Taskforce, which is now known as the Ministerial Industry Strategy Group (MISG).

1.9 Consistent with this goal, the UK Government announced in 2004 that it was setting a new target for attracting R&D into the UK across the whole economy

"... because we want Britain to be the most attractive location in the world for science and innovation, we are setting a new and ambitious target of increasing UK R&D investment as a proportion of national income from its current level of 1.9 per cent to 2.5 per cent by 2014 over the next decade."²

How is the 'UK' pharmaceutical industry defined?

1.10 The next chapter considers the rationale for pursuing industrial policy in the pharmaceutical sector. A prerequisite for doing so is to be clear on the definition of the UK pharmaceutical industry: that is whether policies are directed at supporting firms

² Source: The UK Government's 'Science and Innovation Investment Framework 2004-2014', published in July 2004.

that operate within the UK, or firms with UK ownership. This distinction is important as either option will be based on different rationales and will result in different policies.

- 1.11 There appears to be some confusion on this issue as some previously published statistics and analyses relating to the pharmaceutical industry have neglected to make this distinction. For example, data identified in the Department of Trade and Industry's R&D scoreboard as 'UK R&D' is the sum of R&D invested in the UK by foreign firms and all R&D conducted by UK-owned firms, whether conducted in the UK or not. The 2000 PICTF valuation of the Pharmaceutical Industry makes a similar conflation (as discussed in the next chapter).
- 1.12 It is our understanding that UK industrial policy is orientated towards encouraging firms to invest within the UK rather than supporting UK-owned firms. For example, the 2004 PICTF report on competitiveness and performance indicators states that, *"the indicators help in monitoring the competitiveness of the UK relative to other countries as a location for the pharmaceutical industry"*.
- 1.13 *'The Science and Innovation Framework 2004-2014: Next Steps'*, a report published in 2004 and produced jointly by several government departments, also sets out the importance of the UK as a location for R&D:
- '...the Government published its Science and Innovation Investment Framework 2004-2014 in July 2004 to set a long-term strategy to improve the UK's R&D and innovation performance. In order to remain attractive as a **location** for research and innovation, the UK needs to build on this strategy...'*
- 1.14 By contrast, if industrial policy were aimed at UK-owned companies, the implication would be that it would involve preferential treatment for UK-owned companies over companies that are not UK-owned. We do not believe that either Government or the key industry associations would support such a policy position.
- 1.15 There is a further, practical, difficulty with any policy that aimed to support UK-owned firms: given the global nature of share ownership, it is unclear to what extent any firm is solely or even mainly owned by UK citizens. Indeed, in practice where the literature refers to UK-owned firms, in most cases it seems that the reference is in fact to firms that are registered in the UK rather than owned by UK citizens.

Overview of the annexe

- 1.16 The rest of this annexe is structured as follows:
- Chapter 2 considers the economic rationale for seeking to attract R&D investment to the UK, and reviews a previous attempt at quantifying the value of the pharmaceutical sector to the UK economy
 - Chapter 3 gives an overview of the performance of the UK in attracting pharmaceutical investment

- Chapter 4 assesses whether PPRS gives explicit incentives to invest in the UK, and assesses legal constraints on pursuing industrial policy goals through pharmaceutical pricing
- Chapter 5 analyses the key factors that determine the location of footloose investments and the relative performance of the UK against these factors, and
- Chapter 6 provides some high level policy implications.

2 ECONOMIC RATIONALE FOR INDUSTRIAL POLICY

Introduction

- 2.1 The UK Government has set a target of increasing UK R&D investment as a proportion of national income from its current level of 1.9 per cent to 2.5 per cent by 2014. In this chapter we consider the potential rationale for such a policy – both within the economy as a whole and within the pharmaceutical sector in particular.
- 2.2 The principal theoretical justification for government intervention in R&D is based on market failures caused by the existence of positive externalities. Firms will benefit from R&D carried out by others, as productivity-enhancing knowledge 'spills over'. These spillover benefits that do not accrue to the firm undertaking the investment may lead to underinvestment in R&D.
- 2.3 In addition to R&D spillovers, there are other possible motives for industrial policy:
- market failures arising from uncertainty: an asymmetric distribution of information between investors and firms about the risk of undertaking R&D may lead to underinvestment
 - strategic trade policies: by subsidising R&D in imperfectly competitive markets, governments can enable firms to take a larger share of the economic rents
 - macroeconomic or regional policies: the support of R&D can be used as a tool for stimulating the economy generally, or to regenerate a locality or region.
- Analysis of these potential justifications follows below.
- 2.4 The first subsection analyses and assesses the potential economic justifications for industrial policy and the second evaluates a previous attempt at quantifying the benefits to the UK of the pharmaceutical industry.

Justifications for industrial policy in the pharmaceutical sector

Spillovers

- 2.5 Spillovers are positive externalities that occur when the social returns to a productive activity outweigh the private returns. These spillovers principally take the form of 'knowledge (or technology) spillovers' that increase the productivity of other firms: benefits accrue both to other firms operating in the same industry and to firms in other industries that use similar processes. They are quantifiable as the difference between social and private returns.
- 2.6 In addition, there may be some negative spillover effects resulting from product market rivalry. R&D undertaken by firms who are product market rivals may sometimes lower the productivity of their competitors (for example, if they are involved in a race to register a patent). However, these effects have been shown to be vastly dominated by

the positive technology spillovers,³ with social returns being several times greater than private returns.

Geographical range of spillovers

- 2.7 The market failure caused by spillovers could potentially be addressed by industrial policy to promote R&D. However, the suitability of government intervention depends crucially on the geographical range over which spillovers occur. If spillover effects are international, then a policy to attract R&D to the UK will not be necessary. The UK will not retain the spillovers from its own R&D and may be able to benefit from R&D investment made elsewhere.
- 2.8 It is therefore relevant that in the literature on knowledge spillovers, there is evidence supporting the notion that geographical distance is an important determinant of their effect.⁴ The fact that some knowledge spillovers are localised may provide a rationale for policy to attract R&D to the UK.

Size of spillovers

- 2.9 Using data from the US, Bloom, Schankerman and Van Reenen (2005) find that the net social returns are greater than private returns for R&D (3.5 times). They examine both R&D as a whole, and analyse three high-tech sectors in detail: pharmaceuticals, computer hardware and telecommunication equipment. They find that the social returns to R&D in the pharmaceutical sector are the same as the overall returns to R&D. As noted below, a research exercise conducted through PICTF estimated the net social return to spillovers in the UK pharmaceutical sector to be 51 per cent and the private return to be 14 per cent. This estimate was produced by averaging a range of sources, not all of which are revealed.
- 2.10 The table below shows a range of estimates which have been published for the private and social returns to R&D. While precise estimates vary, all of the studies suggest that social returns exceed private returns.

³ Bloom, Schankerman and Van Reenen (2005), *'Identifying Technology Spillovers and Product Market Rivalry'*, CEPR Discussion Papers 4912.

⁴ Jaffe, Trajtenberg and Henderson (1993) find evidence for localised knowledge spillovers by examining the distance of patent citations from the original patent source (there may be 'tacit knowledge' required to use a patent that cannot be directly transmitted but may spill over to other firms). This technique is reproduced in many further papers. Fischer, Scherngell and Jansenberger (2004) conduct a study on high-technology firms in Europe capturing knowledge spillovers using patent citations. They too find evidence that geographical distance has an impact on knowledge spillovers. In addition they find that national border effects are significant and dominate geographical distance effects. In the recent literature, there has been some debate over specific aspects of the methodology used to test for knowledge spillovers (within the general patent citation framework). The broad consensus seems to be that geographical distance is important in determining spillover effects.

Table 2.1: Estimates of private and social returns to R&D

Author (Year)	Estimated rates of return (%)	
	Private	Social
Nadiri (1993)	20-30	50
Mansfield (1977)	25	56
Terleckyj (1974)	29	48-78
Sveikauskas (1981)	10-25	50
Goto-Suzuki (1989)	26	80
Bernstein & Nadiri (1988)	9-27	10-160
Scherer (1984)	29-43	64-147
Bernstein & Nadiri (1991)	14-28	20-110

Source: DTI (2003), originally adapted from Griliches (1992) and Nadiri (1993)

- 2.11 The available research indicates that spillovers are positive, and may be sufficiently large to warrant intervention. However, this does not provide an argument for Government to adopt a policy of general intervention in R&D funding across all sectors or stages in the development process. It must instead focus on those where the spillovers are judged to have potentially significant positive spillover effects but for which the market by itself does not provide adequate incentives. The funding of basic (university) research is a good example of this.

Strategic trade policy

- 2.12 Industrial policy could take the form of strategic trade policy: pursuing policies to support domestic firms in international oligopolistic markets so they get a larger share of economic rents, at the expense of foreign firms.
- 2.13 The theoretical literature on strategic trade policy suggests that under certain conditions, countries may be able to increase their welfare by pursuing industrial policy (subsidising R&D) in imperfectly competitive sectors.⁵ However, there are several caveats to this argument. In particular, the nature of the policy intervention suggested by the theory may vary greatly from one market to another and depend on aspects of the market about which the government may be poorly informed. Moreover, the size of the potential gains from strategic trade policies may be insufficient to warrant intervention.
- 2.14 Such policies are also sensitive to the actions of firms in the relevant market and of other governments. For example, other governments may retaliate by subsidising the R&D of foreign firms that are in the same market. If both domestic and foreign firms are subsidised, there may be overproduction in the market as firms are not taking into account the true cost of R&D. Since both domestic and foreign firms are subsidised,

⁵ Theoretical justification for strategic trade policy: Spencer and Brander (1983, 1985), Brander (1995) provide theoretical support for strategic trade policy in oligopolistic markets. Leahy & Neary (2000) argue that investment (R&D) subsidies may be an optimal government policy in an oligopolistic market robust to whether firms set prices or quantities.

there may be minimal gains in producer rents for either firm. The allocative inefficiencies caused by the distortionary effect of the subsidies would cause a loss of welfare in both countries.

- 2.15 In considering strategic trade policy in the context of the pharmaceutical sector, it is important to note that the targeted gain is the economic rent. This implies that it is the ownership of the companies to be targeted, rather than the location that is important. However, as argued above, it seems apparent that industrial policy in the pharmaceutical sector targets UK-based firms, not UK-owned ones. On this basis, strategic trade policy would not be a valid rationale for industrial policy in the pharmaceutical sector.

Macroeconomic policy

Fiscal policy

- 2.16 The support of R&D could be used as a tool for stimulating the economy generally (that is as a macroeconomic policy or regional policy) in order to improve macroeconomic objectives, such as output, employment and the trade balance. This is perhaps the most commonly-articulated justification for Government support for industry.
- 2.17 This rationale for attracting pharmaceutical investment to the UK is based on the assumption that there is some rigidity in the economy (such as wage stickiness in the labour market), which has the potential to keep the economy at less than full employment. In this case, additional investment into the UK could increase aggregate demand and stimulate employment and output.
- 2.18 However, there are important reasons why this sort of macroeconomic policy may not be warranted. Government investment may 'crowd out' private investment either via the effect of increased expenditure on the interest rate, or via increased taxation (the investment must be financed either by borrowing or taxation).
- 2.19 More importantly, by using industrial policy, governments will be reducing the ability of markets to allocate resources to their most productive uses. On the grounds of economic efficiency, government intervention is only justified in the case of market failure (inefficiencies in the operation of markets or institutions). This position is reflected in the Treasury's *'Green Book'*:⁶

'The achievement of economic objectives by addressing inefficiencies in the operation of markets and institutions; and,'

The achievement of an equity objective, such as local or regional regeneration.'

⁶ HMT (2003), *'The Green book: Appraisal and evaluation in central government'*, London: Stationary Office.

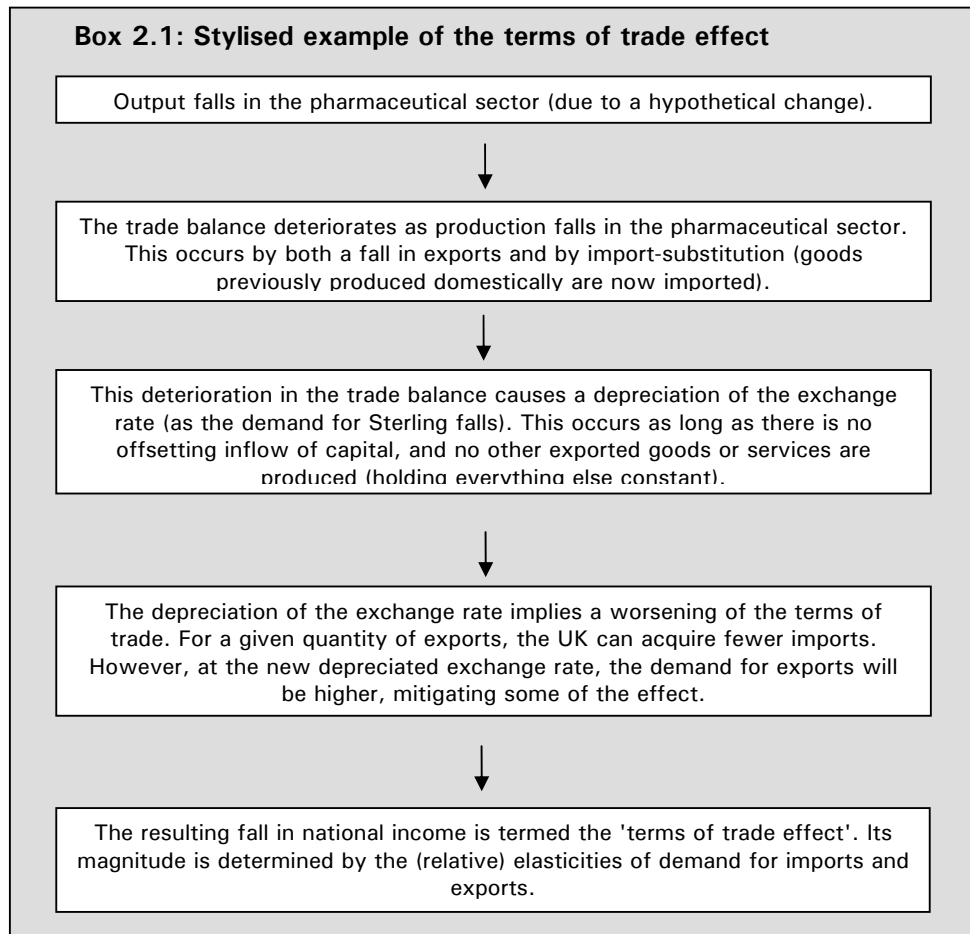
2.20 Finally, if the Government did subscribe to the view that price-wage rigidity warranted a fiscal stimulus, benefits would be common across all companies in the economy. Hence this rationale does not on its own justify singling out the pharmaceutical sector for special treatment.

Terms of trade effect

2.21 The pharmaceutical industry also makes a significant positive contribution to the UK's trade balance. Significant changes to the trade balance may affect the exchange rate and alter the terms of trade (the price of a country's exports in terms of its imports). A fall in the terms of trade indicates that a country can acquire fewer imports for a given number of exports and so represents a fall in welfare, everything else being equal,.

2.22 The pharmaceutical industry therefore contributes to the value of UK output via its effect on the trade balance and thus the terms of trade (that is via a terms of trade effect). Industrial policy to support the pharmaceutical industry aims therefore indirectly to increase the value of UK output via the effect on the terms of trade.

2.23 Box 2.1 below illustrates the mechanism whereby changes in the production in a particular industry result in changes in national income via the terms of trade.



Summary of rationale for industrial policy

- 2.24 Of the rationales discussed above, the existence of R&D spillovers is the most significant. Other rationales have limited justification. Government should therefore be encouraged to focus its attention on policies that focus on the provision of R&D which is judged to have potentially significant spillover effects but for which the market by itself does not provide adequate incentives.

PICTF valuation of the pharmaceutical industry (2000)

- 2.25 This section provides an analysis of the Pharmaceutical Industry Competitiveness Taskforce's (PICTF) estimations for the valuation of the pharmaceutical industry in 1997. The following analysis shows that the PICTF estimations are likely to be overstated. These estimations can be used to show the economic rents that will be affected by industrial policy.
- 2.26 The PICTF report is based on an 'economic rent approach'. That is to say, the pharmaceutical industry is valued net of the opportunity cost of the resources that it uses. This gives the value of the industry over and above the value of the resources used in their next most productive use. This net value is the economic rent. In these calculations, the PICTF use the manufacturing sector as a benchmark for the opportunity cost of investment in the pharmaceutical industry.
- 2.27 There are five categories identified by PICTF under which benefits to the UK accrue:
- producer (export rents) and tax revenues from them
 - labour rents
 - R&D spillovers
 - terms of trade effect, and
 - extra benefit to patients
- 2.28 In terms of the valuation of the industry, the distinction between UK-based and UK-owned firms involves substantial overlap. However, by including rents earned under all of the above categories, the PICTF study has confounded those that are relevant to UK-owned firms, and those that are relevant to UK-based firms.
- 2.29 For the purposes of analysing the potential benefits arising from industrial policy it is necessary to differentiate between those benefits that accrue to UK-based and to UK-owned firms. Producer (export) rents and the terms of trade effect are only relevant benefits if UK-owned firms are the target of industrial policy. Labour rents and R&D spillovers, on the other hand, are relevant to firms located in the UK. The different justifications for industrial policies discussed above also relate to benefits that are identified by the different categories listed above. For example, strategic trade policy targets producer (export) rents.

2.30 Box 2.2 below summarises the results of the PICTF's pharmaceutical industry valuation:

Box 2.2: PICTF report on the value of the pharmaceutical industry to the UK economy

The PICTF report identified the following benefits that might accrue to the UK depending on the ownership and location of pharmaceutical firms:

Sources of benefit from UK-owned and UK-based pharmaceutical firms

		Ownership	
		UK	Overseas
Location	UK	Gross profits Employment income Better terms of trade R&D spillovers in UK Benefits to patients	Tax revenues to UK Employment income Better terms of trade R&D spillovers in UK Benefits to patients
	Overseas	Net Profits Employment income of UK nationals	

Note: In order to calculate the net benefit accruing to the UK, PICTF adjusted the above benefits to net off the opportunity cost of UK resources.

Estimated net value of the pharmaceutical industry to the UK

	£ million p.a.
Extra benefit to patients (from UK location of R&D)	Not quantifiable
Producer rents (from exports and overseas activities)	500–1,500
Labour rents	80–160
Research and development spillovers (to other sectors)	120–360
Net benefit	700–2,000
Terms of trade effect	1,000–2,000

The table below shows how the benefits estimated by PICTF break down into benefits arising from pharmaceutical firms located in the UK and benefits from UK-owned firms located overseas.

		Ownership	
		UK	Overseas
Location	UK	Net benefit: £300-920m Terms of trade effect: £1-2bn	
	Overseas	Net benefit: £400-1,100m	

- 2.31 The next section provides a step-by-step presentation and analysis of the PICTF calculations.

Producer (export) rents

Method of calculation

- 2.32 The method used to estimate export rents involves forming an approximation of the pharmaceutical industry capital base, making an assumption for the depreciation rate of R&D capital and then comparing estimated returns of capital for the pharmaceutical industry and the manufacturing sector.
- 2.33 The additional return of capital employed in the pharmaceutical industry compared with manufacturing ranges from 1.0 per cent (14.2 per cent pharmaceutical as opposed to 13.2 per cent manufacturing, on the assumption that R&D takes 15 years to depreciate) to 5.5 per cent (21.3 per cent pharmaceutical as opposed to 15.8 per cent manufacturing, on the assumption that R&D depreciates immediately). This results in £180 million to 520 million economic rent.
- 2.34 There is a 31 per cent marginal tax rate and it is assumed that 70 per cent of post tax rent is retained in the UK (due to foreign share ownership) resulting in a downwards revision to £140 million to 410 million. A downwards adjustment is made to £100 million to 400 million in case some of the previously calculated rent is in fact attributable to transfer payments from the NHS and UK private healthcare.
- 2.35 The PICTF calculations also include economic rent resulting from UK-registered companies' overseas operations. They take a DTI estimate of overseas rents assuming no R&D capital of £2.3 billion. This is revised downwards for capitalisation of R&D to £850 million (assuming that capitalising R&D expenditure has the same proportionate downward effect on the estimated rents as in the case of UK activities). They assume that overseas corporation taxes are the same as UK taxes and that the companies are 70 per cent UK owned. This results in an overseas rent estimate of £400 million to £1100 million.

Analysis

- 2.36 The producer rents, as calculated above, contain the economic rent earned both by UK-based firms, and by UK-owned firms located overseas. These benefits are clearly attributed to firms of UK ownership rather than location. Of the rationales for industrial policy discussed above, only strategic trade policy specifically targets producer rents as its explicit objective. Since, as argued previously, the relevant targets for industrial policy are firms based in the UK, producer rents are not relevant for the justification of industrial policy and the quantification of its potential benefits.
- 2.37 Concerning the calculation of rent for firms operating in the UK, there appear to be three main steps. First, an estimate is made of the extent to which the profitability of the UK pharmaceutical sector exceeds the manufacturing sector. Second, it is

estimated how much of this accrues to UK shareholders. Third, the resulting figure is adjusted for the extent to which the profits represent transfer payments from UK rather than foreign customers. We see problems with each step:

- step 1 - although the range given for economic rent is very wide (based on assuming a depreciation period for R&D of between zero and 15 years), there are a number of uncertainties which do not appear to have been taken into account. First, the average depreciation period and rate may differ between pharmaceuticals and manufacturing. Second, cash flows for successful pharmaceuticals tend to increase between marketing approval and patent expiry, with the highest cash inflow tending to be just before patent expiry, implying that economic depreciation rates for pharmaceutical R&D may be substantially different from straight-line depreciation. Third, measured profitability differences may reflect differences in the cost of capital rather than in rents. Finally, it is not clear that manufacturing sector is the appropriate counterfactual (that is, the next best use of pharmaceutical resources)
- step 2- the basis for assuming 70 per cent UK share ownership is unclear. Many of the pharmaceutical companies operating in the UK have their base overseas and may be expected to have relatively few UK shareholders, and
- step 3- the downward adjustment for transfer payments reduces rent only by between two and 29 per cent. Our analysis of companies' annual financial returns under the PPRS shows that home sales represent 42.5 per cent of revenue on prescription medicines with export sales accounting for the remaining 57.5 per cent (see Annexe H)⁷. Assuming similar profit margins on home and export sales, this suggests around 42.5 per cent of any rent results from payments by home customers (principally the NHS). Some of this would accrue to foreign shareholders.

2.38 The uncertainties associated with the first step of the calculation are such that it is not obvious that there are any material producer rents accruing to the UK. It is the ostensible purpose of the PPRS profit control to prevent the NHS paying prices at which producers earn excess profits (rents). However, if rents do accrue from the pharmaceuticals sector, it is likely that UK consumers (principally the NHS) are contributing their share of those rents since UK prices are not obviously lower than prices elsewhere in the world (see Annexe F). This means net producer rents accruing to UK persons could even be negative: they will be negative if tax payments and profits accruing to UK shareholders from export sales are less than profits accruing to foreign shareholders from home sales. Assuming a marginal tax rate of 31 per cent, home sales of 42.5 per cent of total sales and a similar profit margin on home and export sales, net producer rent to UK persons would be negative if UK shareholders account for less than 17 per cent of the total ownership of companies earning the rents.

⁷ These figures may however be more relevant to manufacturing than R&D activities.

Labour rents

Method of calculation

- 2.39 PICTF estimate a wage bill for the pharmaceutical industry of £1.6 billion. Employees receive eight per cent wage premium.⁸ Therefore labour rents are £120 million. Allowing for the fact that some of the rent may be earned from UK (predominately NHS) business and that there is some uncertainty, the report suggests a range of £80 million to £160 million.

Analysis

- 2.40 The labour rents accrue to workers living in the UK. Hence this estimate is relevant in the consideration of UK-based companies.
- 2.41 The original estimate of £120 million seems fair, but the revision for the possibility that some of the rent was earned domestically does not appear to be consistent with that made for the producer rents. Our comments above regarding this adjustment may also be relevant here.

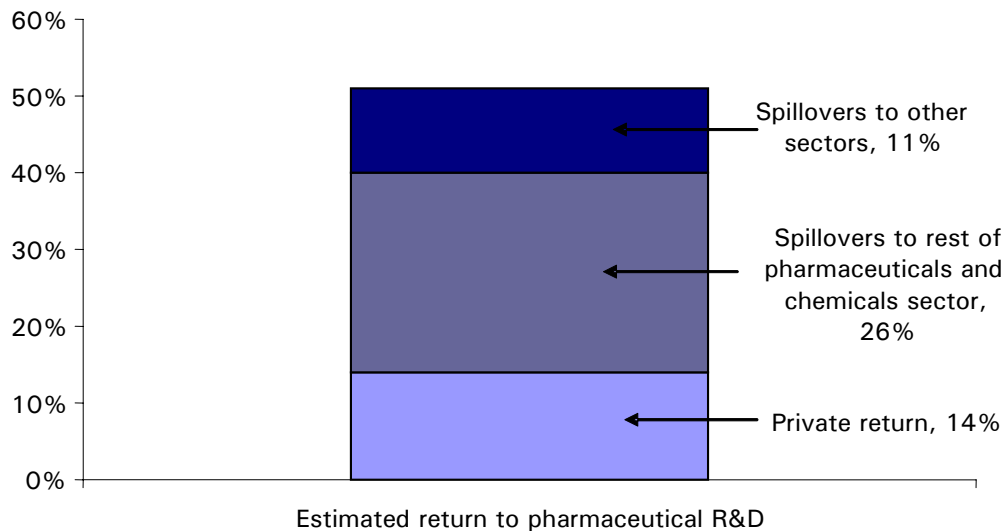
R&D spillover effects

Method of calculation

- 2.42 The social return to R&D within the chemicals industry is estimated to be 40 per cent and the private return is estimated to be 14 per cent. This implies a 26 per cent spillover effect within the pharmaceutical industry. A 37 per cent estimated total margin (averaging a range of sources across the literature) between private and social return implies an 11 per cent spillover to firms outside the industry (total R&D expenditure of £2.2 billion). This amounts to £120 million to 360 million of spillovers (spillovers to other firms in the pharmaceutical sector will already be reflected in their economic rents).

⁸ Based on Van Reenen (1998) '*Econometric analysis of data from the Labour Force Survey*'.

Figure 2.1: Spillovers to R&D in the pharmaceutical sector



Source: PICTF (2000), *'Value of the Pharmaceutical Industry to the UK Economy'*

Analysis

- 2.43 It was argued above that the R&D spillovers have a significant geographic component. This implies that they are relevant to the consideration of the pharmaceutical companies located in the UK.
- 2.44 This estimation is quite crude and the range of sources is not mentioned in the report. However, the confidence interval is large and may account for the uncertainty in this calculation.
- 2.45 As is acknowledged in the report, possible spillovers arising from the R&D expenditure component of the alternative use of resources are not accounted for. However, the expenditure on R&D by the rest of UK-based industry is proportionally far lower than in the pharmaceutical industry.

Terms of trade effect

Method of calculation

- 2.46 The calculation of the terms of trade effect is made by considering the effect on the trade balance and exchange rate of the pharmaceutical industry ceasing to exist. The PICTF paper estimates a deterioration of the trade balance of £11.1 billion (£5.9 billion from exports and £5.2 billion from import substitution). This trade balance deterioration may cause Sterling to depreciate, reducing the relative price of exports to imports and consequently making the UK poorer.

- 2.47 The PICTF report bases its calculation on a similar calculation (Hale and Towse (1995)) which is then scaled up to account for the greater size of the pharmaceutical industry in 1997. The resulting terms of trade effect is estimated at £1-2 billion.

Analysis

- 2.48 The terms of trade effect arises from the depreciation of the exchange rate caused by a fall in the trade balance. Since it is UK-owned firms that contribute to the trade balance, the terms of trade effect is an outcome relating to policy aimed at UK-owned firms.
- 2.49 This terms of trade effect is overstated because the counterfactual (the alternative use of pharmaceutical resources) is not considered (as is acknowledged in the report). The offsetting effect caused by the redeployment of these resources to their next best uses is likely to be large (the magnitude is in part determined by the proportion of new output produced that is tradable).
- 2.50 The PICTF report has acknowledged this offsetting effect but not attempted to quantify it. The result is that the terms of trade effect has been significantly overestimated.
- 2.51 Hale and Towse (1995) made the same assumption in their 1995 valuation of the pharmaceutical industry. They acknowledge that the resources could be used elsewhere to produce exportable goods or to replace imported goods. However, they neglect to include any compensating effect, stating:

"The resources to produce this increased output are available, in principle, from the resources freed by the pharmaceutical industry. However, the UK has a competitive advantage in the market for pharmaceuticals."

- 2.52 The UK may also have competitive advantages in the next best available uses of the resources. Even if resources are being used more productively in the pharmaceutical sector than in their next best use, in order to properly evaluate the rents arising from this effect, an assumption needs to be made about the counterfactual – namely, the proportion of goods produced in alternative uses that would be tradable. By ignoring this offsetting effect, it has been implicitly assumed that no alternative tradable goods are produced. This assumption is clearly unrealistic.

Summary of PICTF report

- 2.53 The PICTF report does not provide a clear distinction of whether the pharmaceutical industry consists of UK-based or UK-owned firms. From the perspective of possible industrial policy intervention, overseas UK-owned firms are irrelevant.
- 2.54 The estimations are mostly quite crude with large confidence intervals.
- 2.55 The magnitude of the terms of trade effect is especially dubious and should be revised downwards. Its magnitude is important since it forms the largest part of the PICTF estimation of the economic rent generated by the pharmaceutical industry.

- 2.56 The upper bound of the PICTF estimates is £2 billion plus a terms of trade effect of up to £2 billion. As noted above, this estimate includes benefits for both UK-owned firms and UK-based firms and is likely to be overstated. Including only R&D spillovers and labour rents (which are attributable to UK-based firms) will lead to a far lower estimate: following the same methodology to the PICTF report, this would lead to an upper bound of £520 million.

Conclusions

- 2.57 Out of the possible rationales for industrial policy in the UK, we find that only the market failure caused by positive spillovers to R&D (and possibly labour rents) provide adequate justification. The other potential rationales discussed above do not justify industrial policy as they are either not market failure based or do not focus on UK-based firms.
- 2.58 Finally, an examination of the estimation of the economic benefits of the UK pharmaceutical industry by the PICTF report suggests that these estimates are significantly overstated, and that only a portion is attributable to UK-based firms. This implies that the economic rents that will be affected by any changes in industrial policy in the pharmaceutical sector are likely to be significantly smaller than estimated in the PICTF report. There may be merit in revisiting some of the calculations in light of more recent data and the considerations set out here.
- 2.59 The purpose of this chapter has not been to take issue with the Government's aim of attracting pharmaceutical investment into the UK but rather to shed light on the situations in which the case for support is strongest. This provides a more robust basis for the analysis in subsequent chapters, which consider the drivers of internationally mobile investments and potential policy implications.

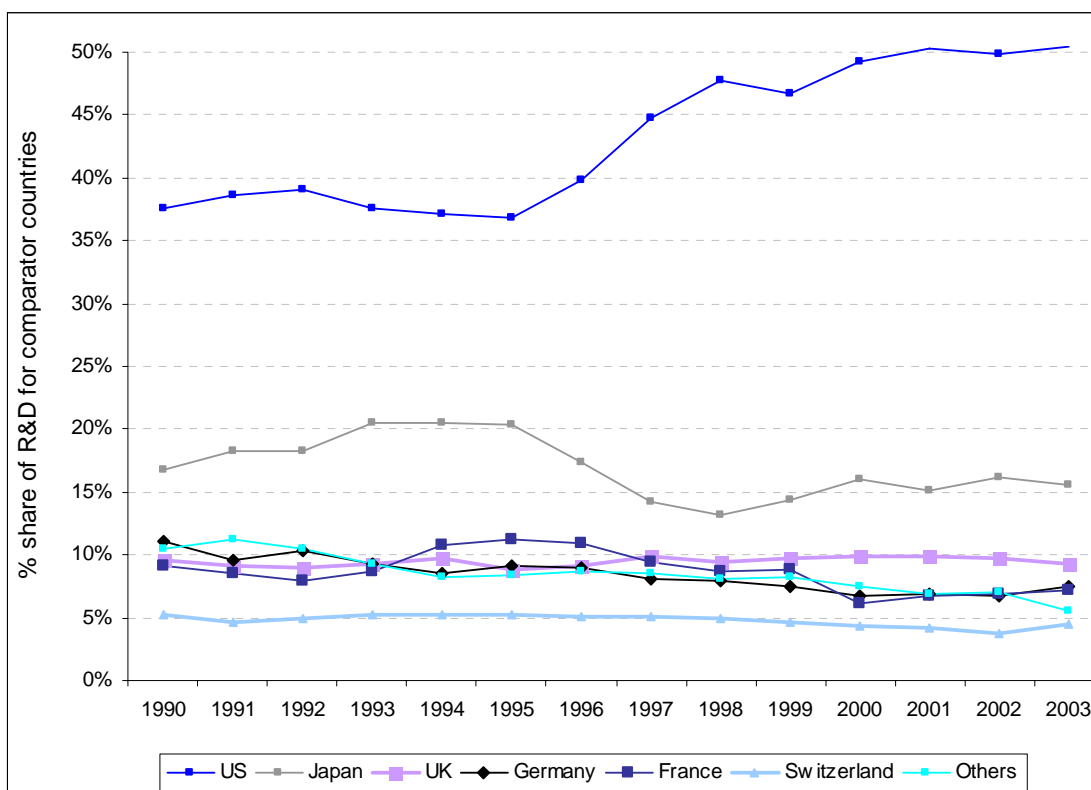
3 PHARMACEUTICAL INDUSTRY R&D EXPENDITURE IN THE UK

3.1 In this chapter we present an overview of the performance of the UK in securing R&D investment in the pharmaceutical sector relative to that of a group of comparator nations. We also assess the relative contribution made by pharmaceutical R&D to total business expenditure on R&D in the UK.

UK share of global R&D spend

3.2 The UK is one of the world's major locations of R&D expenditure. As shown in figure 3.1, R&D carried out in the UK accounted for approximately nine per cent of global R&D expenditure. It therefore ranks third in the world, behind the US and Japan, which account for approximately 50 per cent and 15 per cent respectively.

Figure 3.1: Percentage of 'world' pharmaceutical industry R&D spend⁹



Source: PICTF Indicators 2005

⁹ World is defined as total spend in PICTF comparator countries excluding Australia and New Zealand. This is also a measure of industry R&D within country boundaries and not of companies' total world R&D expenditure.

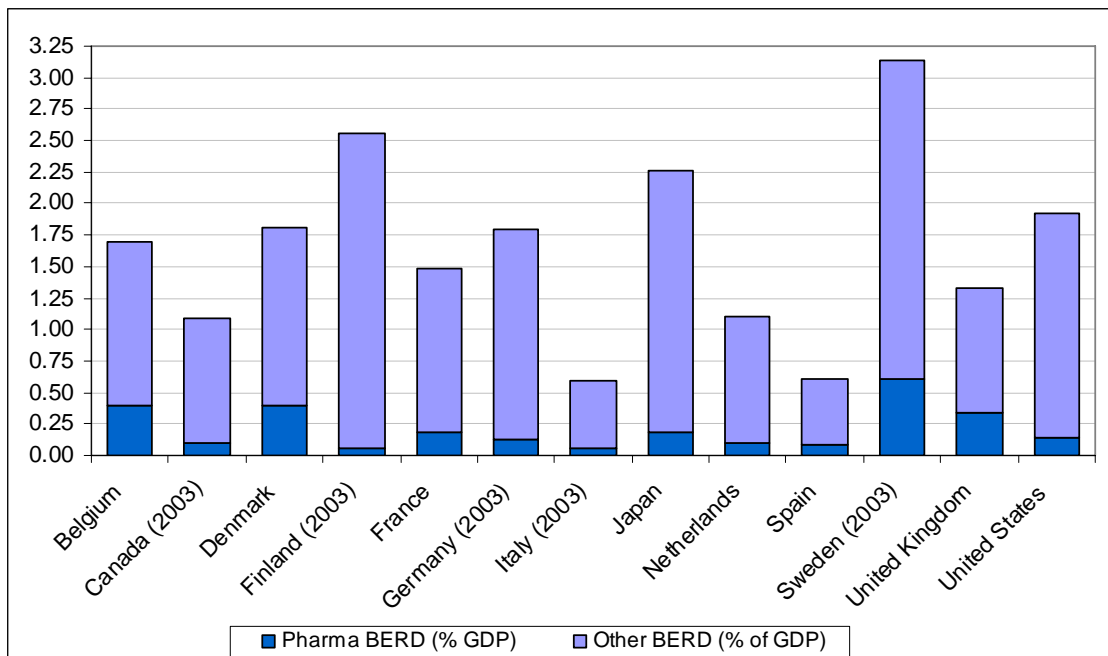
3.3 The chart also shows that pharmaceutical investment in the US stepped up markedly in the second half of the 1990s, largely at the expense of Japan. Expenditure in the UK remained relatively constant over this period.

Relative success in attracting R&D investment

3.4 The above figures largely reflect the relative size of the economies of the countries concerned– it is, for example, perhaps unsurprising that the US is the world's leading destination for R&D investment given that it is by far the world's largest economy.

3.5 The level of R&D expenditure divided by GDP therefore provides a more accurate picture of relative success in attracting R&D investment. The following graph shows total Business Expenditure on R&D (BERD) as a percentage of GDP across several countries. Against this measure, the UK is the fourth highest performing country in the world. In 2002 pharmaceutical industry business expenditure on R&D accounted for 0.33 per cent of GDP in the UK. This compares with Sweden (0.61 per cent), Denmark (0.4 per cent) and Belgium (0.39 per cent). Notably, the UK is the highest performing of the larger economies, ahead of France and Japan (both 0.19 per cent), the US (0.14 per cent) and Germany (0.13 per cent). This is shown in figure 3.2.

Figure 3.2: Pharmaceutical BERD as a percentage of GDP in 2002/2003



Source: OECD (Figures relate to 2002 unless otherwise stated)

Contribution of pharmaceutical sector to overall R&D spend in UK

3.6 As noted above, in 2004 the Government published a ten-year framework for investment in science and innovation, in which is outlines the need to increase the UK's R&D intensity in order to sustain productivity growth. For this the government has set

out a target for the UK to increase R&D intensity to reach a total of 2.5 per cent of GDP in 2014. The government itself commits to invest substantially more in R&D and hopes that this increase is matched by the private sector. In detail the scenario presented in the report projects the following:

Table 3.1 Indicative scenario towards a 2.5 per cent R&D/GDP target

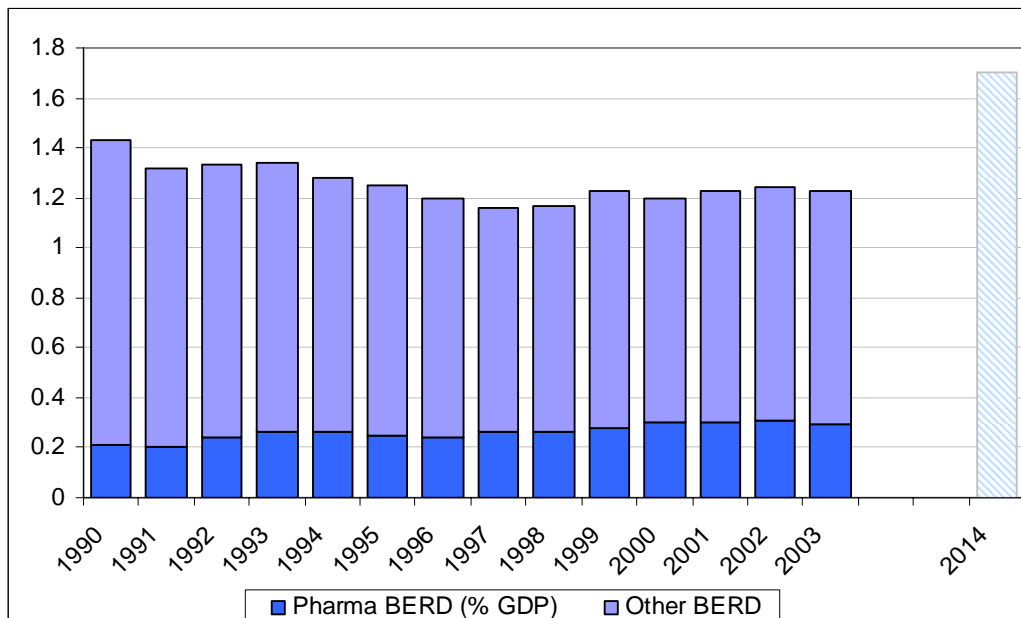
R&D investment as percentage of GDP		
	2004	2014
Government R&D	0.66%	0.8%
Private Sector	1.24%	1.7%
UK total	1.9%	2.5%

Source: HM-Treasury, Science & innovation investment framework 2004-2014

3.7 As figure 3.2 above suggests, the pharmaceutical sector in the UK contributes a particularly high proportion of the overall R&D conducted in the country; at just over 25 per cent, the UK ratio of pharmaceutical BERD to total BERD is the highest of all the 13 countries shown. The Government is, therefore, particularly dependent on the pharmaceutical sector for meeting its overall R&D target.

3.8 However, the Government is a long way from reaching its target. As shown in the chart below, total BERD/GDP fell from 1990 to 1997 and has only slightly risen since then, reaching 1.23 per cent of GDP in 2003. Pharmaceutical business R&D/GDP, on the other hand, has risen steadily, from 0.21 per cent of GDP in 1990 to 0.31 per cent in 2002, before a slight decline in 2003 to 0.29 per cent. For 2004 and 2005 there are no data available.

Figure 3.3: Progress against the Government's R&D target, 1990 – 2003



Source: ONS and OECD BERD data, HM-Treasury

Summary

- 3.9 The UK is the world's third most important location for pharmaceutical R&D investment, behind the US and Japan. It has maintained levels of investment in recent years, while those in the US have risen and those in Japan have fallen. The UK has also performed strongly in relation to the size of its economy, with the fourth highest ratio of pharmaceutical R&D to GDP in the world, behind Sweden, Denmark and Belgium.
- 3.10 The pharmaceutical sector makes a greater contribution to overall levels of R&D expenditure in the UK than in any other country. The UK Government is therefore particularly dependent on the sector for meeting its goal of R&D expenditure constituting 2.5 per cent of GDP by 2014. Recent progress has been limited, with R&D as a proportion of GDP at under half the target level (1.23 per cent) in 2003.

4 THE PPRS AND R&D INVESTMENT IN THE UK

Introduction

- 4.1 In chapters four and five we consider the factors that affect the location of footloose investment, particularly R&D investment. This chapter assesses whether the PPRS profit cap provides any explicit incentives to invest in the UK. We find that it does not and, further, that any reform of the scheme that attempted to do so would almost certainly fall foul of EC rules on the free movement of goods and / or State Aid.

Does PPRS provide incentives to engage in R&D investment in the UK?

Scheme objectives

- 4.2 Some stakeholders have indicated to us that they view the PPRS as an important component of the Government's industrial policy towards the pharmaceutical industry – that is, as a means of attracting and retaining pharmaceutical R&D investment within the UK.
- 4.3 The DTI's Bioscience Unit argued in its submission to the OFT, that it was,
“strongly of the view that PPRS has been an important factor in making research-based pharmaceuticals one of the UK’s most successful industries.”
However, such views are not universally shared in all parts of Government.
- 4.4 The confusion appears to have been caused by the fact that in the past, PPRS agreements have aimed to meet industrial policy goals. Since 1957 there have been nine periodic agreements under the PPRS and its predecessor, the Voluntary Price Regulation Scheme (VPRS). There were VPRS schemes in 1957, 1961, 1969 and 1972 and PPRS schemes in 1978, 1986, 1993, 1999 and 2005. It was in the third VPRS, in 1969, that direct reference to the sponsorship role of government was first made. The scheme referred to the importance of a 'strong, efficient and profitable' industry, and continued,
“As sponsor for the industry the Department of Health and Social Security recognises the industry’s contribution to the economy of the United Kingdom as a whole and wishes further to encourage its competitive efficiency both at home and abroad.” (DH 1969)
- 4.5 Industrial policy goals remained part of the scheme's stated objectives until the end of the 1993 scheme, the objectives of which were to:
- *“secure the provision of safe and effective medicines for the NHS at reasonable prices*
 - *promote a strong and profitable pharmaceutical industry **in the United Kingdom** [added emphasis] capable of such sustained research and development expenditure as should lead to the future availability of new and improved medicines, and*

- *encourage in the United Kingdom [added emphasis] the efficient and competitive development and supply of medicines to pharmaceutical markets in this and other countries."*

4.6 The objectives of the most recent schemes (in 1999 and 2005) have been amended to exclude any reference to investments in the UK (the wording is identical except that the words 'in the United Kingdom' have been deleted).

4.7 It appears clear, therefore, that there has been a shift in explicit objectives of the scheme, away from favouring investments in the UK. As discussed below, this is likely to be due to concerns about the legality of any such use of a pharmaceutical pricing scheme.

4.8 Furthermore, our analysis of the workings of the profit cap element of the PPRS suggests that the scheme does not contain any systematic incentives to locate investments within the UK. In the following paragraphs we consider in turn the following instruments:

- R&D allowances under the scheme
- the calculation of allowed rates of return and the determination of the capital base
- transfer pricing arrangements

R&D allowances under the PPRS

4.9 The profit cap is discussed in Annexe H. The R&D allowances provided for under the scheme can, in principle, relate to R&D investment **anywhere in the world**. In their Annual Financial Returns (AFRs), companies are able to supplement R&D in their UK accounts with R&D 'injected' from anywhere in the world and, where they import materials or finished products from their affiliates abroad, the transfer prices are assumed to include an R&D component (21 per cent under the current scheme and 15 per cent under the 1999 scheme).¹⁰

4.10 The allowances, therefore, provide no incentive to locate R&D investments in the UK. This is illustrated in the table below, which shows the number of companies that added injected R&D to R&D in their UK accounts (injected R&D can, in principle, be carried out anywhere in the world, although in practice most of it is UK R&D which has been recharged to overseas affiliates). 12 companies injected expenditure totalling around £180m, equating to 16 per cent of total R&D allowances across all 35 AFR companies in 2004. The R&D component of transfer prices (also shown in Table 4.1) accounted for a further £180m of R&D allowances. In total, therefore, about £360m was injected or transfer price R&D which need not be carried out in the UK. This equates to over 30 per cent of total R&D allowances under the scheme.

¹⁰ One company based its AFR on accounts of a business extending beyond the UK and its R&D expenditure would therefore include R&D incurred outside the UK. This is not included in Table 4.1.

Table 4.1: R&D injections and transfer prices in 2004

R&D injections	
Number of companies injecting R&D expenses	12
Total R&D expenses injected	£178m
Percentage of R&D expenses allowed for these	48%
Percentage of R&D expenses allowed for all	16%
Percentage of sales across all companies	3%
R&D component of transfer prices	
Number of companies using transfer prices	21
Total R&D from transfer prices	£183m
Percentage of R&D expenses allowed for all	16%
Percentage of sales across all companies	3%

Source: OFT analysis of DH assessment of AFRs submitted by 35 companies.

- 4.11 Strikingly, in discussions with the OFT, many scheme members seemed to believe that R&D allowances were only available for R&D undertaken in the UK. These tended, however, to be large firms for whom R&D investment in the UK alone exceeded their maximum R&D allowance under the scheme. Firms that were reliant on R&D undertaken outside the UK to claim their allowance were more aware of the rules.

Setting allowed rates of return and capital base

- 4.12 We now consider whether the calculation of allowed rates of return and the determination of the capital base under PPRS give an incentive to invest in the UK rather than elsewhere. The ABPI has suggested:

“The pharmaceutical industry is encouraged through the return on capital allowance to invest in the industry in the UK, and partly as a result the UK balance of trade benefits by £3.75 billion.” (ABPI submission to study)

- 4.13 In the following paragraphs, we consider in some detail the implications of the rules of the PPRS profit control for the incentive to invest in the UK compared to elsewhere. Under the PPRS, companies have a target rate of return which is the higher of six per cent of sales and 21 per cent of capital employed allocated to NHS sales. We have described the scheme in detail elsewhere (see Annexe H) but capital employed is in most cases based on an allocation to NHS sales of capital employed in the company's UK accounts.¹¹ As with R&D, capital may be injected from businesses elsewhere, if it is directly relevant to the supply of medicines to the NHS, but – unlike R&D – such injections are small.¹²

¹¹ Unless, as is the case with one company (see footnote nine to paragraph 4.9), its AFR is submitted on the basis of a business wider than the UK.

¹² In 2004, one company injected £3.1m of R&D assets into its capital employed.

Overview

- 4.14 Under the PPRS, a firm can increase its price if its profits are less than 40 per cent of its target (the profit floor), but has to make a repayment to DH if its profits are more than 140 per cent of target (the profit ceiling). Incentives to locate investment under the PPRS depend on the treatment of a firm manufacturing with UK assets relative to a firm importing from an affiliate abroad:
- a company manufacturing in the UK with relatively few UK assets, or having its products manufactured by an independent contractor, can earn a profit of up to 8.4 per cent (1.4 times 6 per cent) of NHS sales. It can obtain a price rise if its profits drop below 2.4 per cent (0.4 times 6 per cent) of NHS sales
 - a company manufacturing in the UK with sufficient UK assets can earn a profit of up to 29.4 per cent (1.4 times 21 per cent) of assets attributed to NHS sales¹³. It can obtain a price rise if its profits drop below 8.4 per cent (0.4 times 21 per cent) of assets attributed to NHS sales. This applies as long as assets are more than 28.6 per cent of sales¹⁴
 - companies importing from affiliates abroad are required to confirm that the transfer prices used are as accepted by HMRC for corporation tax purposes. In the absence of a detailed breakdown, transfer prices are assumed to comprise 59 per cent manufacturing, 21 per cent R&D and 20 per cent profit. Since transfer price profits are included in target profit, such companies can earn a profit of up to 8.4 per cent (1.4 times 6 per cent) of sales plus 28 per cent (1.4 times 20 per cent) of transfer price payments to affiliates abroad and can obtain a price rise if profits fall below 2.4 per cent of NHS sales plus 8 per cent of transfer price payments. Additionally, under the PPRS, manufacturing costs (cost of goods sold, COGS) are limited to no more than 45 per cent of sales, so transfer price payments are limited to 76.3 per cent of sales. With transfer prices at this level, companies can earn a profit of up to 29.8 per cent of sales and can obtain a price rise if profits fall below 8.5 per cent of sales.
- 4.15 In many cases, companies manufacture some of their products in the UK and import others from affiliates abroad. In order to illustrate the potential impact of the PPRS, we compare, in Table 4.2 below, maximum profits for three hypothetical companies:
- a company manufacturing in the UK assessed on a return on sales (ROS) basis
 - a company manufacturing in the UK assessed on a return on capital (ROC) basis with allocated capital employed of 80 per cent of sales, and

¹³ Where medicines are manufactured in the UK for both NHS and export markets, companies are able to allocate costs and assets more than proportionately to NHS sales to reflect fixed costs. This fixed cost adjustment represents 7.5 per cent of costs and assets allocated proportionately to exports (see Annex H).

¹⁴ From this point on, references to sales and assets or capital employed are to those relevant to the PPRS: in other words to NHS sales and to assets or capital employed attributed to NHS sales.

- a company importing from its affiliate abroad, assessed on a return on capital basis, with a similar cost structure to the UK ROC company. The table assumes a transfer price such that the PPRS breakdown of transfer prices gives COGS similar to the COGS of the UK ROC company (this implies a transfer price payment of 60.1 per cent of NHS sales).

4.16 In each case, we have assumed the company has an R&D allowance of 21 per cent of NHS sales and costs of 20 per cent of sales.

Table 4.2: Comparison of profits: UK companies versus importer

	UK ROS company	UK ROC company	Importer	Transfer price reallocation	
Capital employed (UK)	25	80.0	< 28.6		
Sales	100.0	100.0	100.0		
Transfer price payment					60.1
COGS	41.0	35.5	35.5	59%	35.5
R&D	21.0	21.0	12.6	21%	12.6
Injection of R&D*			8.4		
Other costs	20.0	20.0	20.0		
Profit †	18.0	23.5	23.5	20%	12.0
Max PPRS profit	8.4	23.5	25.2		
Repayment (headroom)	9.6	0.0	(1.7)		

Notes: Transfer price payments (60.1) are such that the importer's costs are similar to those of the UK ROC company. Difference between COGS of UK ROS company and UK ROC company is equal to additional cost of capital at 10 per cent.

* Companies can inject R&D up to their maximum R&D allowance (providing they have sufficient sales outside the UK)

† Profit represents NHS sales less total costs (COGS + R&D + R&D injection + other costs)

4.17 The table illustrates that the maximum PPRS profit for a UK ROS company is lower than that of both the UK ROC company and the importer (see Annexe H). Under the assumptions in the table, the importer has some headroom to charge a higher price than the UK ROC company, that is, the scheme provides no advantage to the firm simply because it has invested capital in the UK as opposed to elsewhere in the world.

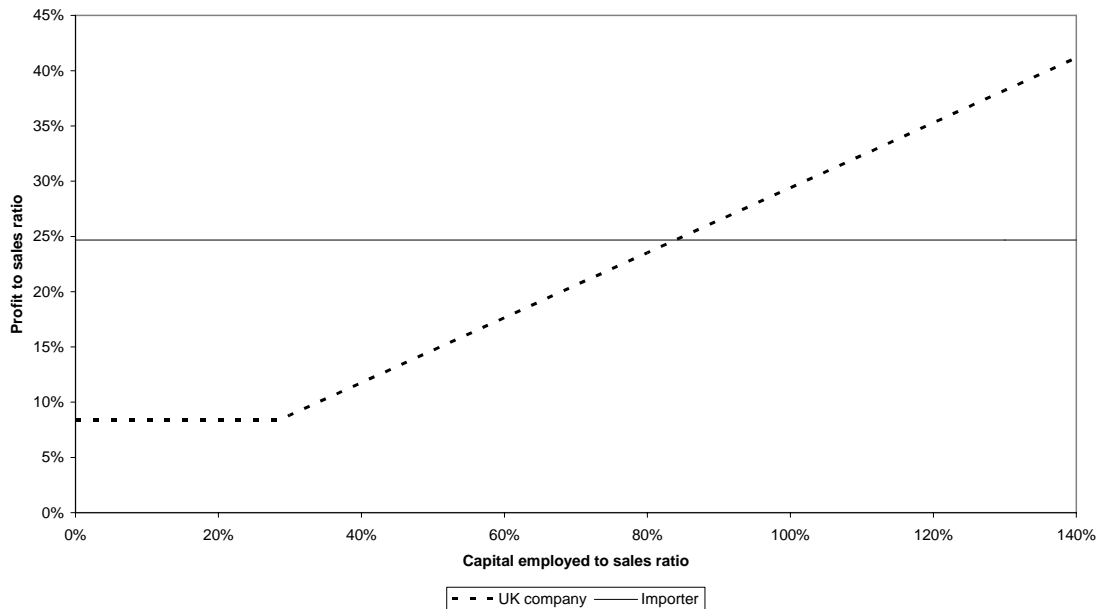
4.18 A similar example could be constructed to show the opposite: this would occur if the UK company's capital employed were higher relative to sales, and/or the importer's transfer price payment was lower relative to sales.¹⁵ The next few sections explore the sensitivity of this finding to capital employed / sales ratios and other factors such as the level of the R&D allowance and the transfer pricing methodology employed.

¹⁵ The level of R&D allowance and other costs are also relevant but are of less importance to the treatment of a UK ROC company compared to an importer.

Sensitivity of results to capital employed / sales ratio

- 4.19 Figure 4.1 shows maximum allowed level of PPRS profit for UK ROCE companies and importers across a range of capital employed to sales ratios:
- the dotted line shows the maximum profits of a UK company as a percentage of sales. This increases as the company's capital employed relative to sales increases, and
 - the continuous line shows the maximum profits of an importer as a percentage of sales. This is 25 per cent for all levels of capital employed to sales (assuming, as in Figure 4.1, an R&D allowance of 21 per cent and other costs of 20 per cent). On these assumptions, an importer's profits as a percentage of sales are maximised if its transfer price payment is 58 per cent of sales, and this implies a profit of 25 per cent of sales. A higher transfer price payment would give rise to a lower profit, while a lower transfer price payment would give rise to a lower PPRS profit ceiling.

Figure 4.1: Profits of UK company and importer (R&D allowance is 21 per cent, and other costs 20 per cent, of sales)



Source: OFT analysis

- 4.20 The two lines cross at a capital employed to sales ratio of 84 per cent, which we describe as the critical capital employed to sales ratio. PPRS rules are such that, at lower levels of the ratio, an importer can have a higher profit as a percentage of sales, and at higher levels of the ratio, a UK company can have a higher profit as a percentage of sales.
- 4.21 Figure 4.1 assumes an R&D allowance of 21 per cent of sales and other costs of 20 per cent of sales. Table 4.3 below shows how the critical capital employed to sales ratio varies as the R&D allowance and other costs vary.

Table 4.3: Impact on critical capital employed to sales ratio of different assumptions about R&D allowance and other costs

R&D allowance as percentage of sales	Other costs as percentage of sales	Critical ratio of capital employed to sales
Varying the R&D allowance		
20%	20%	85%
25%	20%	80%
28%	20%	76%
Varying other costs		
21%	15%	89%
21%	20%	84%
21%	25%	78%
21%	30%	73%
21%	35%	68%

Source: OFT calculations

Sensitivity of results to transfer pricing methodology

- 4.22 In the case of a UK company, a higher profit to sales ratio implies a higher maximum price level. In the case of an importer this is also true as long as the importer sets a transfer price such that its COGS is the same as that of a similar company manufacturing in the UK (as in Table 4.2). Cost-plus is one basis for transfer-pricing and if we additionally assume cost-plus pricing, we can infer that a company with a capital employed to sales ratio above the critical ratio would have a higher maximum price if it invested in the UK.¹⁶
- 4.23 However, there are a number of different bases for transfer pricing which are acceptable to HMRC (see Annexe H). The majority of pharmaceutical companies do not base their transfer prices on a cost-plus methodology but use a resale-minus basis. Under resale-minus, the transfer price is set at the actual selling price minus a resale price margin reflecting UK costs and an appropriate profit margin of a suitable independent comparator. As we discuss elsewhere (see Annexe H), the resale-minus transfer pricing methodology takes price as its starting point and consequently the PPRS ceiling on profits does not constrain prices (except to the extent that UK costs, for example marketing and general and administrative costs, used to calculate resale-minus transfer prices are above those allowed under the PPRS).
- 4.24 To summarise, a comparison of the PPRS's treatment of importers with UK companies suggests that importers setting transfer prices on the basis of a resale-minus pricing methodology, are effectively unconstrained by the PPRS profits control in respect of the prices they can charge. UK companies; however, are constrained to a return on capital employed of no more than 29.4 per cent (or 8.4 per cent of sales if their capital employed is less than 28.6 per cent of sales).

¹⁶ The actual cost of manufacturing in the UK and alternative locations is also relevant.

- 4.25 Turning to the PPRS profit floor, similar reasoning suggests that an importer using a resale-minus methodology is unable to obtain a price rise as its profits would never fall below the floor. On the other hand, a UK company is able to obtain a price rise if its profit falls below 8.4 per cent of capital employed (or 2.4 per cent of sales if its capital employed is less than 28.6 per cent of sales). However, importers can base transfer prices on actual costs if they provide an audited breakdown of the make-up of the costs.¹⁷ Thus, if an importer's price falls below its actual costs, it is able, in principle, to obtain a price increase in the same way as a UK company.

Summary

- 4.26 Summing up, the rules of the PPRS do not encourage investment in the UK. If anything, PPRS rules are more favourable to companies importing from their affiliates abroad since they are unconstrained by the profit ceiling if, as most do, they base transfer prices on the resale-minus methodology. If there were any material possibility of UK companies being constrained by the profit ceiling, the rules might even deter investing in the UK. In practice, we do not believe UK investment has been deterred since the PPRS constraint on companies has been minimal in recent years: most companies are within the PPRS margins of tolerance (under the 1999 scheme only one company repaid excess profits while no AFR companies obtained a price rise) (see Annexe H).

Legal constraints

- 4.27 We have noted that the current scheme does not provide explicit incentives to invest in the UK. There are, in addition, strong arguments to suggest that the scheme could not be amended to provide any such incentives in the future, as this would be contrary to EC rules on the free movement of goods and state aids rules (Articles 28 and 87 of the EC Treaty).

Free movement of goods

- 4.28 Article 28 EC Treaty¹⁸says,

“Quantitative restrictions on imports and all measures having equivalent effect shall be prohibited between Member States.”

- 4.29 Such restrictions and measures may, however, be justified if they fall within Article 30 EC Treaty, which says, so far as relevant,

“The provisions of Articles 28 and 29 shall not preclude prohibitions or restrictions on imports, exports or goods in transit justified on grounds of public policy; [and] the protection of health and life of humans Such prohibitions or

¹⁷ Importers are only required to use corporation tax transfer prices if they do not provide a breakdown of transfer price costs.

¹⁸ Treaty Establishing the European Community.

restrictions shall not, however, constitute a means of arbitrary discrimination or a disguised restriction on trade between Member States.”

- 4.30 In the cases set out in Box 4.1, Member States' pharmaceutical price regulation measures were held to breach Article 28 (with no justification under Article 30) on the basis that they favoured domestic supplies over imported products.

State aid

- 4.31 Under Article 87(1) EC Treaty:

“Save as otherwise provided in this Treaty, any aid granted by a Member State or through State resources in any form whatsoever which distorts or threatens to distort competition by favouring certain undertakings or the production of certain goods shall, in so far as it affects trade between Member States, be incompatible with the common market.”

- 4.32 Such state aids are consequently unlawful unless they fall within a derogation in Articles 87(2) or 87(3). In simple terms, there are four basic elements to the test for State Aid:

- aid granted by a Member State – there must be a loss or potential loss of State resources. A regulatory provision with no state resources involved would not constitute a transfer in this sense¹⁹
- advantage to a particular undertaking or a class of goods – the aid must confer an advantage on the recipient(s), for example a loan on better than commercial terms or higher than market price paid for goods. In addition, in order to confer an advantage, the transfer must be selective for example tax credit made available to undertakings in a particular sector²⁰ or geographical location or a higher than a fair market price for goods paid to only a subset of a particular group
- distorts or threatens to distort competition – in practice, this test appears to have a low threshold and is satisfied in most if not all cases where the first two criteria are met
- affect on trade between Member States – again, in practice this test appears to have a low threshold although it is not always satisfied (for example in respect of local visitor attractions which are not regarded as destinations by visitors from afar).

- 4.33 The following derogation in Article 87(3) may be relevant in the context of the PPRS:

“Article 87(3)(c) - aid to facilitate the development of certain economic activities or of certain economic areas, where such aid does not adversely affect trading conditions to an extent contrary to the common interest”

¹⁹ See for example ECJ Case C-379/98 *PreussenElektra AG v. Schlesweg AG*

²⁰ See for example ECJ Case C-143/99 *Adria-Wien Pipeline GmbH*

4.34 From 1 January 2007, the European Commission's new Community Framework for State Aid for research and development and innovation²¹ will come into effect. Part of its purpose is to provide, "for the assessment of measures falling within its scope, not only rules on the compatibility of certain aid measure (Chapter 5) but also, due to the increased risk of certain aid measures to distort competition and trade, additional elements concerning the analysis of the incentive effect and necessity of aid (Chapter 6) and an additional methodology to be applied in case of detailed assessment (Chapter 7)²²".

4.35 In the Belgian case²³ discussed in the box the European Commission took action against the system of programme contracts as amounting to unlawful state aids within Article 87(1). In its Decision it said:²⁴

"The price increases authorized within the framework of the conclusion of programme contracts constitute State aid within the meaning of Article [87] (1), since they enable the beneficiaries to carry out investment and/or research, to take on staff and to promote exports without having to bear the normal costs of such measures."

4.36 It also said,

"In addition, the aid does not fulfil the conditions laid down in order to qualify for one of the exemptions provided for in Article [87](2) and (3)".

²¹ http://ec.europa.eu/comm/competition/state_aid/reform/rdi_en.pdf

²² See Chapter 1.2

²³ C-249/88 in which the Commission took action against Belgium in respect of the programme contracts alleging that they infringed Article 30 EC (now Article 28).

²⁴ Commission Decision 92/327/EEC, OJ 1992 L182/89.

Box 4.1: Relevant cases under Articles 28 and 29 of the EC Treaty

Roussel Laboratoria BV v État Néerlandais (Case 181/82, [1983] ECR 3849)

The Netherlands introduced measures under which the price of imported medicines was tied to the manufacturer's usual basic price for products intended for consumption in its home state. The price of domestic medicines was based on a price freeze at a fixed date.

The European Court of Justice (ECJ) said,

- any measures which are capable of hindering, directly or indirectly, actually or potentially, trade between Member States are to be regarded as measures having an effect equivalent to quantitative restrictions
- systems regulating prices applicable to domestic products and imported products alike do not in themselves constitute measures having an effect equivalent to quantitative restrictions but may have such an effect when the prices are fixed at a level such that the sale of imported products becomes either impossible or more difficult than that of domestic products
- article 28 precludes a Member State from introducing in respect of pharmaceutical products imported from other Member States legislation which refers to the manufacturer's basic prices usually charged for products intended for consumption within the territory of the Member State in which they are produced, where the legislation applicable to domestic production is based solely on a freeze of the level of prices at a given reference date, and
- a situation of that kind can have the effect of placing the sale of imported products at a disadvantage by rendering such sale more difficult, impossible or, in any event, less profitable than the sale of domestic products whenever the level of prices applying to imported products is lower than that applicable to domestic products.

Commission v Italy (Case 56/87, [1988] ECR 2919)

Italy adopted a method of fixing prices for pharmaceutical products which expressly provided that:

- the development of the national industry and research on the national territory should be promoted, and
- the cost components related thereto may be taken into account to a greater extent than the corresponding cost components for imported products,

Under these terms the supplementary costs and charges inherent in importation were not mentioned among the factors to be taken into consideration in the fixing of prices of imported products. The ECJ held that this constituted a measure having an effect equivalent to quantitative restrictions on imports within the meaning of Article 28.

Commission v Belgium (Case C-249/88, [1991] ECR I 1275)

In Belgium pharmaceutical prices were very tightly regulated, with maximum prices set at a low level that could only be increased under very strict conditions. As a result, profit margins were low and it was difficult for pharmaceutical companies in Belgium to invest in employment and R&D. The Belgian authorities' response was to pass a law under which the state and pharmaceutical companies could enter into 'programme contracts'. Under these contracts, pharmaceutical companies were allowed to increase the price of their products in return for

undertaking to promote laboratory research, investment and employment in Belgium and Belgian exports. The conditions attached meant, in practice, only pharmaceutical products developed and manufactured in Belgium could be covered by the contracts.

The ECJ said:

“The introduction by a Member State in the pharmaceutical products sector of a system of programme contracts from which only national undertakings can benefit, and which, in return for the commitments on investment, research, employment and exports, allows derogations to be granted from the general rules on price control and places the products that benefit from the system at an advantage as regards approval for re-imburement, constitutes an infringement of Article 30 [now Article 28] of the Treaty. That system is such as to place imported products at a disadvantage and, therefore, constitutes a measure having equivalent effect to a quantitative restriction prohibited by that provision.”

Conclusion

- 4.37 The PPRS does not provide explicit incentives to invest in the UK. The R&D allowance under the scheme relates to R&D wherever in the world it is carried out. Theoretically, PPRS rules on transfer pricing could even produce a disincentive to invest in the UK. In practice, however, this effect is not currently likely to be significant effect because the profit cap has not been binding for most firms. Further, any pricing scheme that did contain explicit incentives to locate in the UK would be likely to fall foul of EC rules relating to the free movement of goods and state aid.
- 4.38 In the next chapter we consider the factors that are likely to drive the location of internationally mobile investments.

5 DRIVERS OF THE LOCATION OF FOOTLOOSE INVESTMENT

- 5.1 This annexe identifies the key factors influencing the location of internationally mobile investments in the pharmaceutical sector. It draws on interviews and discussions conducted with many companies in the UK and abroad²⁵ supplemented with internal OFT analysis. Our findings are in many ways similar to those of the study conducted by NERA presented to the MISG.
- 5.2 Companies have identified a number of factors that are likely to influence decisions to locate footloose investments:
- quality factors
 - cost / financial factors
 - historical and cultural factors
 - market conditions (although this factor, as will be discussed below, is more contentious).
- 5.3 The following sections identify the key factors that are most important for driving investment decisions at different stages of the pharmaceutical supply chain: pre-clinical R&D; clinical trials; and manufacturing. We then examine drivers that cut across the various stages of the supply chain and have an impact on investment decisions more generally. We also attempt to benchmark the current performance of the UK against each of these factors, using data from PICTF and other sources.
- 5.4 This analysis provides a basis for the high level policy implications considered in the final chapter.

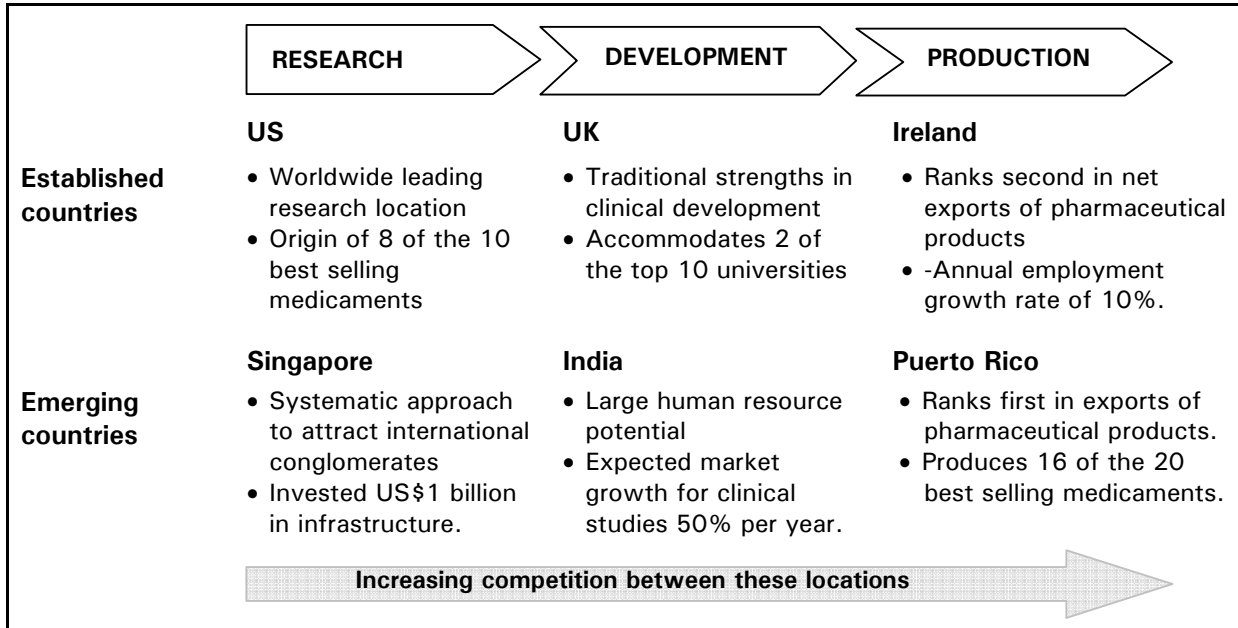
Overview

- 5.5 Pharmaceutical investments are becoming increasingly mobile, with a growing number of countries able to provide a viable infrastructure for such investments. Competition for resources in the pharmaceutical industry is becoming, therefore, more global and the UK is in competition not only with other industrial nations but more and more with transition economies.
- 5.6 The UK has been successful to date, and continues to be so, in key areas that are vital to pharmaceutical industry R&D location. The UK is well known for its clinical trial infrastructure, government spending on research, opinion leaders in the field of pharmaceuticals, its quality of skilled staff, and as a location where business leaders' perceptions of the business environment are positive. The environment for manufacturing is less attractive, due in part to the advantageous tax regimes provided by other countries.

²⁵ These are Australia, Canada, France, Finland, Germany, the Netherlands, Spain, Sweden, Switzerland and the US. See Annexe K.

5.7 Other countries see the UK as one of the leading countries in providing a good environment for pharmaceutical R&D. A recent German study finds for example that although competition is increasing among R&D locations, the UK is still competing among the top six locations, especially in the field of clinical trials (see Figure 5.1).

Figure 5.1: Successful countries along the pharmaceutical value chain



Source: AT Kearney (2005), 'The Research Based Pharmaceutical Industry as a Chance for the Business Location Germany', Michael Nusser, Annett Tischendorf.

5.8 In the following sections, we identify and discuss key drivers of investment within different stages of pharmaceutical development, such as the research and pre-clinical trial phase, the clinical trial phase and the production and the marketing phase. We also look at drivers in the overall economy and consider the more contentious question of whether there is a link between drug prices and the location of pharmaceutical investment. Where appropriate we draw on other research exercises, such as the NERA report.

Drivers of R&D investment in basic research and the pre-clinical stage

5.9 We start by identifying drivers that are of high importance for the very early stages of drug development, that is, the pre-clinical research stages.

5.10 The basic research and pre-clinical trial stage in drug research is characterised by a high amount of cost-intensive research in different molecules. A significant proportion of this primary research is often eventually deemed not useful. That is, this research is characterised by high attrition rates²⁶. These high attrition rates help explain the high

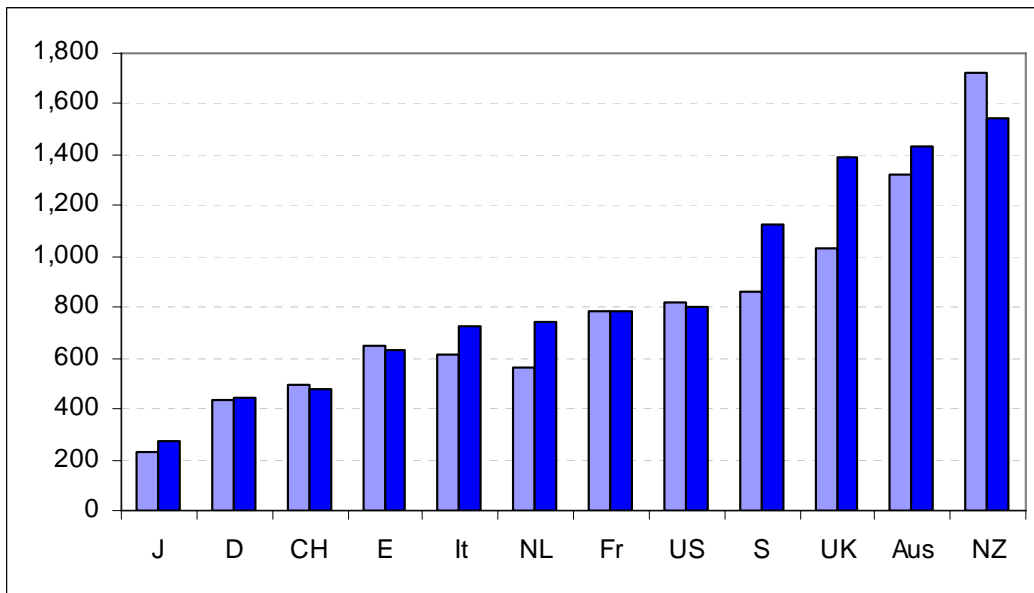
²⁶ The rate at which investigational drugs (fail to) progress to the next stage of testing.

level of risk involved in this first stage of research and highlight the need for good research networks and high quality researchers.

Skilled workforce

- 5.11 Industry mentions that quality scientists are their key resource in early stage pharmaceutical development. Thus a key factor of R&D location is the availability of a strong and reliable supply of good quality science graduates and the attractiveness of the location for a small number of leading scientists in the area.
- 5.12 The UK has sustained a high reputation for the quality of its skilled workforce in the field of sciences. Figure 5.2 below shows that the UK is ahead of the US in terms of new science graduates and has been catching up with Australia and New Zealand between 2000 and 2003. However, the data is collected differently in each nation and it is not a measure of the quality of science graduates.

Figure 5.2: Number of new graduates in degrees in science relevant to the pharmaceutical industry (2000/2003)



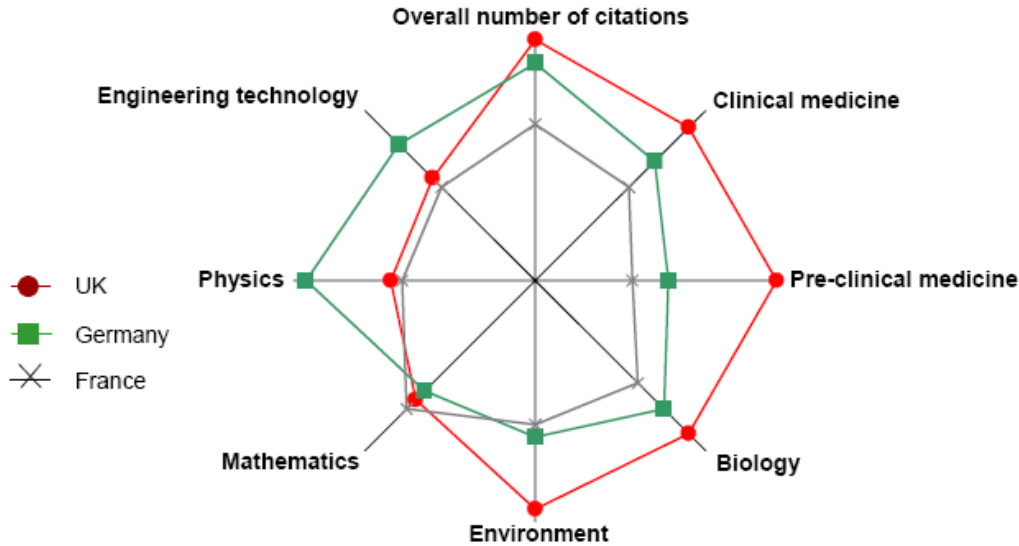
Source PICTF Indicators 2005, Number of graduate scientists per 100,000 persons in the labour force 24-34 years of age (2000/2003)

- 5.13 To date, the UK has consistently provided a large number of good quality science graduates for the pharmaceutical industry. The existence of two of the world's ten top universities in Britain and the attraction of British universities to foreign researchers and students is one of the drivers of the high quality of staff available in the UK.
- 5.14 As well as science graduates, the ability of the UK to attract leading scientists in many areas of pharmaceutical research also provides the industry with necessary human resources. The UK's good academic facilities and the excellent reputation of its

universities are certainly helpful. Furthermore, high living standards and salaries in the UK generally attract talent from all over the world.

- 5.15 As can be seen in Figure 5.3, within Europe the UK is a leader in several fields of research related to the pharmaceutical industry, such as medicine and biology. This also serves to make the UK a more attractive place to conduct research.

Figure 5.3: Country ranking per field of research



Note: The chart is based on the number of citations in scientific research between 1993 and 2002. Source: Nature 2004, 'The scientific impact of nations', A.T. Kearney (2005)

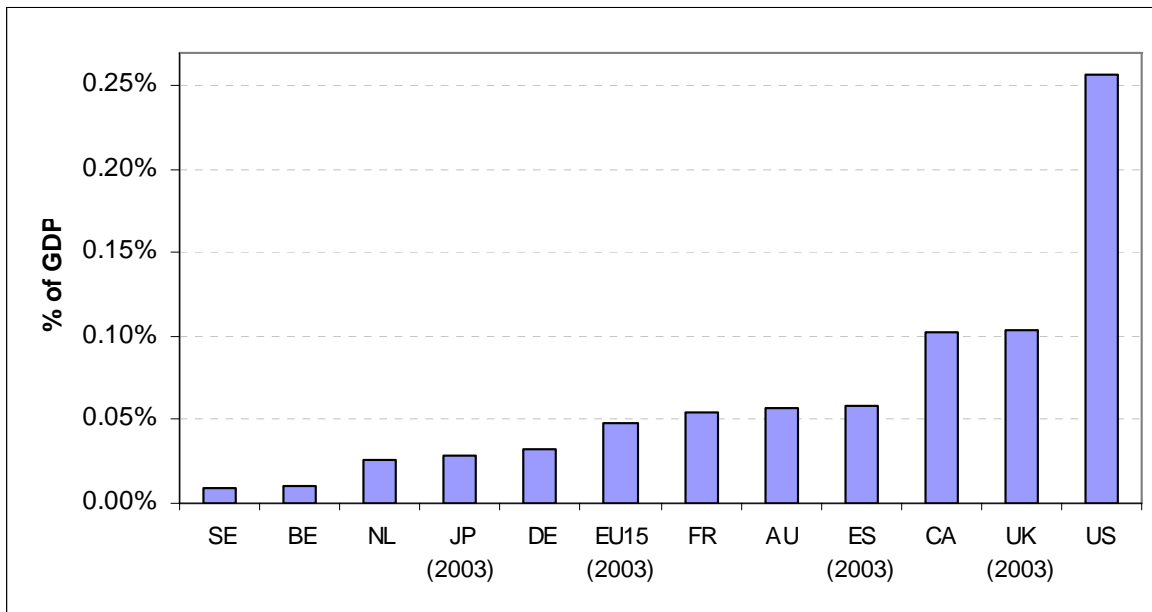
- 5.16 Nonetheless, many business leaders are concerned that the UK is losing many of its top academics and graduates to the US ('brain drain') and that competition from Eastern European nations – which have good quality science graduates, skilled staff in the sciences and lower costs – is growing increasingly strong.
- 5.17 In its report, '*Sustaining the Skills Pipeline in the Pharmaceutical and Biopharmaceutical Industries*' (October 2005), the ABPI highlighted at that time further action was needed by all stakeholders to enhance the pipeline of skills to ensure UK R&D competitiveness.

Government spending on research

- 5.18 Pharmaceutical companies often spend large amounts of time and resources on early basic research. Networks between industry and universities or public research laboratories allow synergies to be exploited and give pharmaceutical companies the possibility of buying into promising research projects. Public research can also help create pools of skilled researchers that can attract further investment.

- 5.19 The NERA report and research by Charles River Associates²⁷ also recognise this as an important driver of R&D and argue that firms want to locate near universities and research centres because of cost-sharing and risk reduction possibilities.
- 5.20 The UK can certainly take advantage of these research synergies as it is a global centre for medical research, for which Government is a major source of funding; Government spending on health-related R&D, as a proportion of GDP, is second only to the US. As shown in figure 5.4, the UK Government spent 0.10 per cent of GDP on medical research in 2003. This is significantly more than in countries such as Germany, France or Japan. US spending on medical research, on the other hand, accounted for 0.25 per cent of GDP in 2004.

Figure 5.4: Public expenditure on health R&D as a percentage of GDP, 2004



Source: OECD GBAORD Database, 2004;

- 5.21 The Office of Science and Technology (OST) is responsible for the allocation of the Science Budget (currently over £3 billion per annum) into research via the Research Councils UK launched in 2002. The Medical Research Council, one of the eight UK Research Councils funded through the OST, had a budget of £476.4 million in 2004/5.
- 5.22 The UK government also provides research funding through the Department of Health, which had approximately £650 million in funding for its policy research programme and NHS R&D programme for 2005/6. Furthermore, the Treasury announced in March 2006 that the budgets for the MRC and NHS research will be combined into a single budget in the future. The budget will be worth an estimated £1 billion.

²⁷ Charles River Associates (2004) *Innovation in the Pharmaceutical Sector: A Study undertaken for the European Commission*.

5.23 The UK Clinical Research Network (UKCRN)²⁸ aims to increase the quality, speed and co-ordination of clinical research, to strengthen the research collaboration with industry and tries to ensure that the health research needs of industry are met. Additionally, the National Institute of Health Research (NIHR) has launched a new funding stream to support 'high technology platforms' for clinical research, that is cutting edge technology infrastructure necessary for clinical research²⁹.

5.24 The need for links between private and public research is also recognised by the Cooksey Review³⁰, which recommends that:

"OSCHR (Office for Strategic Coordination of Health Research) and the TMFB (Translational Medicines Funding Board) should work with the healthcare industries and other interested stakeholders (e.g. the medical charities) to develop proposals for joint public and private investment in new technologies for medicines discovery, along the lines laid out in the FDA's Critical Path programme and the European Innovative Medicines Initiative"

5.25 The report recognises that specific programmes need to be established to support the development of new technologies in medicines discovery. It recommends research to be conducted into how to speed up the drug discovery, development and clinical trial process by identifying new 'end points', 'biomarkers' or disease models. Other important research topics identified by the FDA were data pooling and simulation models, research into innovative and efficient clinical trials, and research into better identifying at-risk populations.

5.26 Government investment in research into these areas could help both to identify more quickly which particular patients will benefit from which drug, and could help drugs to be targeted at more specific patient groups, thus allowing scarce health care resources to be allocated more effectively.

5.27 However, the Cooksey Report identifies the need for a,

'clearer picture as to the support available to translate the results of research and take ideas through to commercialization'.

This is especially important for smaller firms that might not initially have the economic strength to push a drug through the entire development chain.

R&D tax credits

5.28 R&D tax credits were introduced in 2000 in the UK primarily to help boost R&D investment and try to promote innovation and productivity. Small or medium sized

²⁸ www.dh.gov.uk/assetRoot/04/13/71/36/04137136.pdf

²⁹ www.nihr.ac.uk/infrastructure_technology_platforms.aspx

³⁰ An independent Treasury review led by Sir David Cooksey which aimed to build agreement on the best institutional arrangements for a new single fund for health research. It was published on 11 December 2006 and is available at www.hm-treasury.gov.uk/independent_reviews/

enterprises (SME) can claim up to 150 per cent R&D tax relief on qualifying costs related to R&D expenditure. These qualifying costs are generally considered to be costs associated with material and staff costs. SMEs can choose to receive a payable cash amount of expenditure related to the qualifying cost for R&D if they are suffering a loss.

5.29 Large companies can claim 125 per cent tax relief on qualifying costs. This allows them to deduct 125 per cent of the current (qualified) spending on R&D when calculating its taxable profits.

5.30 Between April 2000 and April 2005 there were approximately 17,000 claims for R&D tax credits totalling £1.3 billion. At present there is no evidence to suggest how well tax credits are working and their impact on the pharmaceutical industry in the UK. Because effects are expected in the long run, and due to the relatively recent introduction of the scheme, any beneficial effects may not yet be observable.

5.31 Nevertheless, a cross-country study carried out by the Institute of Fiscal Studies³¹ in 2002 noted that changes in tax incentives seem to be bringing about long-term beneficial effects in R&D expenditure. That is, R&D expenditure is reacting positively to the introduction of R&D tax credits. The study also suggests that the pharmaceutical industry³² may be one of the most responsive sectors to these incentives. Overall, the authors conclude that:

"tax changes significantly effect the level of R&D even after controlling for demand, country-specific fixed effects and world macro-economic shocks. ... over the long run [effects] may be substantial."

5.32 The UK is not the only nation offering tax credits; other countries' low corporate taxes may make up for tax credits offered by the UK. For example, the NERA report states that China offers foreign investment a 150 per cent deduction on R&D (provided R&D increased ten per cent from the previous year) and Korea provides up to seven years tax holiday for high-tech businesses.

5.33 However the effect of tax incentives must not be overestimated. Companies are aware that tax regimes may be subject to drastic change (often of a political nature). This is especially important in the case of long research programmes. Nevertheless, so as not to lose ground in comparison to other nations, it is important that the UK closely monitors its reputation as an R&D location.

³¹ Institute of Fiscal Studies, 'Do R&D tax credits work? Evidence from an international panel of countries 1979-1994', Nick Bloom, Rachel Griffith, John Van Reenen, 2002;

³² Review findings from HM Revenue and Customs 'R&D tax Credits Final Report December 2005' - claimants responding to survey were 419 (43%).

Animal rights

- 5.34 UK animal rights activists were perceived in our discussions with companies as a potential problem in the UK. Recent high-profile opposition to animal testing, including that to Oxford University's new £18 million biomedical research centre, make the UK a less attractive location for pre-clinical trials than countries with less vocal animal rights lobbies.
- 5.35 New legislation is perceived to have improved the situation over recent years, but activists might still jeopardise new investments in the UK. The NERA report supports this assessment:

"Interviewees suggested that pressure against such activities [animal testing] from the animal rights movement has in the recent past placed in serious jeopardy the maintenance of R&D in the UK. However, they also acknowledged that legislation has substantially assisted the industry in dealing with these pressures."

The clinical trial phase

- 5.36 The second important stage in R&D is the clinical trials stage. Key factors when considering the location of clinical trials are speed, quality and costs. Costs can have an impact but generally the quality of the trials is the main factor. Other factors determining where to locate trials depend on judgement of the overall cost effectiveness for a particular project, whether or not a particular project would benefit from opinion leaders, and whether or not sufficient patients can be recruited in order to conduct the clinical trial.

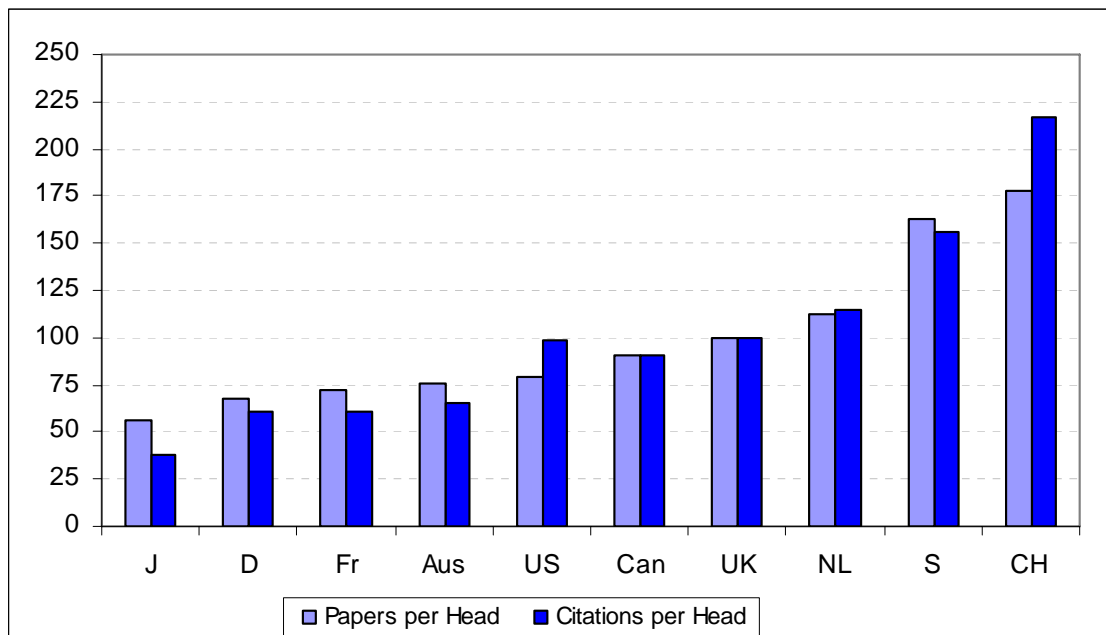
Quality

- 5.37 An important requirement for a clinical trial site is a culture of good clinical practice. This includes highly skilled staff for managing, monitoring and reporting the trials and dealing with regulatory requirements in addition to suitable high quality infrastructure – such as access to leading-edge technologies – that ensures that reliable data is produced. Furthermore, expert scientists with sufficient expertise are needed to carry out and supervise trials and to help interpret results.
- 5.38 A badly undertaken trial can delay regulatory approval and ultimately the market introduction of a product, which may significantly harm a pharmaceutical company. Risks involved with trials are thus great and quality and good practice in one country can often outweigh cost aspects. However, there is a wide range of countries in which good quality can be achieved. Locations as diverse as the US, Central and Eastern Europe, Japan, Brazil, Australia, Israel, South Africa, Morocco and Egypt can provide suitable infrastructure for clinical trials.

Opinion leaders

- 5.39 The attraction and employment of highly recognised pharmaceutical and medical experts, or 'opinion leaders', was argued during consultation with stakeholders to be an important contributing factor in the decision for the location of that trial.
- 5.40 Opinion leaders in the UK are highly regarded, and this is arguably reflected in the UK's ability to attract R&D investment to date. As shown in Figure 5.5, the UK publishes more scientific papers and has more citations published per head than the US and most other comparator countries (falling behind only the Netherlands, Switzerland and Sweden).
- 5.41 One benefit of accessing key opinion leaders for companies is their potential to increase the uptake of a new drug. However, relatively slow uptake rates in the UK might compromise some of these effects. It is therefore important for the UK to address its slow rates of uptake, for example, by providing more opportunities for interactions between NICE and clinicians working on clinical trials.

Figure 5.5: Scientific research papers / citations per head of population, 1994 - 2003



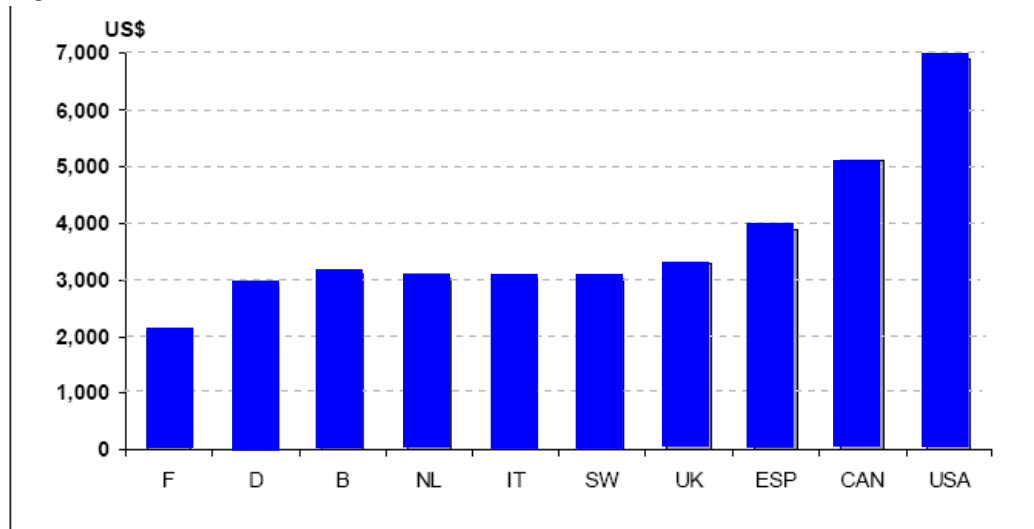
Source Indicators PICTF 2005

Costs

- 5.42 Some in the industry have acknowledged that the cost of clinical trials in the UK is rising and the lack of transparency of these costs is an issue. This rise in costs can be a result of increasing labour costs, increasing costs for recruiting patients for a clinical trial, or costs associated with long initial waiting periods or regulatory barriers.

5.43 The costs of conducting clinical trials in the UK are below the costs in the US, Canada and Spain. Other EU countries have lower per patient costs as shown in Figure 5.6. However, a high percentage of trials are conducted in the US and the UK despite the relative cost disadvantage. Therefore, in certain instances there may be little or no correlation between high costs and the location of clinical trials; decisions may be based on other factors such as the location of the appropriate knowledge about a particular drug category.

Figure 5.6: Per patient cost for clinical studies in phase III in 2001



Source: CRA 2004: Innovation in the pharmaceutical sector

5.44 However, companies are increasingly shifting clinical trials to new locations in Eastern Europe, China and India. Like the UK, these countries have highly skilled scientists, but the recruitment of patients for trials is sometimes significantly easier. Government investment in public research on clinical trial practice (to reduce future costs) is therefore increasingly important if the UK is to maintain its position as an attractive location for clinical trials.

The manufacturing phase

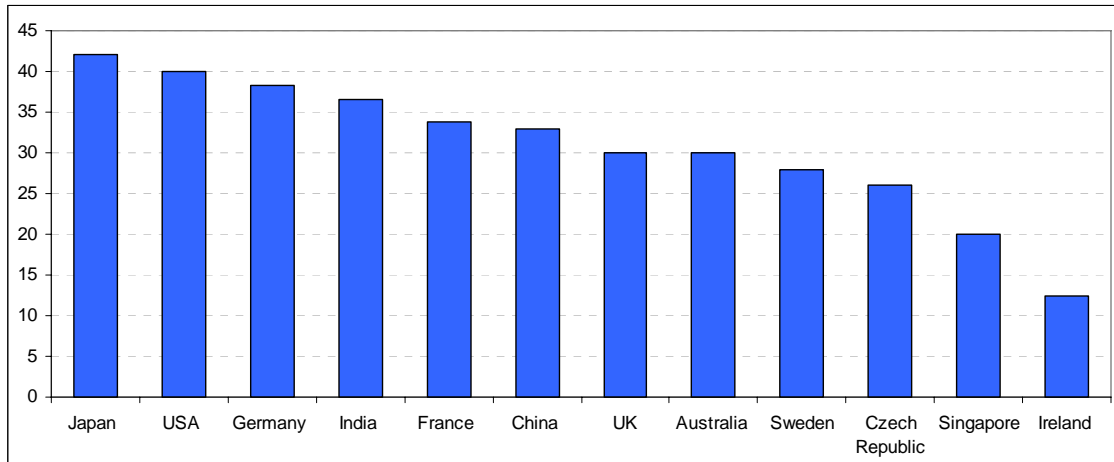
5.45 Although other factors are relevant, a country's tax regime appears to be the biggest driver in the manufacturing stage of the pharmaceutical supply chain.

5.46 The UK's main corporate tax rate is 30 per cent for larger companies and 19 per cent for smaller companies³³. The UK has been perceived in the past as having a competitive corporate tax rate and therefore has benefited from inward investment. As shown in Figure 5.7, the UK in 2005 had one of the lowest main corporate tax rates among comparator nations. However, this is only a measure of the main corporate tax and

³³ OECD data 2003 – rate has remained unchanged for the main tax rate Inland Revenue.

does not include other taxes such as VAT, labour taxes, and other tax levies, which may affect investment decisions.

Figure 5.7: Main corporate tax rates in selected countries in 2005

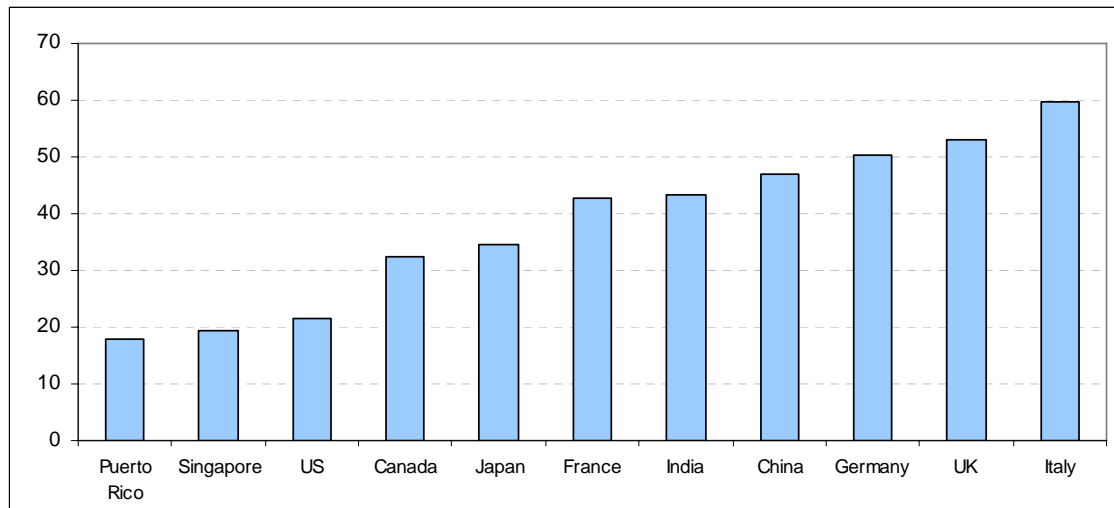


Note: The Singapore rate used was taken from the UKTI website, however some stakeholders suggested that the effective use of various incentive schemes allowed effective tax rates close to zero

Source: KPMG, KPMG's Corporate Tax Rate Survey 2005

5.47 If we compare the tax payable as a percentage of gross profits as shown in Figure 5.8 below, the overall tax bill for companies in the UK looks high in comparison to other countries. According to the World Bank's database of business regulations and their enforcement (DoingBusiness.org), the UK's tax payable is 52.9 per cent of gross profits. This includes all tax levies associated with doing business in the UK.

Figure 5.8: Tax payable on gross profits in 2005



Source: World Bank, Doing Business org

5.48 Because of these differences in tax rates, the UK is viewed as a less viable option to locate the manufacturing side of the pharmaceutical business. Countries such as Singapore and Puerto Rico, which have lower tax payable as a percentage of gross

profits (19.5 and 17.8 per cent respectively), are seen as more competitive locations for the manufacturing side of the industry. The NERA study found that Singapore was observed by business leaders as,

"an excellent example of a country which has successfully achieved significant levels of investment as a result of its delivery of a [favourable business] environment [including low taxes]".

Cross-cutting drivers

- 5.49 There are several factors that influence the overall perception of a country's suitability for R&D investment across all stages of the pharmaceutical development process. In addition to basic issues like political stability and Intellectual Property protection, companies look for a stable pro-business environment with low regulatory burden, low levels of bureaucracy and few restrictions. Tax incentive schemes and the general business tax level also play an important role as companies seek to maximise their profits over their investment location decisions.

UK business environment

- 5.50 Pharmaceutical companies maintain that the business environment in a nation is a key factor in the decision making process for locating R&D investment. If perceived negatively this may overshadow other positive attributes. Consultation with key stakeholders suggests that the UK has historically been perceived by business executives as a good place for doing business, not only because of the regulatory and competitive tax environment, but also because of pro-business government.

- 5.51 Labour laws, flexibility, costs and quality can have an influence on a company's decision regarding where to produce pharmaceuticals. As the NERA report mentions,

"the flexibility of the labour force and labour law appear to be more significant drivers than labour costs per se in influencing location decisions".

This is because a highly sophisticated industry like pharmaceuticals needs to rely on good quality procedures and flexibility – mistakes cannot be tolerated.

- 5.52 The more flexible the labour market, the easier it is for companies to adjust their production according to demand and new products, and the easier it becomes for workers to adjust to a new production line or a new process of production. Consequently it becomes more attractive for a company to locate its sites in this country.
- 5.53 With regards to labour laws, the UK is one of the more liberal countries in Europe, granting companies enough flexibility for short term contracting and hiring. The UK also provides companies with a skilled and well qualified workforce, which is essential to a high quality production line.
- 5.54 However, in consultation, stakeholders suggested to us that countries like China, India, Puerto Rico and Ireland can also provide qualified and equally skilled workers at lower

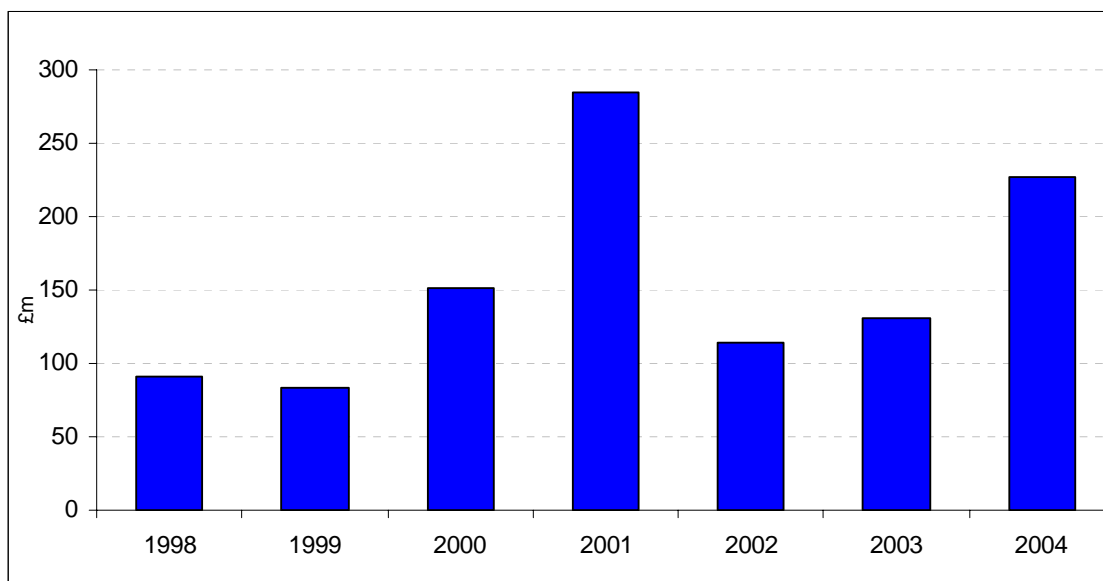
costs. The advantage of the UK may therefore lie in the technical expertise required to produce new high-tech pharmaceutical products (in contrast to traditional chemical based drugs) and high quality infrastructure for specific production needs³⁴. The UK should therefore aim to compete in those areas of production where quality and technical expertise are important.

Venture capital

- 5.55 Access to capital is one of the most important determinants of R&D activity in the pharmaceutical sector. Developing a new drug is a very lengthy process and companies cannot generate positive cash flows from a product before the drug is launched on the market. Additionally, compared to other technology sectors, significantly higher levels of investment are required to bring a product to market and high risks are involved with the investments due to high attrition rates. This frequently precludes venture capital financing at the early stages.
- 5.56 As a result, companies in the pharmaceutical and biotechnology industry face difficulties attracting investment to develop and commercialise their products. This is particularly true of small companies, which may not have a large existing portfolio of products on the market from which to earn revenues.
- 5.57 According to PICTF, flexibility and accessibility of the capital markets is vital to the pharmaceutical industry because of the nature of its long term business. The PICTF argues that over the last four years the funding of biotech companies has been made more difficult as a result of a retrenchment in the private equity market and the closure of the public capital markets to new issues. It notes that approximately 20 per cent of the European bioscience companies started in 2000 have since gone out of business and suggests that developments in the financial markets are the cause.
- 5.58 The Biotech Industry Association estimates that the necessary equity required to fund a top-tier profitable bioscience company in the US costs on average \$600-\$700 million. In the UK, the sector raised £392 million, which is far below what is necessary to finance a top-tier company from the start up to profitability.
- 5.59 The Biotech Finance Forum of the EC has estimated that there is a €1 billion funding shortfall in European bioscience companies; of which 50 to 70 per cent lies within the UK.
- 5.60 As shown in Figure 5.10, venture capital investment in pharmaceuticals/biotechnology peaked in 2001 and, following a decline in 2002-2003, has now increased again. This trend is not exclusive to the pharmaceutical industry but is reflected globally in many sectors of the economy.

³⁴ Such as cooling facilities, good infrastructure to serve different markets, etc.

Figure 5.10: Venture capital invested in the pharmaceutical/biotechnology industry



Note: number of companies receiving investment: 2000: 98; 2001: 119; 2002: 146; 2003: 139; 2004: 135;

Source: PICTF and British Venture Capital Association Reports on Investment Activity 2000-2004

5.61 It should be noted, however, that venture capital raised in the UK does not necessarily have to be used exclusively on UK projects. The economies of scale and scope associated with the City of London make it a leading world financial centre and an attractive location for raising capital for firms operating (exclusively) abroad.

Market conditions

5.62 Having reviewed the different drivers of reform along the pharmaceutical value chain, this section discusses, at a theoretical level, whether it is possible for a government to use its drug pricing and procurement policy to promote its domestic pharmaceutical industry. We ask whether the prices that a government is willing to pay for drugs can drive R&D location decisions, and discuss the credibility and rationale of these so-called strategic arguments often made by industry.

5.63 Some of the statements made by the pharmaceutical industry imply a link between the price which the NHS pays for drugs and the attractiveness of the UK as a location for the industry. For example, in a press release dated 24 January 2006, the ABPI stated:³⁵

“No company can be expected to invest in the UK if the environment here is not sufficiently welcoming. Areas that the Government needs to watch carefully include the danger of over-regulating the industry and placing further pressure on prices for products that can advance the productivity of the NHS.”

³⁵ www.abpi.org.uk/press/press_releases_06/060124.asp

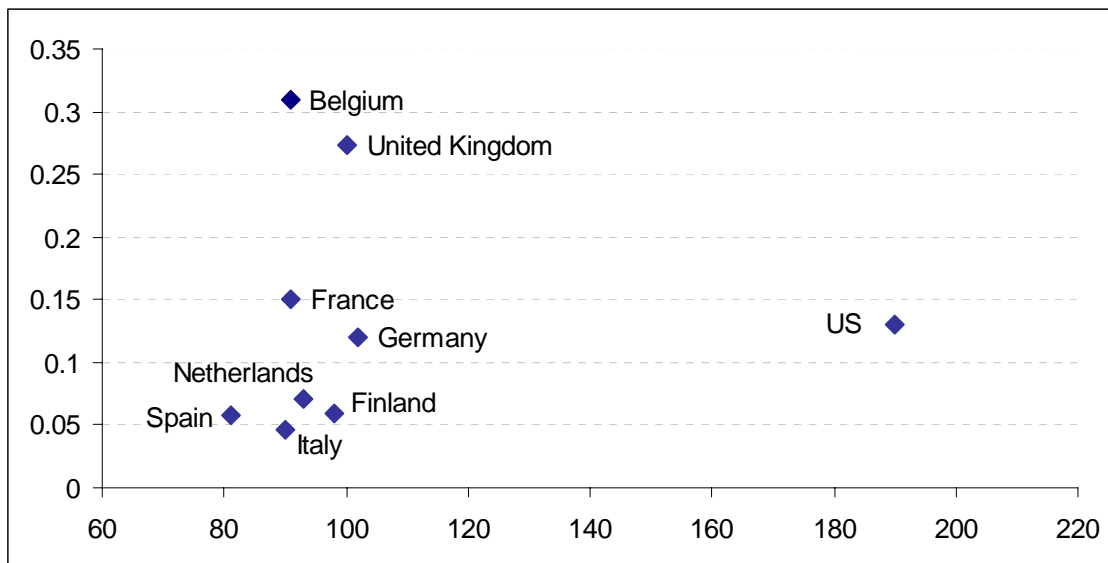
“While it is right that the NHS should get its medicines at a fair price, this has to be carefully balanced against the enormous benefits that the industry’s continued presence and investment bring to patients and to UK plc.”

- 5.64 At first glance, it is not obvious why there should be a link between price and level of R&D investment, provided that pricing decisions made by the NHS have an equal effect on both imported drugs and drugs manufactured in the UK. This would mean that pharmaceutical companies located outside the UK could free-ride on the 'high prices' in the UK. The argument put forward by some that the price of pharmaceuticals in the UK is an incentive to invest in R&D in the UK therefore overlooks the fact that products can be sold globally, regardless of where the initial research has been conducted.

- 5.65 There are no credible economic mechanisms to suggest that product market characteristics could over-ride other incentives for investments, such as costs of production, availability of a skilled labour force, tax incentives or a favourable research friendly business environment.

- 5.66 Figure 5.11 shows that despite the fact that US consumers pay high prices for medicines, US R&D intensity as a percentage of GDP is lower than that of the UK. Belgium, on the other hand, shows a very high R&D intensity despite paying lower prices than the UK and other European countries such as Germany or Finland. Thus, there is no obvious correlation between success in attracting R&D and the prices paid for pharmaceuticals within a nation.

Figure 5.11: Pharmaceutical R&D as a percentage of GDP related to drug prices, 2003



Source: Data is directly drawn as pharmaceutical R&D/GDP from the OECD database, DH price indices

- 5.67 In this annexe we have been considering the drivers of 'footloose' investment by pharmaceutical companies – that is, investment that could be carried out anywhere in the world where a suitable environment exists, regardless of where final sales are made. There is, however, one component of R&D for which it could be argued that

decisions over where to locate are related in part to market conditions. The location of clinical trials may in part be driven by a desire to market a product to clinicians in a particular country so as to improve subsequent uptake. These incentives will not, however, be strong in countries where revenues are expected to be low in any case. As the NERA report argues,

"the benefits of familiarising opinion leading clinicians with new medicines will not be high if cost-cutting bodies are to prevent clinicians prescribing them anyway"³⁶.

5.68 Such arguments are only likely to be significant in larger markets, however.

Political bargain

5.69 Another way in which price could, in theory, affect location decisions would be if there was an implicit bargain between the government and industry. In other words, the government would agree to pay higher drug prices in return for an (implicit) agreement by industry that pharmaceutical R&D would continue to be located in the country in question.

5.70 However, such an argument seems weak in the UK context as other (supply-side) factors make the UK an attractive location for the pharmaceutical industry. The industry's threat to 'punish' Government by relocating overseas if prices are cut is less credible if there are strong supply-side reasons why the industry would wish to remain in the UK. These reasons might include:

- a skilled labour force and science base (likely to be particularly important for R&D investment)
- a high level of publicly-funded health R&D
- access to a high quality clinical trials infrastructure
- flexible and accessible capital markets
- a relatively low rate of corporation tax compared to other countries (likely to be particularly important for manufacturing), and
- availability of R&D tax credits.

5.71 If companies have their decisions led by preferential treatment today, they may be vulnerable to political change in the future. Using rational reasoning a company might not want to agree in such a risky bargain but rely on supply side fundamentals. Overall, it seems unlikely that a political bargain of the above mentioned nature would be credible or sustainable. In policy terms, instruments that target supply-side factors directly are likely to be much more effective than attempting to inflate price as part of a loose quid-pro-quo bargaining arrangement.

³⁶ NERA report p35.

- 5.72 Even if (for the sake of argument) high drug prices do have some effect on location decisions, it is not clear that this is the best way for Government to achieve its industrial policy objectives. In particular other policies, such as investment in private-public partnerships or research networks could be more effective at achieving the government's industrial policy objectives (for the same amount of money). It is particularly likely that policy support which is directly targeted at companies locating in the UK and companies with efficient new drugs would be more effective than paying high prices across the board as part of an (unenforceable) bargain with industry, and
- 5.73 Generally, alternative (better) policies are likely to focus on improving the supply-side environment for the pharmaceutical industry, rather than on the demand-side. Examples of possible policies to attract R&D investment include:
- enhanced tax incentives for R&D
 - increased public funding for health R&D
 - improvements to science education and training, and
 - public investment in clinical trials infrastructure.

Conclusions

- 5.74 This section has analysed a number of key factors that influence the location of footloose investments in the pharmaceutical sector at the main stages in the development process (the basic research and pre-clinical stage, the clinical trial stage and the manufacturing stage). Additionally, it examined some general, cross-cutting, driving factors. Finally, it examined theoretically whether the price of pharmaceuticals in the UK has any influence on UK R&D investment decisions.
- 5.75 This section has a number of key conclusions, summarised as follows:
- the quality of the higher education system, the success of public-private partnerships, the presence of tax credit schemes and the strength of the animal rights lobby are important factors that influence UK R&D investment in basic research and the pre-clinical stage
 - the quality of support infrastructure, the presence of highly recognised pharmaceutical and medical experts and the level and structure of costs are important drivers of UK R&D investment in the clinical trial stage
 - other important, cross-cutting, drivers include the perception of the UK business environment – which is largely determined by the flexibility of the UK labour market – and the availability of venture capital
 - the size of the UK market is unlikely to explain the UK's strong pharmaceutical industry
 - price setting is unlikely to be a successful tool with which Government can attract UK R&D investment.

5.76 The next, and final, section will outline some general conclusions and high-level policy implications arising from the discussion in this annexe.

6 CONCLUSIONS AND POLICY IMPLICATIONS

- 6.1 This annexe has evaluated the argument put forward by some stakeholders that the PPRS is currently or can in future be used as a means through which the UK Government can influence pharmaceutical R&D investment in the UK. Its conclusions are twofold: not only does the PPRS **not** contain explicit incentives to locate R&D investment in the UK, but any future attempt to incorporate such goals in a pricing scheme would fall foul of EC legislation.
- 6.2 This study finds that there is very little evidence to link the price of pharmaceuticals in the UK with the overall attractiveness of the UK as a pharmaceutical R&D investment location. It recommends that any future reform to the UK's pharmaceutical pricing scheme must retain the current policy of not discriminating between firms on the basis of the location of their investment. Indeed, this policy should be made more explicit as several key stakeholders misunderstand the scheme's current aims in this regard.
- 6.3 This annexe has analysed a number of factors that do influence firms' decisions to locate R&D projects in the UK. It did so individually for different stages in the pharmaceutical development process. In summary, we found that the spillover effects from R&D research are positive and potentially significant. Targeted Government support for R&D projects for which the market by itself does not provide adequate incentives may therefore be in the social interest. The funding of basic (university) research is a good example of this.
- 6.4 We identified public-private partnerships as a particularly strong and important driver of R&D and should be further strengthened by Government initiatives. As also identified by the Cooksey Review, *'there needs to be a clearer picture as to the support available to translate the results of research and take ideas through to commercialization'*. This is especially important for smaller firms that might not initially have the economic strength to push a drug through the entire development chain.
- 6.5 It is important that Government strengthens the UK's capacity to conduct leading pre-clinical and clinical research by investing in education, skills and research networks. The Cooksey Review recognises in this respect that:
- "In order to exploit the strengths of the UK's health research, the [Cooksey] Review believes the UK must maintain the quality and quantity of its excellent basic medical research. But it must also address the barriers to translation of basic research that result from the gaps identified between basic and clinical research, and between clinical research and clinical practice. The Review envisions cultural change in both the Department for Health and the MRC, to address cultural barriers to research collaboration, and to the willingness to undertake further research to support the application and translation of basic research into patient and economic benefits".*
- 6.6 In this respect, we welcome the continued development of the UK Clinical Research Collaboration (UKCRC). Established in 2004, the UKCRC brings together the key

organisations that shape the clinical research environment in the UK, the main funding bodies, academia, the NHS regulatory bodies, industry and patients. Its aim is to co-ordinate research funding, build up infrastructure supporting clinical research, create incentives for research in the NHS, and build up a skilled research force. The UKCRC has established a UK-wide infrastructure to underpin clinical research, has developed initiatives to fund Public Health Research Centres for Excellence and has launched a £134 million coordinated initiative to build a national framework for experimental medicine research. Although it will undoubtedly take time to develop full potential of these initiatives, the analysis of this annexe suggests they are likely to have positive effects in the long term in attracting R&D investment to the UK.