Annexe L

Evaluation of options for reform to the PPRS

February 2007
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EXECUTIVE SUMMARY

This annexe explores possible alternative approaches to the PPRS for the pricing and reimbursement of branded prescription medicines in the NHS. It builds on the analysis contained in the other annexes of the report, which consider the role of the PPRS within UK and international markets.

The discussion considers the objectives that a pricing scheme should attempt to meet as well as a number of questions that need to be considered in the design of a workable scheme. It then draws up options for reform of the PPRS, considering first off-patent brands (both originator and non-originator products) and then on-patent branded drugs.

An efficient price for a branded medicine must balance, among other considerations, securing value for money to the NHS with providing appropriate incentives to manufacturers to invest in innovative new drugs. A scheme must ensure that drugs are affordable to the NHS, so that patients can benefit from them, but also that innovation is rewarded when new drugs provide medical breakthroughs or significantly improve on standards of care delivered by existing treatments.

Off-patent brands

Under current arrangements, off-patent brands (which are priced under PPRS) can be many times more expensive than bioequivalent generics, which bring precisely the same benefits to patients. We also have concerns that aspects of the pricing and reimbursement regime – namely, price modulation provisions under PPRS and the significant margin differences that exist between brands and generics – have the potential to undermine competition between brands and generics and generate higher costs for the NHS.

We recommend pricing off-patent brands in line with bioequivalent Category M generics (allowing a margin of 25 per cent in the case of originator brands). We believe our proposals will address the competition concerns identified and deliver efficiency gains to the NHS in excess of £60 million per year.

On-patent brands: options for reform

In considering how best to meet the high level objectives of the scheme, we consider four options for the pricing of on-patent brands. They are:

- an incremental option that sets out reforms to existing price and profit controls
- a value-based system under which companies would retain freedom of pricing for new active substances at launch, but where a drug’s price would be reviewed some years later and a maximum price set at a level judged appropriate by cost effectiveness analysis (an 'ex post' value-based approach)
• a second value-based system, which would use the same pricing principles as the first but establish maximum prices before launch (an ‘ex ante’ value-based approach), and

• removing the PPRS altogether and replacing it with more localised bargaining between primary care organisations and manufacturers.

In our opinion the best long-term arrangement for the UK would be Option three: to replace PPRS profit controls and price cuts with an ex ante value-based approach to pricing. We recognise, however, that this would require some time to implement.

On balance, we do not support Option four because there is great uncertainty if it could be implemented in practice and about the outcome if it could be implemented. Neither do we support Option one. There are major difficulties in making any meaningful assessment of profitability in the pharmaceutical sector, for example due to the global cost base and high level of intangible capital employed by many firms. More fundamentally, reforms to the profit cap, would not best achieve the high level objectives of the scheme since they would not give strong incentives to companies invest in the drugs that are the most useful to patients.

Neither would we recommend further reliance on price cuts in the future. The cuts – which have increased over time – necessarily have an element of arbitrariness since they apply to all branded drugs irrespective of therapeutic value. Companies may also anticipate future cuts when setting launch prices for New Active Substances. We do not, therefore, consider this to be a sustainable model of pricing in the future.

In short, incremental changes to existing controls would not address our main concerns with the PPRS – that neither the profit cap nor the price cuts addresses the therapeutic value of the drugs they affect. As shown in Annex M of this report, under current arrangements drugs that are clinically substitutable sometimes have widely divergent prices. This does not represent value for money. Further, failing to reflect relative clinical benefits in prices does not provide manufacturers with strong incentives to invest.

We recognise that other aspects of UK pharmaceuticals policy – such as the creation of NICE, SMC and AWMSG – in part compensate for the fact that the PPRS does not operate at the level of individual medicines. While these bodies are highly expert in the assessment of clinical and cost effectiveness and have made a major contribution since their creation, we believe that the restricted remit they have been given limits the extent to which they can ensure resources are used cost effectively. Our Options two and three are aimed at addressing these restrictions.

We believe either Options two or three would represent an improvement on current arrangements, since they are based on the same underlying value-based principles. Taking up the system of ex post reviews proposed in option two would involve fewer changes compared to today and allow companies commercial freedom in pricing newly launched drugs, but the trade-off would be a delay in achieving value-reflective prices and, possibly, delays in the uptake of cost effective treatments.
The ex ante value-based approach in Option three addresses these concerns and is therefore our preferred option. Fast track ex ante assessments would provide a rapid, pragmatic approach for most drugs. In certain cases, such as some drugs for chronic conditions, it may be more difficult to gain a full view of therapeutic value at launch, before data from clinical use become available. The option to pursue risk-sharing contracts – under which definitive prices would only be set after some years, once appropriate data were available – may then be useful in some cases but would call for more administration and negotiation. In either case, we argue that NICE, SMC and AWMSG, together with other resources in the NHS and UK departments of health, possess ample specialist expertise compared to authorities in many other countries that appraise every new drug at launch and review public reimbursement listings annually.

Details of our recommendations

We propose that under a fully reformed PPRS starting from 2010 maximum prices for branded drugs would be set on value-based principles. The cost effectiveness analysis required to form a view on value-reflective prices would be undertaken by NICE, SMC and AWMSG. The maximum price of a branded drug would be set on the basis of the additional therapeutic benefits it delivers compared to a next-best alternative (or placebo where no substitute is available) in the various licensed indications and patient groups for which the drug might be prescribed.

Some companies have expressed to us the view that on-patent brands should not be compared against generics in considering cost effectiveness as this will reduce incentives to invest in new drugs. We do not agree with this position. In our view, given the limited resources the NHS has at its disposable, it cannot afford, on grounds of both efficiency and fairness to patients, to ignore relevant comparators on the grounds that they are ‘too cost effective’. If the best available treatment is a generic then new treatments must demonstrate their benefits in relation to the generic to receive higher prices. In the long run, we agree this will have effects on incentives to invest, but we believe they will be entirely positive, encouraging companies to target areas of unmet clinical need.

Because medicines often provide different benefits across various indications and patient groups, there is no guarantee that a single list price applied to all prescribing volumes would be efficient, from the point of view of rewarding therapeutic benefits actually delivered and giving appropriate incentives for marketing to pharmaceutical companies. We therefore consider various ways in which ‘non-linear’ price structures could be implemented. Because multiple list prices for pharmacy reimbursement would be impractical, non-linear prices would be best implemented through rebates.

Under our recommendations, the work of NICE, SMC, AWMSG and other NHS bodies would be coordinated by agreement between the devolved health departments. However, these bodies would not be able to set prices or make reimbursement decisions on their own account. Any revised NHS list prices or rebate regime would have to be formally negotiated with companies by the Secretary of State for Health. In practice, we propose that a pricing
unit within DH carry out this task, on the basis of analysis carried out by NICE, SMC and AWMSG.

Part of the appeal of this framework is its practicality since it would not require new legislation. It reflects the fact that pricing decisions are not devolved, but are set at a UK level. At the same time, most aspects of devolved arrangements would be untouched because devolved bodies would continue to exist in their present form. The pharmaceuticals-related work of NICE, SMC and AWMSG would be coordinated under a UK-wide health technology assessment programme to ensure efficient use of resources but guidelines issued by those bodies (SIGN in Scotland) would continue to be issued locally, as would non-drug-related guidance.

We also consider further options for the longer term under which the joint working arrangements proposed here could be extended. Possibilities include bringing NICE, SMC and AWMSG under the aegis of a UK-level commission that, as well as appraising drugs, would negotiate prices with companies independently of government. However, such an arrangement is not necessary to ensure the smooth working of value-based reforms to the PPRS.

In both the medium term and long term structures, we think there could be an important role for a PPRS-style agreement between industry and government, to provide high-level input into pharmaceutical pricing and reimbursement arrangements. A value-based PPRS would clearly be a different sort of document to the present agreement, containing high level principles for the conduct of reviews and setting out certain key parameters.

**Costs and benefits of reform**

Several companies indicated to us that they see merit in the principle of value-based pricing, but were concerned at the resource implications of any move in this direction. It is clearly right that reform only be implemented if the benefits outweigh the costs.

We consider extra resources that would be required by NICE, SMC and AWMSG to operate our recommended options for reform. Indicative financial costs would be about £6 million per year beyond current expenditure on health technology assessment. There would also be costs for pharmaceutical companies, for submitting more information than today to evaluation bodies. However, some of these costs would be offset as under the proposed system because companies would only be required to submit ex ante reviews to a single cost effectiveness body, when multiple submissions can be required at present.

More importantly, more efficient price structures should result in better incentives for efficient marketing and thus lower marketing costs. In fact we believe any increases in required informational expenditure caused by a move to value-based pricing could entirely be offset by reduced marketing costs. That is, resources could be reallocated from marketing to submission of cost effectiveness information on drugs. It would only require a small reallocation of marketing spend to achieve this: in 2004, £850 million was spent by AFR companies on marketing drugs in the UK.
We recognise, however, that, in a more value-conscious NHS, it is important to support companies in developing robust cases for the cost effectiveness of their products. Several recommendations to help companies do so are discussed in the recent Cooksey Review of UK health research funding (December 2006), which we welcome.

Set against the costs of introducing our proposed reforms, the potential benefits of value-based reforms to the PPRS are very large. Benefits are of a different order of magnitude altogether to the costs.

The most immediate benefits are set out in Annexe M of this report. They are potential efficiency savings from adjusting the current prices of certain on-patent branded medicines to be more in line with their clinical benefits relative to close therapeutic substitutes available generically. Possible efficiencies run to over £500 million per year. These efficiency savings, which could under an alternative scheme be reallocated to improve access for patients to new and existing drugs, provide an initial indication of some of the gains that could be achieved through value-based pricing.

Substantial further gains may be available over the longer term because setting prices to reflect incremental therapeutic benefits delivered beyond existing medicines would give manufacturers stronger incentives to invest in areas of unmet patient need. The influence of UK prices on the investment decisions of the global pharmaceutical industry should not be dismissed since the UK affects prices and demand in many other countries – which between them represent around 25 per cent of global sales.
1 INTRODUCTION

1.1 This annexe explores possible alternative approaches to the PPRS for the pricing and reimbursement of branded prescription medicines in the NHS. It builds on the analysis contained in the other annexes of the report, which consider the role of the PPRS within UK and international markets, analyse the scheme’s profit and price controls and review alternative pricing and reimbursement arrangements in ten major countries.

1.2 The discussion starts with a blank slate before working up concrete options for reform of the PPRS. It begins in Chapter 2 by setting out a list of objectives that an ideal pricing scheme would achieve – and some of which various systems around the world seek to achieve.

1.3 The most important objectives are that a scheme should help achieve short run and dynamic efficiency – that is, deliver value for money for the NHS while providing the right incentives to companies to invest in drugs in the future. These goals are at the heart of the current PPRS stated objectives. A number of other detailed objectives are identified, which are subsidiary to these high-level goals.

1.4 The discussion continues in Chapter 3 by translating these high-level objectives into five cross-cutting design issues and working through each in turn. Each design issue is a set of related questions that need to be addressed in the process of devising a scheme to meet the objectives. Considering each issue in turn organises and simplifies the discussion. The issues relate to:

- the assessment of value
- whether to negotiate prices of drugs before or after they come onto the market
- price structure
- setting the budget / level of prices, and
- institutional design.

1.5 Chapter 4 sets out proposed reforms to the pricing of off-patent brands, considering both originator products and non-originator products (so-called 'standard branded generics').

1.6 Chapter 5 draws up four possible alternative arrangements for the pricing of on-patent brands, evaluating the advantages and disadvantages of each in the light of the objectives previously discussed. The first is an incremental option that sets out potential reforms to existing price and profit controls. The second and third are arrangements that would set the prices of branded prescription drugs to reflect their therapeutic value to patients. These two options have similar conceptual

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1 The latter have been the subject of DH consultations to remove them from the PPRS. However, this consultation has been on hold pending the outcomes of this study.
underpinnings but differ in their mechanics. The first is closer to current PPRS arrangements, retaining freedom of pricing up front and reviewing drugs when they are already on the market (an 'ex post' approach), while the second involves an assessment before new drugs come onto the market (an 'ex ante approach'). The last option would remove the scheme altogether, replacing it with more localised bargaining between PCOs and manufacturers.

1.7 Chapter 6 sets out our recommended option – a value-based approach to pricing – and provides a high level estimate of the potential costs and benefits of this proposal. It also considers to what extent additional public and private resources would need to be found to implement a value-based approach to pricing.

1.8 Chapter 7 concludes by considering how the institutional framework to implement our proposals could be structured in the short and long term.

1.9 Several companies and Government stakeholders have told us that while value-based pricing may be attractive in principle it is very important to be clear on the details of how any such scheme would work in practice, in particular how institutions would work and the rules and procedures they would be implementing. This annexe therefore explains in some detail how the alternative scheme could work in practice.

1.10 The objective of the annexe is not simply to set out our ideal approach, however, but also to explore alternative options and explain where appropriate why we have rejected them. We do so because a key role of this study is to improve the terms of debate about pharmaceutical pricing and reimbursement, not just in the UK, but internationally.
2 OBJECTIVES IN THE PRICING OF BRANDED PRESCRIPTION MEDICINES

2.1 This chapter sets out the high-level objectives that, in our opinion, should guide the design of a pricing scheme for branded prescription drugs. All the objectives are important although the first – short and long run efficiency – is fundamental, whereas the others could be considered instrumental to this fundamental aim. The high-level objectives are:

- economic efficiency in the short and long run
- workability
- appropriate allocation of risks
- transparency.

2.2 As will be discussed, a number of subsidiary goals fall under each of the high level objectives. In practice, designing a pricing scheme will involve trade offs between different goals.

Economic efficiency

2.3 We would regard achieving economic efficiency to be the most important objective of any drug pricing scheme. It captures the twin goals of delivering value for money for the NHS while providing the right incentives to companies to invest in drugs in the future. It is therefore central to the interests of patients in the short and long run.

2.4 This concept of short and long run efficiency is at the heart of stated objectives of the PPRS, which are to:

- 'secure the provision of safe and effective medicines for the NHS at reasonable prices'
- 'promote a strong and profitable pharmaceutical industry capable of such sustained research and development expenditure as should lead to the future availability of new and improved medicines'
- 'encourage the efficient and competitive development and supply of medicines to pharmaceutical markets in this and other countries.'

2.5 In the sections below we discuss in a little more detail the related notions of short run and dynamic efficiency, while Box 2.1 gives a more formal definition.

Short-run efficiency

2.6 Since health budgets are limited, a pricing scheme should aim to deliver value for money for the NHS - that is, to maximise benefits to patients from a given amount of expenditure. Through the application of cost effectiveness analysis, the concept of value for money can apply not just within therapeutic categories but across different
categories and between drugs and different healthcare interventions. Concepts of equity – that is, a fair allocation of resources – can also be accommodated within this broad notion of value for money.

2.7 Short run efficiency also embraces the goal of minimising costs for a given level of output. Box 2.1 considers some issues in relation to the costs incurred by companies. But equally relevant are the public sector costs of administration. A scheme should be designed to have proportional running costs and realistic personnel requirements. Other costs that must be weighed include the burden of compliance on industry and transitional costs, for example to implement any new legislation that might be needed. Chapter 6 and 7 of this annexe provide estimates of the implementation costs of our proposals.

Dynamic efficiency

2.8 Dynamic efficiency is achieved when prices give companies the right incentives for continued investment in drugs in the future. This means, for example, rewarding manufacturers more for developing innovative and effective products that make major improvements to patients’ lives than for developing drugs that add little to established standards of care.

2.9 The concept of patient value is therefore central to achieving dynamic as well as short run efficiency. Over the long run, value-reflective prices should encourage investment in the research and development that is most useful to society: into drugs for previously untreated conditions or ones that bring significant improvements over existing therapies.

2.10 The concept of dynamic efficiency is more important in the UK than the size of the UK market alone (some 4 per cent of global demand) would suggest. This is because many countries link the prices of products sold to their health systems to those obtaining in the UK. This is discussed further in the next chapter.

**Box 2.1: Economic efficiency in drug pricing – a more formal definition**

Economic efficiency is said to be achieved when:

- costs are efficiently incurred (productive efficiency)
- medicines are supplied to all patients for whom the benefit exceeds the marginal cost (allocative efficiency), and
- investment, including R&D, is up to the point where the present value of the total benefits to all patients (for whom the benefit exceeds the marginal cost) is greater than the present value of total costs (dynamic efficiency).

For the purposes of the current study, we are taking as given the international system of IPR recognition (notably the length of patents together with supplementary protection certificates for pharmaceuticals). If we do this, the correct signal for dynamic efficiency is given when a drug is supplied to all patients for whom its incremental benefit exceeds marginal costs, and price during the period of patent/SPC protection equals average incremental benefit across
those patients (compared to the nearest alternative). Under this condition, allocative efficiency also is achieved.

The above suggests three criteria for assessing the efficiency of pharmaceutical markets:

- whether costs are efficiently incurred
- whether prices, during the period of patent protection, are in line with average incremental therapeutic benefits, and
- whether drugs are supplied to all patients for whom the benefits exceed marginal cost (and no others).

Much of our concern in this annexe is with the second and third criteria. As regards the first criterion, a company generally has good incentives to control costs as long as its prices are not linked to its own costs (we refer to this in discussing incremental change to the PPRS since a binding profit control links prices to costs and gives poor incentives for cost control). There is also a question, however, as to whether current linear price structures give companies incentives to incur costs efficiently. We consider issues related to price structure in Chapter 3.

Workability

2.11 Any pricing scheme needs to be workable in practice. We have identified three dimensions of workability for a pricing scheme – that it be practicable within information constraints, maintain stability of supply and be legally defensible.

Practicable within information constraints

2.12 A theoretical scheme that is not practicable within information constraints would not be operational in practice. Information requirements can be high for all of the basic approaches to pricing set out in chapter 3 – international reference pricing, cost-based approaches and value-based pricing. We would argue, however, that, unlike the other two categories, the information required to implement value-based pricing is a prerequisite for ensuring rational and cost effective prescribing – whether or not a value-based approach to pricing is employed.

2.13 The information required by an ideal pricing regime may be highly detailed, potentially concerning the clinical benefits of drugs in different uses and patient groups. A well-designed scheme would rely only on information that is likely to be available in reality – but would not necessarily be limited to working with information that is available at present. The optimal scheme would give incentives to companies to provide the most revealing data achievable about the relative merits of their products. It would also be connected to the NHS closely enough to be able to exploit data generated by clinical practice.

Speed of access to market and uptake and stability of supply

2.14 To attain the goals already outlined a pricing scheme would require substantial inputs of information and, possibly, time to process all drugs equitably. But it is also in the
interests of patients and companies that patients have access to beneficial new drugs quickly at launch and that they be taken up by prescribers in indications for which the drug is cost effective. A workable arrangement would balance evaluation and access, and would manage the effects of uncertain evaluations on the uptake of new drugs.

2.15 A pricing scheme should also aim to ensure the stability of supply of drugs in the long run. Rapid fluctuations in access to certain products would be harmful to patients for whom switching to an alternative treatment might lead to undesirable side effects.

Legally defensible

2.16 An ideal pricing scheme should be legally defensible and thus avoid frequent litigation. Frequent litigation would be costly, lead to delays in decision-making and would create uncertainty both for manufacturers and the NHS. In addition, it would undermine public confidence in the system.

2.17 In particular, any pricing scheme in an EU member state must be compliant with EC legislation, including the EC Directive relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems (Directive 89/105/EEC the 'Transparency Directive')

2.18 In practice, as elaborated upon in Annexe G, the Transparency Directive is not prescriptive as to the particular form of a pricing scheme, but rather sets the high level principles to which it should adhere – in particular that pricing and reimbursement decisions should be made on the basis of ‘objective and verifiable criteria’2. It also imposes certain procedural requirements. Almost all the cases successfully brought under the Transparency Directive have related to a failure to keep within the prescribed time limits or to provide reasons for decisions.3

2.19 This objective could therefore be met by a wide variety of forms of pricing scheme, providing the institutions that implement them had robust and fair processes.

2 Of particular relevance in interpreting this requirement is UK (R (on the application of Pfizer Ltd.)) v. Secretary of State for Health [2003] 1CMLR 19 in which Court of Appeal was asked to consider the decision of the Secretary of State that Viagra was not to be reimbursed on the NHS. It was alleged that the decision to restrict the use of Viagra, on the basis not of clinical or cost effectiveness but rather on the Secretary of State’s assessing the need it addressed as having a lower priority than other calls on NHS funds, failed to contain a statement of reasons ‘based on objective and verifiable criteria’ as required by Article 7. Lord Justice Brown held on the contrary that, “For the criteria to be ‘verifiable’, all that is necessary is that they should be published and available, in particular to would-be importers, to satisfy themselves that they do not contain disguised restrictions on intra-Community trade. And the measures are ‘objective’, in the sense used by the Court in Duphar, if they are based on a legitimate aim, that of improving the economics of the state health system.”

3 Annexe G provides further details.
Appropriate allocation of risks

2.20 Both companies and public bodies have told us that stability is a very important attribute in a pricing scheme, in particular financial stability (for companies, stability or at least predictability of revenue and for Government, predictability of expenditure). In practice, this goal may be difficult to achieve when unforeseen events occur (such as the entry of a highly beneficial drug onto the market), calling for flexibility (that is, the ability to respond appropriately and rapidly to changing circumstances).

2.21 The design of a scheme must therefore recognise there is a trade off between stability and flexibility and that, in many cases, there is also a trade off between the degree of stability afforded to payers and that afforded to companies. Getting this balance right means allocating risks appropriately, which in our view implies that specific risks should be allocated to the entity most able to bear and manage them.

2.22 Therefore, companies should bear commercial and development risks, such as the risks relating to a product’s efficacy relative to those of substitutes, since this gives them good incentives to compete by investing in better products in the future. However, in a market in which there is considerable buyer power, it is optimal to insulate companies to the extent possible from opportunistic behaviour on the part of the payer since companies have little means of managing or responding to these risks, with the potential result, in the long run, that incentives to invest in useful products may be undermined.

2.23 Achieving the right balance is difficult in practice, since companies cannot be guaranteed revenues today for products the characteristics of which will only be known at some point in the future. Measures that can help include:

- transparency and clarity over the rules and principles to be applied to pricing decisions (possibly set out in guidance or a longer term framework contract)
- the creation of an independent institution to make pricing and reimbursement decisions in pursuance of objectives set out in statute
- more radical measures still, such as fixing a drugs budget and having it move over time according to exogenous parameters such as an inflation index.

2.24 The measures are all based on the idea that by constraining the discretion of the payer in some way, incentives to invest can be improved. While the first is a prerequisite for most successful pricing schemes, the latter two are more radical departures from the current regime and require greater scrutiny. We consider arguments for and against all these measures in Chapter 3.

Transparency

2.25 Transparency is important for a number of reasons.
First, it underpins all the other objectives set out here. Companies must understand
the risks to which they are exposed and the incentives that arise out of them to
respond efficiently to a well-designed scheme (notably to invest in drugs that society
values the most).

Second, to gain the support of stakeholders a scheme should not only work well but
be seen to work well. Companies, NHS bodies and patients should all be confident
that decisions are made on a fair and equitable basis, with the reasoning clearly set
out. The interests of the taxpayer should also be met in ensuring there is proper
accountability for the use of public resources.

Transparency is also important on an international level. As noted elsewhere in this
report, because R&D is a global fixed cost, individual countries have an incentive to
‘free ride’ on the expenditure of other countries, paying prices near to marginal cost
in the hope that high prices elsewhere will ensure companies continue to invest in
drugs. However, there is a danger that other countries will respond to such activities
by adopting the same approach, undermining the sustainability of investment in the
future. To avoid this outcome, it can be important for a payer not only to contribute
to global costs but also to be transparent about doing so, to send clear signals to
other countries to pay their fair share towards the cost of innovative new medicines.
As noted, UK prices have a particularly strong signalling effect internationally.

We note that complete transparency cannot always be achieved – for example, on
grounds of commercial sensitivity.

Conclusion

It will be noted that the objective of securing investment in the UK is not one of the
objectives considered here. This is because, as discussed in Annexe E, 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 legislation relating to the free
movement of goods and state aids. Further, Government has much more effective
instruments at its disposal for attracting investment into the UK, 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.

The objectives set out above should not be controversial in themselves, and indeed
are either explicit or implicit within the current stated objectives of the PPRS.
However, achieving them in practice involves difficult trade offs, and raises a number
of different issues that need addressed in designing a pricing scheme. These issues
are set out in the next chapter.
3 DESIGN ISSUES

3.1 To achieve the objectives outlined in Chapter 2 there a number of issues that any system for the pricing of branded prescription medicines would be called upon to address. We discuss five main design issues. Considering these issues separately from other features of pricing schemes helps organise the task of developing and assessing concrete options for reform of the PPRS.

3.2 Before considering the issues, we give a brief overview of different types of pricing and reimbursement arrangements around the world, drawing on the international case studies we conducted as part of this study. Each individual system represents a number of specific choices against the design issues discussed in this chapter. We briefly review alternative, non-value-based approaches to pricing, such as pricing in relation to costs and international reference pricing. Most systems, however, involve some notion of pricing in relation to therapeutic value. A very wide range of potential approaches fall under this umbrella, and a major focus of this annexe is to explore these different options.

3.3 The first design issue we consider is how to establish the value of a drug for pricing purposes. This is perhaps the most fundamental issue faced by a pricing scheme because obtaining value for money and giving manufacturers efficient dynamic incentives to invest in helpful drugs should be central aims of any rational drugs pricing policy – and both rely on being able to determine the clinical value of medicines. In considering how to assess therapeutic benefits in practice, we address a number of important issues, such as sources of information on therapeutic value, how to deal with the fact that value may differ by indication and subgroup and finally how to set prices in relation to therapeutic value.

3.4 A second design issue is the question of when to negotiate the prices of branded drugs, in particular whether to negotiate prices before drugs come on to the market (ex ante controls) or after a period of use (ex post controls). It is worth noting that this question influences decisions in relation to several of the other design issues. For instance, whether the assessment of therapeutic benefits occurs ex ante or ex post affects how it is feasible to conduct the assessment. There are major logistical issues around the data and time required to price drugs on the basis of therapeutic value. The challenge is to balance full consideration of all available data with getting beneficial new medicines to patients as quickly as possible. The choice between ex ante and ex post controls also affects the bargaining relationship between public payers and pharmaceutical manufacturers. This links to the fifth design principle, below.

3.5 A third design issue relates to the structure of prices, which can also have an important impact on achieving the ultimate objectives of a pricing scheme. Prices are currently linear. Changing this (through more complex tariffs and/or side payments) has the potential to improve incentives on both the demand and supply sides and hence to help deliver efficient outcomes. Also relevant are the international
implications of any change in price structure, through effects on parallel trade and international reference pricing.

3.6 The fourth design issue concerns the level of prices and budget setting. There are two basic approaches – either fixing the drugs budget in advance and letting prices be determined ex post or (more commonly) fixing prices in advance and letting the budget be determined ex post. Each approach has merits although logistical considerations often dictate that the latter approach is used.

3.7 The fifth and final design issue concerns institutional design and how pricing rules are interpreted and implemented in practice. To work well any system would depend on its institutions being technically competent and credible both within the NHS and in the eyes of industry. The system also needs to be underpinned by a balanced bargaining relationship that shares risks efficiently and equitably between companies and the NHS. This involves considering the range of instruments that could support the bargaining position of the payer, including statutory, contractual and reimbursement mechanisms.

Overview of different pricing schemes

3.8 This section briefly reviews alternative approaches to setting drug prices (often reimbursed prices) drawing on the international case studies conducted as part of this study. Each individual system represents a number of specific choices against the design issues discussed in this chapter. A summary overview of features of the systems we have reviewed is presented in Table 3.1 below.
Table 3.1: Overview of different drug pricing & reimbursement systems

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*non-innovative drugs  ** innovative drugs

IRP: International Reference Pricing
PVA: Price Volume Agreements

3.9 There is a lot of complexity in the pricing and reimbursement arrangements adopted by countries around the world, of which this table only provides a high level summary. For example, the US is a highly disaggregated system with many different payers (public and private) and intermediaries negotiating prices and reimbursement status. The table reflects the fact that, in almost all cases, there is some form of assessment and negotiation until the drug can be included on the formulary of reimbursable drugs.

3.10 Further, although the UK is one of the few countries in the world (along with Germany) not to impose an automatic requirement for a decision on price before a product is reimbursed this only applies to New Active Substances. Provisions for the pricing of non-New Active Substances are set out in the PPRS. Furthermore, bodies such as NICE and SMC increasingly conduct early reviews of drugs in order to provide guidance on their use to prescribers in the NHS. Another difference between the UK and other countries is the fact that many other countries have a system in which the reimbursed price can differ from the priced actually paid by patients.

3.11 For a detailed discussion of the systems summarised here, please see Annexe K. The UK system is described at length in Annexe A.

4 Free pricing takes place for all products except for non new-active substances.
Despite the complexity of different systems, it is possible to identify three basic approaches to setting the price (more commonly the reimbursed price) of pharmaceuticals:

- approaches based on international reference pricing
- cost–based approaches, and
- value-based approaches (a broad term comprising systems that set prices with respect to the price of substitute products or, if none is available, a placebo).

**International reference pricing**

International reference pricing (IRP) involves setting prices with reference to those set in other countries. Countries that use IRP as the sole approach to price setting effectively avoid taking an independent view on the appropriate prices of pharmaceuticals and rely entirely on the judgements of other countries. This might be a pragmatic solution for smaller countries, given the relatively high costs of carrying out independent assessments.

However, IRP involves a number of significant practical difficulties. First, it is often difficult to establish the prices that are actually paid in the countries referred to, given the extensive use of rebates in pricing and reimbursement systems. The approach also suffers from the numerous technical difficulties in making comparisons (such as those involved in selecting matching products — exact presentational matches or broader matching over the same active ingredient). These issues are discussed in Annexe F.

Even if these issues could be addressed, the use of IRP would not be a viable approach for the UK to adopt. This is because a significant number of countries already reference to the UK. We estimate that countries accounting for around 25 per cent of global demand reference the prices of some of their products to the UK. These countries are shown in the figure below.

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5 In practice, most countries use IRP as one of a range of measures to price setting or only use it for a limited range of drugs. Canada and France provide examples.

6 The Pharmaceutical Forum is currently considering how to improve the transparency of pricing and reimbursement data exchanged between Member States, partly in response to such concerns.
Furthermore, our international research has confirmed that UK prices are used in implicit price comparisons (that is, as part of company / country negotiations) even where they are not used in formal international reference price schemes.

Currently the UK, along with Germany, is one of the few major European countries that does not reference to other countries. Because the UK is a de-facto price leader in Europe we do not think it feasible to set prices here by international referencing since any attempt to do so would quickly render European prices circular. International reference pricing is therefore discounted from the following discussion of how to design an ideal pricing scheme for the UK.

**Cost and profit-based approaches**

An alternative approach is to seek to control the profitability of companies selling drugs to the public health system. The PPRS profit control is perhaps the only operational approach of this type in the world. While systems in Spain and Australia refer in principle to costs and profits as factors to be taken into account in deciding pricing and reimbursement, in neither country are these criteria used in practice.

In Annexe H we discuss at length the issues with attempting to regulate the profits of pharmaceutical companies. The principled concern we have with a system that attempts to remunerate on the basis of inputs (costs) is that there is little systematic
link between the costs and outputs of innovative activity in the pharmaceutical sector – through skill and ingenuity different firms will enjoy very different levels of success in producing useful drugs from a given level of expenditure on R&D. To these can be added practical difficulties, relating to the identification and allocation of costs, which arise primarily from the international nature of the industry.

3.20 However, some companies have suggested that some form of profit control should be retained, and that it could even be bolstered, to substitute for price cuts. Therefore we explore options for addressing the concerns above while retaining a cost-based scheme as part of our consideration of option one, as evaluated in Chapter 5.

**Value-based approaches**

3.21 As the table shows, most countries take some account of relative therapeutic benefits when setting the public reimbursement prices of branded prescription medicines. The approaches taken vary widely in terms of methodology and aims, however. There are three main approaches: reference pricing, therapeutic tendering and cost-effectiveness pricing, which we discuss in greater length in the next section, which discusses the first design issue: how to establish the value of a drug for pricing purposes.

**Design issue one: establishing the value of a drug for pricing purposes**

3.22 One of the most fundamental issues faced by any pricing scheme is **how to establish the value of a drug for pricing purposes**, as this is key to achieving the fundamental objectives of value for money and good dynamic incentives set out in Chapter 2.

**Basic concepts of therapeutic value**

3.23 Whatever the disease or circumstances of the individual case, the concept of therapeutic value captures the fundamental purpose of medicines: to extend patients’ lives and improve the quality of their lives.7

3.24 A wealth of knowledge exists on therapeutic value, particularly in the NHS. Drugs are licensed only after years of testing and are comprehensively monitored post-launch by pharmacovigilance programmes that generate further data about their effects and limitations. Increasingly, cost-effectiveness analysis is used to translate these effects into general (that is, non disease-specific) measures of patient value.

3.25 There are significant challenges, however. Different diseases have very diverse characteristics meaning that the clinical benefits of drugs might need to be assessed according to multiple standards. Patients’ circumstances can also complicate

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7 It is sometimes asserted that another fundamental purpose is – or should be - to improve the wellbeing of patients’ families, carers and society at large. This view is discussed below.
matters. Often patients suffer from more than one condition or may be subject to other factors (for example, genetic or environmental) that complicate treatment for the condition at hand, possibly confounding efforts to discern the effects of individual drugs. But these difficulties are not unique to a value-based approach to pricing. Addressing them is fundamental to ensuring rational and effective prescribing behaviour.

3.26 In the rest of this section, we discuss available sources of data on therapeutic value before considering how they can be used in pricing drugs.

**Data on the efficacy of drugs**

3.27 Therapeutic value can be measured and expressed in various ways. Data on the efficacy of drugs is generated either during studies conducted under controlled conditions or through day-to-day clinical practice. Such data provides direct evidence of therapeutic benefits but can also be further analysed to estimate effects on patients’ quality of life.

**Controlled conditions data**

3.28 Studies conducted under controlled conditions include clinical trials carried out as part of the licensing process for new drugs and subsequent studies published in learned journals. Such exercises usually provide statistical data on the efficacy of one or more drugs in some or all of their indications.

3.29 There are many design choices for controlled clinical studies, though the main type used in licensing and cost effectiveness analysis in the UK and most other countries are randomised controlled trials (RCTs). RCTs are considered a gold standard because they carefully isolate the effects of the treatment investigated from other factors. In an RCT patients are randomly allocated treatment or a comparator (for instance a placebo) to control for different initial circumstances which might affect outcomes. Patients are also monitored during treatment and follow-up to control for environmental factors that may have as much impact on outcomes as the drug.

3.30 In contrast to RCTs, another common approach is the observational study (used in epidemiology) that reports associations between the therapies given to participants and their health status, but without controlling for administration or follow-up. There are numerous other variants of study design such as cross-sectional surveys or individual case reports.

3.31 Even within the constraints of an RCT design choices arise, such as whether to compare a drug to a similar drug, some other alternative therapy or placebo (though

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8 Findings on a drug could be confounded if, for example, patients with relatively ‘bad’ initial circumstances (and less likely to improve) were systematically allocated treatment and patients with ‘good’ circumstances were systematically given a placebo.
it may not always be deemed ethical to withhold treatment from a control group).

Another option is over the endpoints to report, which might be intermediate or final. Some of these choices are taken up in Box 3.1.

**Box 3.1: Choices in the design of RCTs**

**Endpoints**

An intermediate endpoint is a laboratory marker or physical sign of the effect of a drug on a system in the body that is known to be affected by the condition treated. Final endpoints are clinical outcomes such as symptom control, survival, time to relapse or death.

The usefulness of intermediate versus final endpoints in determining the efficacy of a drug depends on the type of drug and disease investigated. To illustrate, for a drug used in a chronic condition a final endpoint might be patients’ or carers’ impressions of symptom control (for example in depression). In this case an intermediate endpoint (such as a reading of chemical activity in the brain) may reveal more about the efficacy of a drug than the potentially misleading subjective judgements that have to be made to inform final endpoints.9

In conditions where mortality is a major risk, however, (for example in cardiovascular disease) final endpoints are likely to offer more clarity. To illustrate with drugs that lower cholesterol (statins), the benefits of lower cholesterol on cardiovascular related mortality are well established but the exact causal mechanisms are still debated. The question of which endpoints are most informative often merits careful deliberation.

Well designed studies are rigorous about what can (or cannot) be inferred but even high-quality RCTs have their limitations – often due to constraints of time or money – and can be forced to make compromises. One such compromise is the use of ‘composite endpoints’, indicating that one of several outcomes occurred, which can be called for to increase the effective size of data samples to provide statistical power to an analysis.

**Choice of comparator**

As regards the choice of comparator, the most useful trials for assessing cost effectiveness evaluate a drug against one or more similar medicines (so-called ‘head-to-head’ studies). Clinicians need to know which of several broadly substitutable drugs is most appropriate for specific indications or patient groups encountered in the care of a condition. Head-to-head studies provide direct evidence of the relative qualities of drugs in specific contexts whereas two or more placebo-controlled trials can only provide a comparative picture when meta-analysed. But if there are any differences in trial design (for example in the initial circumstances of the patient cohorts or the follow-up methodologies employed) meaningful comparisons may be complicated.

**Patient group coverage**

It can be impractical or costly to recruit large enough cohorts of patients to give statistical power to all desirable analyses of a drug’s effects on patients with different circumstances. Hence it can take time before there are enough trials to collectively cover all major subgroups. This implies a role for an expert body in estimating and reconciling subgroup effects.

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9 This could be especially important when patients become habituated to their symptoms and inclined to dismiss them despite the seriousness of their underlying condition.
Data generated in clinical practice

3.32 An advantage of data generated in clinical practice is that over time it can be collected from potentially the entire population affected by a condition. It also offers valuable insights into how drugs are really used, and how efficacy is affected by uncontrollable everyday factors such as patient convenience and potential non-compliance with prescriptions. For many reasons the true worth of medicines may be different from what is implied under controlled conditions. A disadvantage of practice data, however, is that without experimental control biases may creep into the appraisal of drugs, for example when patients are in reality most affected by the comfort of being treated rather than the treatment itself (that is, placebo effects).

3.33 Therefore practice data may confuse the appraisal of drugs for conditions where endpoints are less clear, are more subjective, or where placebo effects are more important. In psychiatric or neurological conditions, for example, which can be very emotive, patients and carers are often thankful for any intervention even when the evidence on its real value is weak. Clinical practice data recording that patients ‘seem better’ – which may be the only outcome readily observable in busy primary care settings – might conceal placebo effects. In such cases, trials data collected under controlled conditions may be more insightful.

NHS bodies involved in the collection of data

3.34 It is important to note that, although there are significant informational challenges, many bodies in the NHS, the academic community and the pharmaceutical industry already meet them. For instance, the UK cost effectiveness bodies, NICE, SMC and AWMSG undertake a great deal of analysis of the clinical benefits of drugs to inform their decisions. In addition, many other initiatives and bodies exist in the NHS to inform clinicians and managers about the health and cost implications of drugs, such as at the National Electronic Library for Medicines and the National Prescribing Centre. Primary care organisations employ prescribing advisers to monitor the real effects of drugs on patients and local health economies and a number of groups based in academic centres and teaching hospitals review the evidence on medicines as it evolves. In principle the information generated by all of the above could be captured by a value-based pricing scheme.

Broader measures of patient benefit: QALYs

3.35 Data generated under experimental conditions or in clinical practice can be interpreted, using standard techniques, to provide more general measures of health gain, in terms of improvements to life expectancy or patient quality of life. In health economic evaluation, a popular measure of the therapeutic benefits delivered by drugs and other interventions is the Quality Adjusted Life Year (QALY). In the UK, NICE and SMC often use QALYs to assess the benefits of medicines and inform cost effectiveness decisions. QALYs are also used by many other pricing and cost effectiveness bodies around the world.
QALYs attempt to capture the effects of health interventions on patients’ length of life and quality of life in a single measure. Each year added to a patient’s life expectancy by an intervention can be worth up to one QALY. One QALY is a year in an unimpaired state. But a year spent in pain or discomfort, with impaired mobility, subject to anxiety or depression, or unable to undertake usual activities or self-care would be worth less than one QALY.

To determine the fraction of one QALY experienced by a patient during a year of impaired wellbeing, surveys of patients are carried out. A number of enterprises attempt to simplify the measurement of QALYs by providing pre-scored questionnaires for patients to complete. A widely used example is the EQ-5D framework maintained by EuroQol.\(^\text{10}\)

Annexe B provides a detailed discussion of QALYs, including how they are derived and used in cost effectiveness analysis. In short, as a measure that allows comparisons to be made of the cost effectiveness of treatments across different diseases, we believe QALYs are a key tool in securing value for money across the health economy.

We recognise that there are areas of keen debate over their use. Some companies feel, for example, that the QALY process is biased towards life saving drugs (that is, it is hard to demonstrate QALY gain in drugs which improve the quality of life for patients suffering from certain types of illness but do not increase their length of life). It should be noted, however, that where these issues do arise they often reflect fundamental problems of a lack of information (evidence that a drug does indeed improve a patient’s quality of life) rather than problems created by a particular methodological approach.

In the evaluations of NICE and SMC, QALYs typically form the basis of Incremental Cost Effectiveness Ratios (ICERs) used for determining the value for money of a new treatment relative to an appropriate comparator. This ratio takes the following general form:

\[
\text{ICER} = \frac{\text{Cost}_{\text{New drug}} - \text{Cost}_{\text{Comparator}}}{\text{Benefit}_{\text{New drug}} - \text{Benefit}_{\text{Comparator}}}
\]

If the ICER exceeds a certain cost per incremental QALY (typically in the £20,000 to £30,000 range) the treatment is generally not recommended to the NHS, except in exceptional circumstances.

\(^{10}\) See http://www.euroqol.org
Wider societal costs and benefits

3.42 QALYs were developed to provide a standard unit of measurement for the health benefits provided by drugs and other interventions to patients. But a current question in the debate on Health Technology Appraisal (HTA) is whether and how far to recognise the benefits provided by drugs to people other than those who take them – such as the carers or family of patients or society at large. Non-patient benefits include increased wellbeing and reduced burdens of care on individuals or the state.

3.43 When non-patient benefits are material one way to count them is to include them in the QALYs delivered by a drug and to think of QALYs as a broad measurement of ‘health output’. An alternative approach could be to focus on the non-patient costs saved by drugs as opposed to non-patient benefits delivered. Often costs and benefits are two sides of the same issue: for example, a carer benefit of ‘increased free time’ could be quantified as ‘lost earnings (potentially) recouped’. For this reason when both costs and benefits to non-patients are taken into account it is important to avoid double-counting.

3.44 There is some precedent for non-patient benefits being considered in the UK. NICE considered benefits to carers in its recent appraisal of drugs for Alzheimer’s.

Pricing on the basis of therapeutic value

3.45 Whether a drug is appraised under controlled conditions or in clinical practice, or its efficacy is expressed in some broader measure of health benefits such as QALYs, its therapeutic value can always be construed in either an absolute or a relative sense.

3.46 The absolute value of an effective drug may be high. Any drug that cures, manages or palliates a serious and widespread condition – improving people’s life expectancy and/or quality of life – is very useful to society, and as such has a high absolute value. A good example of a hugely valuable drug is aspirin, which still saves many thousands of lives per year in its applications in cardiovascular medicine and against life-threatening inflammations.

3.47 However, in competitive markets the price is not set equal to the value assigned to the product by all consumers (that is, the price beyond which they would not be willing to consume the product) but at some point below this, through the interaction of supply and demand. This is the case for generic pharmaceuticals, for example,

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11 Such an approach raises theoretical difficulties because the surveys used to derive health-state utilities (and hence QALYs from purely clinical data) are addressed to patients and not other parties affected by treatments. To have theoretically robust ‘social QALYs’ a new system might need to be designed, that would factor in the views of friends, family and government officials about what drugs achieve. Nonetheless, counting non-patient QALYs is a pragmatic approach.

12 The benefits to carers included information on carer psychological well-being from the General Health Questionnaire (GHQ-30). (Clinical and cost effectiveness of donepezil, rivastigmine and galantamine for Alzheimer’s disease, NICE Health Technology Appraisal TA091, Guidance on drugs for Alzheimer’s disease: HTA Report, 2001.)
such as aspirin, the price of which is set through competition between competing manufacturers.

3.48 The position is different for on-patent drugs, where IPR protection means there is only a single supplier and no generic competition. There may be a level of competition between broad therapeutic substitutes, however, and a range of different pricing approaches exist that differ in the extent to which they make use of this competition in setting prices. They are all based, to an extent, on the notion of relative therapeutic value (that is, value relative to a comparator).

**Different approaches to pricing on-patent brands**

3.49 There are three basic approaches to setting the (maximum) price of brands in relation to their relative value. These are:

- **Therapeutic group reference pricing.** This can mean setting a flat reimbursement price for all drugs with a similar chemical action, including drugs with differing relative efficacy. Germany has such an approach in some drug classes.

- **Therapeutic tendering.** Bids are invited to supply the public health service in a list of therapeutic areas. In each area one or two bids are accepted, according to an analysis of the efficacy, costs and logistics of each product. New Zealand is an example of a country that has experimented with therapeutic tendering.

- **Cost effectiveness pricing.** This method, used in Australia and elsewhere, involves setting the maximum price of a product at a level that ensures it does not exceed a given ICER relative to a substitute (typically a cost per incremental QALY).

3.50 The choice of approach – and the way in which they are implemented in practice – can have a major effect on extent to which value for money can be secured and incentives given to companies for investment in new and improved drugs for the future.

3.51 If it is based on flat pricing products with different clinical benefits, reference pricing will fail to reflect incremental value, with harmful short and long run effects. It should also be noted that reference pricing allows patients to pay a premium above the flat reimbursed price to choose the drug of their choice. Therefore efficiency properties depend in practice on the extent to which patients are aware of, and willing to make a co-payment reflecting, the benefits of the more effective drugs. Reference pricing is not currently implementable in the UK, which does not have a variable co-payment system.

3.52 Therapeutic tendering involves trying to increase the competitive pressures between broad substitute products by offering to reimburse only one (or a restricted number of products) and inviting companies to submit bids on price and other parameters to secure reimbursement. Effects depend on how the approach is implemented, including what relative weight is given to clinical and cost criteria.
3.53 In principle therapeutic tendering replicates the normal competitive processes of the market and a variety of different buyers (particularly in secondary care) use this approach in health systems around the world. In chapter 5 we consider the potential for more widespread use of therapeutic tendering at a local level in the UK to replace a national-level scheme. However, a potential concern relating to dynamic effects arises if this approach is used by a purchaser with considerable buyer power (such as a major national purchaser).

3.54 The concern arises because it is not unusual for drugs exploiting the same breakthrough in medical knowledge or technology to be in development at the same time. If companies knew that, through the action of a powerful buyer, the entry of a broadly comparable product onto the market at the same time as their own could mean that the price of their product would be driven down to the level little above production costs, they might conclude that it is not worth investing. The concern is greater in situations in which companies are able to ‘invent around’ the patents of other companies, since this would mean that there would be an active cost to being the first mover – incurring the bulk of the costs of R&D but seeing the value of that investment eroded quickly as follow on products entered the market.

3.55 In our view, pricing according to cost effectiveness offers the best potential for the right balance to be struck between long and short run efficiency.\textsuperscript{13} It does so by setting the maximum price in relation to an assessment of the incremental value of the therapeutic benefits of the drug – as set out in the discussion of QALYs above. The key question in conducting relative assessments that optimally recognise the short- and long-term value of new medicines is what type of products to compare them to.

Relative value and the choice of comparators

3.56 Typically, the relative value of a drug is understood by comparing it to similar drugs used to treat the same condition. But when no existing drug treatments exist – as is often the case for breakthrough products – value can be assessed relative to a next-best (perhaps non-drug) therapy or, if that is unavailable, relative to placebo. Comparing to placebo amounts to making an absolute assessment, which is reasonable where there is no existing treatment available.\textsuperscript{14} The choice of comparator may differ according to whether a new product is coming onto the market (during an ex ante review) or is considered as part of a group of products already on the market (ex post review).

\textsuperscript{13} Again, a key question is how diligently products are compared and how accurately improvements are recognised and rewarded in practice.

\textsuperscript{14} Where a comparator drug or non-drug therapy is used, it must itself be cost effective.
Assessment of new drugs

3.57 Where there are pharmaceutical substitutes, the maximum price of a new branded drug should be set to reflect its additional benefits over another branded drug (for the same or similar conditions) or over a generic. Companies would be permitted to price below this maximum.

3.58 The operation of such an approach is shown in the figure below. In the example, product A is assessed to deliver 1.5 QALYs more than the comparator for a given volume of treatment. This is used to establish a maximum price. In this example, the manufacturer of product A sets a price below this maximum threshold.

**Figure 3.2: Value-based premium**

![Graph showing value-based premium](image)

3.59 For the assessment of new drugs, the choice of comparator is relatively simple in principle – the drug in question should be compared against the best comparator product (whether brand, generic or non-drug treatment). This is in essence the approach currently adopted by NICE and SMC.

3.60 Where a new product chooses a price below the maximum threshold – as in the example above - we do not propose that the price of the existing comparator product should automatically be reduced. This is discussed further below.
Assessment of a group of drugs

3.61 Assessing a group of drugs at the same time makes the choice of comparator more difficult, as many bilateral comparisons are possible. However, it is important to note that where branded drugs are priced relative to other branded drugs, at least one branded price must be set in relation to a treatment the price of which is determined outside the system (such as a Category M generic, a non-drug treatment or a placebo).

3.62 This ‘exogenous’ price is an anchor to the entire system. It could either be used alone or in conjunction with the prices of other comparator brands in setting maximum prices during group reviews. These two approaches have different implications for short-run and dynamic competition and are discussed below.

Exogenous comparator sets price threshold

3.63 In principle the price of the exogenous comparator alone could be used to set the maximum price of all comparator products during ex post reviews. A scheme along these lines is set out in the box below.

Box 3.2: Example of an ex post value-based pricing scheme: exogenous comparator sets maximum price thresholds

The first step in the process is an evaluation of a class of drugs (assumed to consist of products A, B, C and D) by an independent cost effectiveness body, such as NICE. The evaluation is based on a suitable, exogenous comparator, which may be a Category M generic product, a non-drug based treatment or a placebo.

The cost effectiveness body evaluates the drugs’ therapeutic benefits (in QALYs) compared to the comparator. The possible outcome of such an evaluation is illustrated in the box on the right hand side of Figure 3.3a below: products A, B, C and D are assumed to produce 1.5, 1.3, 1.5 and 0.5 additional QALYs respectively over the comparator. This QALY difference is then translated into a maximum price for each drug using the price of the comparator drug (and the value of each QALY, the length of the treatment etc). In the diagram below, each manufacturer has set its price at the maximum threshold allowed by the exogenous comparator.

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15 A drug’s maximum price may also be increased in recognition of benefits not reflected in QALYs, for example from variety and/or delivery method, but this is not assumed in Figure 3.2a.
Figure 3.3a: Setting the maximum price of drugs using QALYs

If a manufacturer decides to set the price of its drug below the maximum threshold (for example at $p_c$ as opposed to $p_c'$), other products in the same class are not affected by this decision (see Figure 3.3b below).

Figure 3.3b: Effect of a brand price being reduced below maximum

Incremental benefits:
- product A = 1.5 QALY
- product B = 1.3 QALY
- product C = 1.5 QALY
- product D = 0.5 QALY

define price thresholds
However, if the comparator price is itself reduced, the maximum prices of all linked drugs are reduced as well. As illustrated in Figure 3.3c, a price change (from \(p_0\) to \(p'_0\)) of the comparator affects the maximum prices of all four products A, B, C and D.

**Figure 3.3c: Effect of the comparator drug price being reduced**

- **Incremental benefits:**
  - Product A = 1.5 QALY
  - Product B = 1.3 QALY
  - Product C = 1.5 QALY
  - Product D = 0.5 QALY
- **Define thresholds**

However, in the example, only products A, B, and D will be obliged to adjust their prices (compared to the position in Figure 3.3b). Product C’s price (in Figure 3.3b) is already within the maximum set by the cost effectiveness evaluation using the lower price of the comparator and does not have to be reduced.

**Prices of other brands set threshold**

3.64 The box above describes a system in which the maximum allowable prices of brands are based on incremental therapeutic value relative to the base comparator alone. The decision of one branded manufacturer to reduce its price below the maximum has no effect on the maximum prices allowed for other brands. An alternative approach would also be possible, in which the most cost effective brand at prevailing prices imposes an additional constraint on the prices of other brands. Where this is the case, however, we would argue that comparisons between branded drugs should take account of the order in which drugs are introduced to the market.

3.65 This can be illustrated with an example. Consider Drug A which is first to market and chooses to price at the maximum threshold – in this case a price of 50. Drug B is second to market, has the same therapeutic benefits (and hence has a maximum price of 50) but the manufacturer chooses to price it below A at 40. A third drug C, again with the same therapeutic benefits, enters the market after A and B. Its
maximum allowable price could either be set in relation to the maximum price of A and B (implying a maximum price of 50) or, alternatively, in relation to the actual price of B (implying a maximum price of 40).

3.66 The argument for the second option is that B is the more cost effective treatment and is arguably therefore the relevant comparator when considering pricing of Drug C. The example showing this option is illustrated in the diagram below, where Drug C is priced at its maximum allowable price of 40.

Figure 3.4: Prevailing brand prices impose additional price constraints

3.67 This approach delivers good value for money for the NHS, since it would ensure that relevant comparators are taken into account in setting maximum thresholds. We would argue, however, that the actual price of a brand should only impose a constraint on the prices of brands that succeed it onto the market.

3.68 If, alternatively, all brands within a group review would be constrained to have equal cost effectiveness, regardless of order of entry, this might have harmful effects in dynamic terms. As noted in Annexe A, follow-on brands sometimes enter the market at a discount to the originator, to gain market share. It would arguably be unreasonable to require a reduction in price of A (on the grounds that it is more

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16 This effect is likely to be relevant for drugs for which demand is price sensitive. As noted in Annexe A, this may particularly be the case for certain off-patent brands that enter the market in competition with originator brands (for products for which there is no Category M comparator).
expensive than B) because this could create a downward spiral: the actual price of B might be reduced to retain its advantage over A and consequently further reductions in A would be required. Such a downward spiral would not provide an appropriate reward to innovators. Alternatively, under a system in which the originator brand was constrained to respond in price terms to such entry, the initial impetus of the follow-on brand to enter at a discount might be dulled (in anticipation of this downwards spiral).

**Conclusion**

3.69 We believe the approach set out above – in which the price threshold for a brand is set through demonstrating incremental benefits relative to the exogenous comparator and further constrained by the price of brands that have preceded it onto the market – achieves the right balance between short and long run efficiency.

3.70 Pursuing the example in Figure 3.4 above, where there is a group of drugs with similar effects, once the patent on the first drug to market (A) had expired, generics would enter and a competitive market for A with much lower prices would be expected to develop. At this point, the maximum prices of the other drugs in the group (B and C) would be reset to ensure their use remained cost effective.

3.71 Consequently, drugs introduced earliest to the market would enjoy the longest period of high prices. Drugs introduced later to the market with no therapeutic advantages over the first drug would get a shorter period of high prices, but drugs with significant therapeutic advantages over the first drug would continue to get higher prices even after the patent expires on the first drug.

3.72 Assuming that generics prices rapidly decrease through competition between manufacturers (as they tend to in the UK under Category M) and that a brand in a market with generics would be awarded a price exceeding a benchmark generic only in proportion to the additional benefits delivered, a company could expect a high return only from bringing to market a significantly better new drug. By contrast, under current arrangements a brand offering no significant advantages in a mature market can continue to earn high returns so long as doctors can be persuaded to prescribe it by brand name.

3.73 The system would therefore give strong rewards for first in class products, by giving them the longest expected period of premium pricing. Unlike certain other systems in the world, however, it would not artificially penalise products that were developed simultaneously with the first in class drug, but arrived on the market marginally later. Products would, rather, be rewarded along a continuum: the closer to the first in class they were brought onto the market, the greater the rewards.

3.74 For companies considering entry several years after the first in class product (and where the chances are commensurately higher of inventing around existing patents), this system would give transparent and efficient signals to pursue research in other areas unless they can demonstrate benefits relative to existing treatments.
This system would also preserve incentives for brand competition during the patent period, allowing follow on brands to enter the market at a discount to the originator if they wished.

Generic comparators and the brand premium

Some companies have expressed to us the view that on-patent brands should not be compared against generics in considering cost effectiveness as this will reduce incentives to invest in new drugs. As explained above, we do not agree with this position. In our view, given the limited resources the NHS has at its disposal, it cannot afford, on grounds of both efficiency and fairness to patients, to ignore relevant comparators on the grounds that they are 'too cost effective'. If the best available treatment is a generic, then alternative treatments must demonstrate their benefits in relation to the generic to receive higher prices. In the long run, we agree this will have effects on incentives to invest, but we believe they will be entirely positive, encouraging companies to target areas of unmet clinical need. Companies are given at least 12 years notice of a product going off patent and should be able to target their development activities accordingly.

However, we recognise that in practice there may be merit in allowing for some difference between the price of a brand and its generic comparator (over and above that suggested by differences in the clinical benefits of the two). There are two reasons for this. First, different drugs may have differential benefits for certain types of patient in ways that have not been demonstrated in clinical trials and formal cost effectiveness analysis – for example because effects occur in subgroups that are too small to be considered significant in broad population trials. Second, it may be desirable to maintain some form of wedge between the price of a brand and a generic to encourage continued generic prescribing, thus producing volumes sufficient to sustain vibrant competition in generics markets. This wedge – which we call a 'brand premium' – is discussed in greater detail in the box below.

**Box 3.3: Brand premium**

It may be desirable to allow a price premium for a brand over a generic comparator even if no benefits of the former over the latter have been demonstrated. This price premium – which we call a 'brand premium' – can be motivated on two counts: to capture potential benefits to patients that have not been demonstrated formally in trials and to encourage sustained generic prescribing.

Our understanding of this view is that it relates particularly to existing on patent brands. It appears to be broadly accepted that new brands must demonstrate cost effectiveness relative to appropriate comparators, whether generics or brands. The concern relates more to the principle that products that are already on the market should have to demonstrate cost effectiveness when a substitute goes off patent. As noted elsewhere in this report, we believe there is an asymmetry in current arrangements – existing products are not always subject to the same constraints as new products. But this asymmetry is not in the interests of patients or of innovative companies and hence, in our view, is not sustainable in the long run.
In relation to the first motivation, the highest-grade evidence on medicines is provided by randomised controlled trials (RCTs) that control strictly for factors other than an investigated product that might explain observed therapeutic effects. To have statistical power RCTs need to be large – and potentially expensive and time-consuming. In some cases, an RCT may show no significant difference between two products when used in large populations, but individual patients may not tolerate one whilst thriving on another.

If an on-patent brand offers potential but unproven benefits beyond a comparator product available generically it may be appropriate to negotiate a brand premium. Any such premium would need to be proportionate, recognising that benefits have not been demonstrated, but are merely plausible. Later in this discussion – and also in Annexe M of this report that quantifies some of the potential benefits of value-based reforms to the PPRS – we suggest that a premium of 50 per cent over the cost of comparable generics might be applied to a number of on-patent branded drugs. This practice has been used in other countries – for example, in its reviews of therapeutic groups, the Swedish pricing authority LFN has allowed for a premium of 25 per cent between clinically equivalent products (such as the PPIs) to reflect the benefits of having a variety of products on the market.

In relation to the second motivation, if a brand with potential but unproven benefits over a comparator generic were priced at parity with that comparator, clinicians may switch prescribing to the brand in large volumes – possibly even larger than strictly required for medical reasons, for example due to clinical conservatism or marketing activities. Because UK generics markets currently work well, and because generics prices are the most appropriate anchor for the prices of branded drugs, it is important not to destabilise them. Applying a premium to brands should help to sustain generic prescribing and generic entry.

A further motivation for recognising possible but unproven value in this way is to secure continued supply, which brand manufacturers might withhold if a pricing regime insisted on pricing brands at the level of equivalent generics. In practice, the level of the wedge would likely be negotiated by the relevant pricing authority and possibly informed by the views of the relevant cost effectiveness body concerning the plausibility of potential therapeutic benefits of the brand. This implies that the brand premium for an off-patent brand in relation to its generic equivalent (with the same active substance) would be lower – the only motivation for the premium at all is generic market stability.

3.78 The operation of the brand premium is shown in the diagram below. In the example, product C is considered to deliver the same benefits as the generic comparator but may still price up to a maximum price of the generic comparator plus the brand premium.
For ease of exposition, this discussion has so far referred to therapeutic value as if it were fixed for a given drug. In practice, it may be greater or lesser in different indications and patient subgroups. For example, a drug could be the most effective chemical in its class for most patients but unacceptably dangerous in patients with other conditions or in combination with certain other medicines. Or it could be usually less effective than some alternative but the alternative may have no effect in some genetic types where the drug in question does.

Several drugs exhibiting varying cost effectiveness are examined in detail in Annexe M of this report, which explores the efficacy of some widely used drugs in their different applications.

Value that varies by indication and subgroup can have a number of implications for cost effectiveness assessment and value-based pricing that depends on it. QALYs can still be used to measure the benefits of a drug in each of its different indications and across subgroups. However, it is not possible to pay companies a different price for each indication and subgroup since data on prescribing against these characteristics are not currently available.

One solution is to set a single maximum price for the drug that ensured that it fell below the relevant cost effectiveness threshold in all licensed indications and subgroups. A second approach is to allow a price that would leave the drug cost ineffective in certain indications and issue guidance to prescribers on the cost effective use of the drug. This is the role currently played by NICE (which, as noted,
is not empowered to negotiate on price). A further solution is to negotiate non-linear price structures, including price-volume agreements and rebates, which seek to ensure that in aggregate the NHS secures value for money from the use of the drug. This latter option is considered in greater detail in a section later in this chapter, which considers options for reform of the structure of prices.

3.83 We do not regard these solutions as mutually exclusive. Indeed, in our view any value-based approach to pricing needs to be supplemented with guidance to prescribers, which provides far richer information on the appropriate use of the drug than price alone can. Accordingly, the different options for value-based pricing we consider in Chapter 5 all incorporate the use of guidance and, where appropriate, the option for non-linear price structures.

**Whether to recognise innovation per se**

3.84 The discussion in this section has been concerned with how pricing schemes should recognise the health benefits delivered by branded drugs. We have argued that prices recognising improvements in patients’ lives provide manufacturers with socially efficient dynamic incentives.

3.85 But some have suggested that a pricing system should also reward stages in the innovative process – ‘innovation in itself’ – over and above clinically beneficial outcomes. In practice, this would mean that a pricing scheme would recognise, in prices, any drug representing a technological innovation (for example by pioneering the pharmacological mechanism) even if it were ultimately ineffective (or at least no more effective than alternatives) and subsequent technological leaps were required before a clinically useful product could be achievable.

3.86 Such arguments – which were touched on above – hold that the development of the first product creates strong externalities (benefits accruing to other firms who build on the initial innovation). Since not all the benefits accrue to the original developer, they may be a role for state support.

3.87 However, it is unlikely to be possible to define any meaningful pricing system that could address this problem. Such a system would call for a great number of discretionary awards based on suppositions about companies’ chances of success against many – potentially esoteric – scientific challenges with no clinical outcomes. In our view, it would therefore not only be inefficient for the NHS to spend money on ineffective drugs that could be allocated to fund proven medicines for patients with other conditions, it would also fail to provide transparent, clear investment incentives to companies.

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18 The following arguments can also apply to other aspects of pharmaceutical innovation. For example, research into new delivery mechanisms or storage solutions for drugs can be very valuable over time but may be trial and error.
3.88 The scheme we set out above would partly address concerns about investment externalities, since it would give the longest period of premium prices to the first in class product, with follow-on products, which have benefited from the original innovation, receiving a shorter period of premium payments. But it would do so solely on the basis of benefits to patients, not discretionary assessments of technological advance.

3.89 An argument that has been expressed to us against this position is that often benefits to patients are not clear when a drug comes onto the market but may be apparent after years of use. According to this argument it is better to pay a premium price in advance, given the possibility that a product will subsequently turn out to be useful. We do not agree with this position. Paying a premium price for a product that has not demonstrated benefits does not give companies the correct incentives to invest in the most useful drugs. Furthermore, it gives companies no incentives to provide the information on clinical benefits that are a prerequisite for efficient prescribing behaviour.

3.90 We do recognise that there are some drugs for which, due to the nature of the disease they treat, it is difficult to provide comprehensive information on clinical benefits at the time of launch. As explained in the next section, we believe this is a strong argument in favour of conducting ex post reviews of clinical effectiveness, once the drug is already on the market. It may also be an argument for agreeing risk sharing agreements where there are plausible but unproven benefits. But in our view this is not an argument for ignoring value to patients when considering the appropriate price of a drug.

3.91 In relation to extreme examples of externalities, we believe science policy is better suited than a pricing scheme to tackling such problems. For example, very basic research the benefits of which cannot be appropriated through formal IPRs is best directly funded through university centres, directly funded research groups and the like.

Conclusion

3.92 There are several approaches to assessing the value of drugs for the purposes of setting maximum prices. Of these, we think an approach based on cost effectiveness assessment offers the best means of obtaining value for money and giving adequate rewards to investment.

3.93 We would recommend imposing maximum prices based on the incremental cost effectiveness of a product relative to a comparator for both individual and group reviews. The specific approach we have set out would give strong rewards for first in class products, by giving them the longest expected period of premium pricing, without artificially penalising products that arrive on the market marginally later. The system would also preserve incentives for brand competition.
Key to the positive dynamic effects of this system is the fact that generics can be used as relevant comparators in both ex ante and ex post assessments: for companies considering entry several years after the first in class product, this would give transparent and efficient signals to pursue research in other areas unless they can demonstrate benefits relative to existing treatments.

We recognise that the principle of comparing existing treatments to cost effective generics will be controversial for some companies. However, given the limited resources at the NHS’s disposal, it inevitably has to restrict access to treatments, and is increasingly doing so for new, innovative drugs that are expensive but nonetheless valuable to patients. In this context, systematically turning a blind eye to major inefficiencies in current expenditure is neither in the interests of patients or of innovative companies. Nor in our view, is it a sustainable policy in the long run.

In relation to the cost effectiveness assessments used to inform price setting, we are sympathetic with company views that account should be taken of non-patient benefits. We do not agree, however, with the proposition that innovation per se (irrespective of patient benefits) should be an important factor in pricing a drug.

When to negotiate the prices of branded drugs

The prices of drugs can be negotiated before they come on to the market (that is, as a prerequisite for obtaining reimbursement status) or after they are already being prescribed. We call the former type of arrangements 'ex ante' controls and the latter 'ex post' controls.

Ex ante assessment and pricing methodologies employed around the world include:

- cost effectiveness pricing (for example in Australia)
- therapeutic group reference pricing (used in Germany and elsewhere)
- international reference pricing (used by many countries in Europe)
- therapeutic tendering (for example in New Zealand)
- price-volume agreements or rebates (for example in Germany, France and Australia).

Such methodologies were discussed in principle above and a detailed account of how they are applied in practice in the countries mentioned appears at Annexe K, which reports on the OFT’s case studies of health systems abroad.

Many countries also employ ex post controls to set or review the prices of branded drugs. Any of the above approaches can be used on an ex post basis. In addition, ex post approaches include:

- across-the-board price cuts (in France, Spain, the Netherlands and the UK)
- systematic reviews of the cost effectiveness of drugs (for instance in Sweden).
3.101 The examples given are also covered in Annexe K. Both ex ante and ex post controls can be negotiated for individual products (often the case for price-volume agreements), at the level of therapeutic classes (by definition for therapeutic group reference pricing) or from both perspectives. Some recourse to therapeutic classes is particularly common, with countries often taking a view of the cost effectiveness of drugs, or linking their prices to other drugs, within the same group of therapeutic substitutes.

3.102 The UK has a relatively liberal regime ex ante (only the prices of non New Active Substances need to be approved up front), with the most significant controls (the price cuts) applied ex post. Most other countries tend to adopt a range of ex ante and ex post measures. This section considers the relative merits of ex ante and ex post controls under four headings:

- efficiency
- informational requirements
- access and uptake, and
- effect on bargaining relationships.

**Efficiency**

3.103 If the pricing control in question helps improve short and long run efficiency, then a straightforward argument in favour of ex ante controls is that they ensure these benefits are delivered at an earlier stage in a product’s commercialisation. Similarly, arguments in favour of ex post controls are that they allow subsequent factors affecting cost effectiveness to be taken into account (such as the genericisation of substitute products).

3.104 In principle, therefore, controls that improve efficiency should be applied both ex ante and ex post in the interests of ensuring that value for money is secured and companies have the right incentives to invest. The frequency and extent of such controls should, of course, depend on the costs of conducting reviews and the informational requirements, as discussed below.

**Informational requirements**

3.105 Much of the information that is required to assess the relative therapeutic value of drugs accurately may already be available for each product at the time of its launch. For certain types of drugs, however, there may be gaps in information which can be filled over time.

3.106 Randomised controlled trials that evaluate drugs in specific indications are always available from launch since they are required for Phase III clinical assessments during the licensing process. Whether they provide sufficient information to support a view on cost effectiveness depends partly on the design of the trial and partly on the nature of the condition the drug is designed to treat.
Acute vs. chronic conditions

3.107 It is likely to be easier to demonstrate efficacy robustly at the time of launch for drugs for acute conditions with clear final end points. For such conditions efficacy can be shown over a shorter period of time, and so should be demonstrable through Phase III trials.

3.108 In contrast, for chronic conditions, relative efficacy can only be demonstrated over a longer period of time, with the result that there may be insufficient data at the time of launch to take an informed view on cost effectiveness. This would suggest use of some form of ex post assessment of efficacy, or possibly a hybrid, risk-sharing approach. This would require the company and payer to agree a contract in which the drug is reimbursed, contingent on claims of clinical effectiveness being realised in practice. This would be assessed through information on the use of the drug in clinical practice. If expected outcomes are not realised, prices would be changed and/or repayments made. This is discussed in greater detail in Chapter 5.

Trial design

3.109 Head-to-head studies, though particularly useful for assessing cost effectiveness, are sometimes not provided by manufacturers at launch and may appear only in the years following launch as academic groups are funded to conduct them. In major disease areas, head-to-head studies can be published at a rate to cover most interesting comparisons of drugs within five to ten years (a good example is the statins for the prevention of cardiovascular disease).

3.110 Though this might seem to be an argument in favour of delaying assessment until such studies are produced, it is important that any pricing scheme give the correct incentives to manufacturers to produce evidence of cost effectiveness up front. Achieving the right balance of incentives is discussed as part of the consideration of Option 3 in Chapter 5. This issue is also addressed through recommendations of the recent Cooksey Review.

Access and uptake

3.111 Ex ante and ex post controls each face particular challenges in terms of allowing access to the market and improving uptake of drugs.

3.112 A criticism often made of ex ante controls is that they can delay market access for new products at launch, harming both patients and manufacturers. Some countries that conduct thoroughgoing analysis to price drugs ex ante, such as France, experience protracted negotiations between government and product sponsors – especially when parties cannot agree on a price – before new products are listed for

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19 The FDA has traditionally expressed a preference for placebo-controlled trials.
20 Chapter 6 contains a discussion of recommendations coming out of the Cooksey review.
reimbursement. By contrast the UK, which does not enter material negotiations over prices ex ante for New Active Substances, is a fast-launch country.

3.113 However, it is not clear that launch delays must inevitably follow from ex ante controls of the prices or acceptable uses of new prescription medicines. Again looking to the experience of the UK, the Single Technology Appraisal of the cost effectiveness of new drugs conducted by NICE in England is a comprehensive exercise that can nonetheless be completed within a few weeks of licensing so as to incur minimal delay once a new drug is launched. SMC in Scotland also provides rapid assessments of all new drugs and formulations for listing purposes.

3.114 For some types of drugs there is also evidence that positive ex ante assessments can improve uptake. This is taken up in the box below.

Box 3.4: Ex ante pricing and uptake

Depending on the attitudes of manufacturers and payers, assessments of therapeutic value and price negotiations for new drugs at launch can be slow, delaying patients’ access to new treatments. This is sometimes claimed to be the principal disadvantage of ex ante controls. But, empirically, systems that employ no ex ante controls and allow entirely free launch pricing can experience delays in uptake.

Absent any ex ante assessment, public health services may be sceptical of the efficacy and in particular the cost effectiveness of a new drug. This can limit uptake, either pending a formal ex post assessment by an official body (such as NICE) or until the health service acquires confidence in the new drug following gradual uptake by specialists.

The OFT has conducted case studies of ten countries (presented in Annexe K of this report) including the major European markets, the US, Canada and Australia. Alongside the UK, only one of the countries we visited – Germany – does not apply ex ante controls for New Active Substances. All others undertake some comparative evaluation of new drugs with therapeutic substitutes before launch (the US is no exception, with PBMs rigorously assessing the clinical benefits of a drug before deciding on formulary listing).

But in both the UK and Germany, prescribing of new drugs by public health services is the slowest among major markets, suggesting that in the absence of an ex ante view on cost effectiveness of prices uptake can indeed be slow.

Evidence of this effect can be found in numerous sources. One is the latest set of performance indicators published by the Pharmaceutical Industry Competitiveness Task Force (PICTF). One recent PICTF indicator\(^\text{21}\) shows the percentage (by value) of the pharmaceuticals markets of ten leading countries accounted for by all products launched within each of the six years to (and including) 2004. The UK has the lowest share of products of each vintage of all countries monitored except Japan.\(^\text{22}\) Germany also has relatively low shares of new products, compared to markets such as Spain, Switzerland,

\(^{21}\)\(2005\) Indicators (latest, published February 2006) Indicator 19, see http://www.advisorybodies.doh.gov.uk/pictf/publications.htm
\(^{22}\) France shows a fractionally lower share of drugs launched in 1998 in all prescribing than the UK.
Further comparative evidence of slow uptake can be found in a recent working paper by Berndt and Danzon. The authors investigate the promotion, use and market shares of new medicines in three broad classes – antihypertensives, antidepressants and antiepileptics – in fifteen countries including the UK over the period 1992 to (end) 2003. Germany and the UK are never ranked above the middle tertile of adopters in any of the three therapeutic classes. Germany is ranked a slow adopter in two (antihypertensives and antidepressants) and a middling adopter in one (antiepileptics). The UK is ranked a slow adopter in one (antihypertensives) and a middling adopter in the other two classes.

It must be noted that these are fairly simplistic comparisons, however, since not all new medicines are cost effective, meaning that there may be good reasons for low uptake in any individual case. Furthermore, low uptake is doubtless a function of other factors peculiar to individual countries, such as prescriber conservatism.

More compelling evidence of the effect of assessments on the uptake of cost effective medicines comes from within the UK where, as discussed in Annexe B, positive NICE guidance often leads to an increase in prescribing.

Effect on bargaining position

3.115 Perhaps the most compelling argument – from the payer’s point of view – for applying some form of ex ante assessment is that failing to do so may significantly undermine the buyer’s bargaining position, creating risks of non-compliance for a pricing authority.

3.116 The ultimate sanction for any payer in negotiating prices is to withhold reimbursement. But any threat to do so is less credible once a drug is on the market, due to patient habituation and political concerns. This fact might lend negotiating power to companies operating under a scheme where prices would be relatively free at launch but subject to later revision. There are potential solutions to such risks – both institutional and contractual – that are set out in at the end of this chapter.

Conclusion

3.117 In the light of the issues encountered by both ex ante and ex post controls, we believe an optimal drug pricing scheme would attempt to combine them in some way, as do a number of countries around the world today (for example Australia and France, as mentioned above and detailed in Annexe K, which describes pricing and reimbursement arrangements in ten countries). An optimal scheme would also give incentives to manufacturers to help address the informational challenges of evaluating drugs by providing the best data they could, which would include more directly revealing head-to-head studies between comparable products. One possibility

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would be to structure the terms of scheme to recognise efforts made by companies to provide insightful data.

3.118 Both ex ante and ex post approaches are possibilities we consider in our options for reform of the PPRS, set out in Chapter 5.

**The structure of prices**

3.119 Currently, prices for reimbursing drugs in primary care are linear across volumes prescribed. That is, if the one pack of drugs of a given form and strength is reimbursed at £1, 1,000 packs of the same drug at the same form and strength will be reimbursed at a total cost of £1,000.\(^\text{24}\)

3.120 In the pharmaceutical sector, linear pricing may not be efficient on two counts:

- pharmaceutical company costs are not linear across volumes supplied, and
- the value drugs bring to the NHS is often not linear across volumes prescribed.

3.121 In this section we consider each of these issues in turn before assessing the potential benefits of non-linear price structures. These benefits include improvements in short run efficiency, through better alignment of the interests of the NHS and companies, and the reduction of socially wasteful expenditure. Non-linear pricing can also improve long run efficiency, particularly given the potential for parallel trade both within and across countries, through ensuring rents are shared exclusively between companies and public purchasers and allowing price differences to be maintained between countries with different abilities to pay for drugs.

**Non-linear costs**

3.122 Annexe D reviews the available evidence on the cost structure of the pharmaceutical industry. As discussed there, costs can be broken down into:

- 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).

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\(^{24}\) It is not the case that prices are always linear in strengths (sometimes different strengths of the same drug will be flat priced). Nor are prices likely to be linear across volumes in secondary care, where, as described in Annexe A, procurement arrangements can secure price / volume deals.
3.123 While the cost structure will vary for different drugs and different types of technology, a high proportion of the costs of the costs of producing most drugs fall into the first two categories.25

3.124 There is an extensive economics literature on the problems high fixed costs create for efficient pricing. The key question is how to recover fixed costs from consumers while minimising distortions to consumption (that is, while still allowing mutually beneficial trades – those for which marginal benefit to the consumer exceeds marginal cost to the firm – to take place). In general, complex tariffs are better able to reduce these distortions than linear tariffs.26

3.125 A complex tariff prevalent in many industries with high fixed costs – such as the utilities sectors - is the two-part tariff. Under a two-part tariff applied to pharmaceutical pricing, the total price of a drug could be broken down into a fixed component and a variable component reflecting the variable costs of supplying the drug. The fixed component could be set at a level to reflect the expected value of the drug to the NHS.

3.126 Such an approach may be beneficial where prescribers are price sensitive, since it would help improve uptake of drugs. However, prescribers in primary care do not seem to be consistently aware of or sensitive to drug prices.27 This is the finding of the survey of 1,000 GPs conducted jointly by the OFT and the National Audit Office, presented in Annex C. This would imply that the benefits of non linear pricing in terms of increasing consumption might be less apparent in pharmaceuticals markets than in certain other sectors of the economy that are also characterised by a high proportion of fixed costs, but in which demand is more price sensitive.

Non-linear value – variation by indication and subgroup

3.127 There is another, more important, argument in favour of complex price structures for pharmaceuticals: the fact that the value drugs bring to patients and the broader NHS is itself often not linear across volumes prescribed.

3.128 As noted earlier in this chapter, therapeutic value can vary significantly across different indications and patient groups. For example, a drug could be the most effective chemical in its class for most people but unacceptably dangerous in patients with other conditions or in combination with certain other medicines. Or it could be usually less effective than some alternative but the alternative may have no effect in

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25 As discussed in Annexe D, a broad brush estimate of the cost structure of the pharmaceutical industry suggests that about 65 per cent of economic costs are internationally mobile (40 per cent R&D and 25 per cent manufacturing) and 35 per cent national in scope.

26 In the economics literature, these distortions are known as 'deadweight loss'. The linear tariff that minimises deadweight loss implements an approach known as ‘Ramsey pricing’ and is considered below under the discussion of parallel trade issues.

27 Hospitals, however, seem to be more price sensitive, though prescribing in secondary care represents only 25 per cent of the total. This is discussed further in Annexe A on competition in the NHS.
some genetic types where the drug does. Or a drug could have sufficiently harmful side-effects in all patients that it is only recommended in high-risk cases. A number of such issues are examined in detail in Annexe M of this report, which explores the efficacy of some widely used drugs in their different applications.

3.129 To take a concrete example, in Annexe M we investigate the angiotensin II receptor antagonists (A2RAs), which are a class of antihypertensive drug. There is a broad consensus of clinical opinion that for 90 to 95 per cent of patients A2RAs are no more effective than any chemical in a similar class – the angiotensin converting enzyme (ACE) inhibitors – all of which are available generically at much lower prices than any A2RA.

3.130 However, for around five per cent of cases ACE inhibitors cause an irritating dry cough that can lead patients to discontinue treatment, in which case A2RAs, which do not cause the cough, are clearly preferable. A non-linear pricing schedule for A2RAs could apply a price no greater than the best ACE inhibitor for 90 per cent of prescribing but a premium price for ten per cent of total annual volumes. Uncalled-for prescribing of A2RAs would then impose no extra financial burden on the NHS. Annexe M gives further examples of drugs for which cost effectiveness is likely to differ significantly by indication and subgroup, such as clopidogrel, an antiplatelet drug.

3.131 Non-linear pricing may be appropriate for A2RAs and clopidogrel because they are one of a number of areas that may be subject to 'indication drift', that is, over-prescribing beyond their cost effective uses. Busy GPs can sometimes be persuaded by marketing to prescribe medicines for indications for which they may not be cost effective, since they have neither the time nor the resources to appraise volumes of evidence on every drug. Further, as shown in Annexes A and C, GPs do not have strong incentives to take account of the costs of prescribing decisions and are, perhaps as a result, not generally aware of the price of the drug they prescribe.

3.132 Since the benefits of drugs are not constant over all volumes dispensed, non-linear price structures could help improve value for money for certain drugs, by ensuring that premium prices are paid only on prescribing volumes that are likely to be clinically relevant.

3.133 For many drugs, non-linear prices could also reduce incentives to incur socially inefficient marketing expenditure. Under current linear prices, there can be very high returns to marketing because the marginal cost of products is typically low and marginal revenues are constant. This can give very strong incentives for companies to market products outside of their cost effective indications. Because large firms can employ thousands in their sales forces, the marginal cost of promoting one drug in a broad portfolio to a receptive GP can be low – but the potential gains from a linear pricing structure far outweigh them.

3.134 Concern is often expressed within the NHS about the amount of money pharmaceutical companies spend on marketing their products. The sums involved are
certainly considerable: in 2004, companies that submitted an Annual Financial Return (AFR) spent a total of £850 million on marketing and sales promotion in the UK (16 per cent of total drug sales value). In response various stakeholders have called for an increase in NHS expenditure on so-called ‘counter-marketing’, for example, the advice given by prescribing advisers to GPs on the cost effectiveness of medicines.

3.135 Others have called for measures directly to curb marketing expenditure by pharmaceutical companies. Yet all these approaches fail to address the root cause of high levels of marketing expenditure: the fact that linear prices give companies very strong incentives to maximise volumes, beyond the point at which prescribing is likely to be cost effective for the NHS.

3.136 Companies are simply responding to the financial incentives they are being given. If the NHS wants to reduce potentially wasteful expenditure, it should give much better incentives to companies, through the prices it is prepared to pay for drugs, to engage in activities that contribute to NHS productivity. This should in turn generate cost efficiencies for the companies concerned.

Possible non-linear price structures

3.137 In principle, it would be possible to implement non-linear pricing by reimbursing pharmacies at different prices for dispensing drugs against different indications and for different patient subgroups. To be implementable, this approach would, however, require the availability of prescribing data broken down by indication and patient group. The provision of prescribing data by indication is one of the objectives of the ongoing NHS National Program for IT (NPfIT) and may arrive within five years. Disaggregated data may arrive sooner in Scotland through the Community Health Index (CHI). Such disaggregated prescription data are not currently available, however, and so this approach is not a viable short term option.

3.138 In the absence of such information, it would be necessary to estimate up front annual prescription volumes for given indications and patient subgroups for which cost effectiveness is likely to differ and then apply different prices to given prescribing volumes accordingly. For example, if a drug was found to be more effective than a comparator in only one indication, and the upper bound estimate of prescriptions against that indication was 10,000 packs of a given strength per year, a premium price would apply to volumes up to 10,000 and a price in line with the comparator for volumes in excess of that.

3.139 We recognise that estimates of relevant volumes would be challenging to produce up front. Companies must therefore be given appropriate incentives and support to demonstrate the cost effectiveness of drugs in different indications and subgroups. Value-based pricing would provide those incentives. The support companies would require has been discussed in the Treasury’s Cooksey Review, and is taken up further in Chapter 6.
3.140 We also recognise that under a volume-based approach to non-linear pricing there would be no guarantee that the drug would always be prescribed in the most cost effective indications. Guidance to prescribers will therefore remain an important part of any revised pricing arrangements. The object of non-linear pricing is, rather, to remove the systematic incentive companies are given under current price structures to encourage prescribers to maximise volumes prescribed, beyond those indications for which the drug is cost effective. In turn this would help companies reduce expenditure on marketing activities and reallocate a proportion of these savings to demonstrating the cost effectiveness of drugs.

3.141 There are two options for implementing volume-based approaches to nonlinear pricing:

- negotiate price volume agreements, whereby the reimbursement price changes after a certain volume of prescriptions is exceeded;
- negotiate rebate arrangements, whereby a payment is made between companies and payers after a certain volume of prescriptions is exceeded.

3.142 The difference between the first and second options – price volume agreements and rebates – is that under the first, the price would change after the relevant volumes had been exceeded whereas under the second the price would be unchanged but a rebate would be made between the company and the payer (in practice likely to be DH, but this could be credited to PCTs on a pro rata basis).

3.143 As discussed in Annexe K, many countries employ approaches of this type, such as France, Australia and the US. Indeed, there is a precedent for rebate-type arrangements in the UK. Companies are able, for example to make a payment to DH in lieu of implementing the periodic price cuts negotiated through the scheme.

3.144 We think the second option – rebate arrangements - would be the most tractable and is therefore to be preferred.\(^28\) This is because applying different reimbursement prices for the same product (form, pack size and strength) would create significant difficulties in the supply chain. It would not be clear, for example, at what price a manufacturer should sell to any given pharmacy. If the sales price were related to the higher ‘premium’ reimbursement price the pharmacy would be at risk of not recovering its costs (if it happened to dispense products at a time in the year in which the maximum premium volume had been exceeded). Similarly if the sales price were related to the lower reimbursement price, the pharmacy might over recover if it dispensed products before the threshold had been exceeded. Differential prices would also create the possibility of parallel trade within the UK.

3.145 Supply chain stability and parallel trade considerations are also directly relevant when considering the effect of differential prices across the EU. We think that here too

\(^28\) Indeed, as noted in Annexe K, many international pricing arrangements that are formally called price volume agreements are in fact implemented through side payments (rather than a change in the price) and hence would be called rebates under the nomenclature used here.
there is a strong argument for allowing for a rebate system, in which the list price might differ from the value-based price paid by the Health Service. We discuss these issues in the next section.

Parallel trade

3.146 For certain products, a value-based approach to pricing may lead to prices that are low by European standards, leading to parallel exports from the UK and reducing companies’ revenues in other countries. The loss of revenue to pharmaceutical companies is a relevant concern, especially if a branded product’s value is low because its patent/SPC has expired in the UK but is still in place in other countries (for instance because the patent was granted at a later date than in the UK). Companies are likely to be resistant to accepting prices that significantly reduce their income in other countries. Furthermore, it is not always clear that these countries will benefit to the full extent from such parallel imports, in view of the costs incurred and profits earned by parallel traders.

3.147 Parallel trade considerations therefore provide a further reason for concluding that it may be mutually beneficial to payers and companies to allow, in a pricing system, for rebates to be paid in lieu of price changes. We recognise that this is an area of keen economic and legal debate and therefore the following sections explore in greater detail the economic and legal arguments in relation to parallel trade in pharmaceuticals.

Economic assessment

3.148 Parallel traders legally exploit price differences in identical products between different countries when they are sufficiently large to cover transport costs and earn a profit. In the pharmaceutical sector, the price differentials that sustain parallel trade are caused by the interaction of two factors:

- the pricing systems set by individual countries, and
- pharmaceutical companies’ willingness to price-discriminate between different markets in order to maximise profit.

3.149 Companies operate within a system in which individual countries operate national pricing regimes. Companies that have market power, and for which a high proportion of the costs of supply are fixed, can price discriminate by charging higher mark ups above marginal cost to the most price insensitive buyers.29 In the context of the pharmaceutical industry, this implies charging different prices in each country. This form of price-discrimination can be welfare-enhancing (over the alternative of a single price) for a number of reasons:

29 In order to maximise profits, they should set the mark up equal to the inverse of the price elasticity of demand (‘Ramsey pricing’). Therefore, less price-sensitive buyers will be charged higher mark ups.
consumers who would not be able to buy drugs at a uniform price are able to do so under price discrimination, resulting in an expansion of output and an increase in welfare.

firms have greater dynamic incentives to invest. Higher profits will provide greater incentives for firms to develop new drugs. In the pharmaceutical industry, where a high proportion of the costs are in R&D, this is particularly important.

3.150 Different prices also reflect the varying pricing regimes applying in different countries. In the pharmaceutical sector poorer countries tend to be more price sensitive (that is, they are more likely to forgo drugs on the basis that they cannot afford them). In this context, price discrimination can have positive implications for equity.

3.151 While parallel trade may provide short term benefits to high priced countries, it is also likely to prevent firms from exercising price discrimination effectively. With untrammelled parallel trade, pharmaceutical companies may be restricted to charging a uniform price at which some countries – most likely the poorest - will be unable to buy their products. Moreover, since parallel traders incur costs and earn profits from their activities, they reduce returns on drugs, undermining incentives to invest.

3.152 To sum up, on a global (EU) level, parallel trade in pharmaceuticals may reduce efficiency, both statically and dynamically, as the allocative benefits of price discrimination and incentives for innovation are reduced.

3.153 In the short term, parallel trading may provide savings for consumers (typically public purchasers) in higher price markets as a result of the lowering of prices. This may be brought about both as a direct result of the purchasing of parallel imported drugs (which will be cheaper), and by the effect that the increase in competition in the markets for these drugs has on the pharmaceutical manufacturer’s pricing for domestically sourced products.

3.154 An important issue in assessing the size of this effect is identifying to whom benefits accrue. Empirical work in this area is taken up in Box 3.5

**Box 3.5: Quantification of short term savings from parallel trade in pharmaceuticals**

In order to assess the size and importance of short run savings accruing from parallel trade in pharmaceuticals, it is important to identify to whom the benefits accrue.

Since parallel trading involves intermediaries (that is, the parallel trader and the pharmacy in the destination country) before it reaches the buyer, it is unlikely to be the case that all the savings are passed on to consumers (or public purchasers). In the UK, DH attempts to identify the savings made by pharmacies on parallel trade through the periodic Margin...
Inquiry. It then operates a clawback system whereby some of the savings made by pharmacies from the buying of parallel imported products are recovered by the NHS. The debate about the effects of parallel trade therefore focuses on whether the Margin Inquiry is able accurately to identify the margins earned by pharmacies on parallel trade and adjust the clawback accordingly.

Some empirical work has been conducted in an attempt to determine the benefits and beneficiaries of parallel trade. Two studies (one by economists at York, and the other by economists at LSE) appear to disagree over the proportion of benefits accruing to public health bodies in certain EU countries. The LSE study identifies parallel traders as the major beneficiaries, whilst the York study only estimates the benefits for governments and consumers. In addition, the York study ascribes a far greater likely impact on competition to parallel imports than the LSE study (which finds no evidence for this effect).

There are two principal differences between the two studies. The first is in the scope of the studies: the York study looks solely at savings to national healthcare insurance, whilst the LSE study is extended to include the benefits to parallel traders and the reduction in industry profits. The second is that the York study is a high level macroeconomic study that makes assumptions for the whole industry, whilst the LSE study specifically looks at just 6 product categories in more detail. While this makes direct comparison of the studies difficult, scaling up of the LSE results to account for market share yields similar benefits to national healthcare insurance to the York study.

The emerging conclusion appears to be that there are some savings to national healthcare providers from parallel imports (compared to the alternative of obtaining branded medicines directly from companies in the country concerned at prevailing prices for locally sourced products). However, these savings may be modest (approx £100 million (1.5 per cent of sales) for the UK in 2002, see Annexe J). Moreover, the revenue to the parallel traders themselves is likely to be significant and may well be larger than the savings to the NHS. Such revenue represents a loss to the supply chain that could otherwise have contributed to companies’ returns on R&D or alternatively to savings for national healthcare providers.

3.155 There is therefore some debate over the precise level of savings accruing to public purchasers from parallel trade in pharmaceuticals. However, it seems clear that there will always be an element of loss to the system – the costs incurred and profits earned by parallel traders. Therefore, pricing systems (such as those based on rebates) that take account of parallel trade effects may offer a win / win outcome for

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30 More recently, DH has been able to use other mechanisms to ensure delivery of a given level of pharmacy margin, such as modifications to the margins delivered through the category M mechanism for reimbursing generics. This is discussed further in Chapter 4 of this annexe.
32 The LSE study estimates benefits to parallel traders of €469 million and benefits to the NHS of €56 million (for the UK; note LSE study just looks at 6 product categories representing about 25 per cent of the UK Brand Prescriptions medicines market). The York study estimates total benefits of €342 million, €205 million of which accrue to the government (the rest going to pharmacies; parallel traders’ benefits are not included in the estimation).
33 Though no attempt is made at quantification of this effect.
industry and government - by encouraging industry to accept a higher price cut than would otherwise be the case and ensuring the benefits are shared exclusively between industry and the public purchaser.

Legal arguments

3.156 A number of legal cases in the last few years have provided some support for the analysis set out above. Relevant cases are discussed in Annexe G. They include:

- the European Court of Justice's ('ECJ') judgement in the Bayer case
- the Advocate General's opinion, and the ECJ's final judgment in the GSK Greece case
- the judgement of the CFI in the GSK Spain case
- the decision of the judge at first instance and the Court of Appeal in the BAEPD case

3.157 Here we focus on the two most recent and relevant cases – GSK Greece and Spain. The GSK Greece case arose, at least in part, out of Member States' systems for regulating the price of pharmaceuticals. GSK refused to meet in full Greek wholesalers' orders for three of its patented drugs, including the anti-epilepsy drug, Lamtical, which drugs were much cheaper in Greece than elsewhere in the EU. The refusal, Greek wholesalers alleged, was designed to stop parallel imports.

3.158 In his opinion Advocate General ('AG') Jacobs argued that, for four main reasons, a dominant pharmaceutical company may not abuse its position in these circumstances:

- a dominant company does not have to meet orders which are out of the ordinary, and can take reasonable steps to protect its legitimate business interests
- extensive regulation of price and distribution in the European pharmaceutical sector sets it apart from other industries because pharmaceutical companies have limited control over their commercial policy

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36 Case CJ/E/06/79 - Judgment of the Court of First Instance in Case T-168/01 GlaxoSmithKline Services Unlimited v Commission of the European Communities.
• the incentive for pharmaceutical companies to invest in research and development could be reduced given the lower returns which could result from unlimited parallel trade, and
• ultimately, the benefit of parallel trade often accrues mainly to the undertakings engaged in it, not to the end consumers of products.

3.159 The GSK Spain case relates to a decision in 1998 of a Spanish subsidiary of GSK to adopt new General Sales Conditions that stipulated that its medicines would be sold to Spanish wholesalers at prices differentiated according to the national insurance scheme which would reimburse them. In practice, medicines intended to be reimbursed in other Member States of the Community would be sold at a higher price than those intended to be reimbursed in Spain. That system was introduced in order to limit parallel trade in medicines between Spain and other Member States, in particular the United Kingdom, where prices were at a higher level.

3.160 In May 2001, the Commission decided that the General Sales Conditions were prohibited by Community competition law, because they constituted an agreement in restriction of competition.

3.161 In September 2006 the CFI found that the Commission’s main conclusion, that the General Sales Conditions had as their object the restriction of competition because they made provision for differentiated prices which sought to limit parallel trade in medicines, was incorrect. In particular, the Commission did not take into account the fact that the prices of medicines reimbursed by the national insurance schemes are not freely determined by supply and demand, but are set or controlled by the Member States. For that reason, it could not be presumed that parallel trade tends to reduce prices and thus to increase the welfare of final consumers, as it would do in the absence of those special regulations.

3.162 The Court considered that GSK had not succeeded in invalidating the Commission’s subsidiary conclusion that the General Sales Conditions have as their effect the restriction of competition. Given the measures taken by certain Member States to recover a part of the profits made by parallel traders, for the benefit of the national insurance schemes and patients, the CFI concluded that parallel trade permits a limited but real reduction in the price and the cost of medicines. In so far as they prevent that advantage from being produced, the General Sales Conditions diminish the welfare of final consumers.

3.163 Last, the Court of First Instance found that the question whether the General Sales Conditions might give rise to an economic advantage by contributing to innovation, which plays a central role in the pharmaceutical sector, was not examined with sufficient thoroughness. The Commission did not take into account all the factual arguments and the relevant economic evidence and did not sufficiently substantiate its conclusions.
Conclusion

3.164 It should be stressed that this economic and legal analysis, and the conclusions we draw from it, are particular to the pharmaceutical sector. They arise from the characteristics discussed above, in particular the cost structure of the sector and the fact that member states actively control drug pricing regimes. Therefore there can be no read through from this analysis to the effects of parallel trade in other sectors.

3.165 Furthermore, it should be stressed that nothing in this analysis suggests that measures to restrict parallel trade in the pharmaceuticals sector are necessarily consistent with competition law. The effects of any individual practice need to be assessed on a case by case basis.

3.166 Our conclusion, rather, is this: that, in designing and implementing a pharmaceutical pricing scheme it is not beholden on either public purchasers or manufacturers to ensure that sufficient price differences across Europe are maintained to sustain an industry designed to arbitrage against those differences. The option of allowing rebates to be paid in lieu of changing prices can in principle be in the interests of both payers and manufacturers and therefore benefit patients in the long run.

3.167 Under such an approach, where value-based pricing led to large price reductions, companies would have the option of retaining the existing reimbursement price and paying a rebate to the NHS equal to the difference between this price and the value-based price. Wholesalers and pharmacies would continue to purchase at prices close to current levels, and there would be no increased incentive to engage in parallel exporting. Rebates could in principle be allocated back to PCTs (to ensure local incentives for good resource allocation). As discussed in Annexe K, many countries in Europe and beyond employ rebate mechanisms.

3.168 In 2003, perhaps reflecting these arguments, a European Commission communication document suggested Governments consider whether there was merit in a pricing system in which free-pricing setting by manufacturers was coupled with the use of rebates to enable Member states to control national health care expenditures.38 The Commission also stated one of the eventual aims of such a system as the facilitation of a single EU ‘ex-factory’ price. We understand that the proposal has not progressed, partly over a concern that any such rebate mechanisms would lack transparency. However, as discussed in the next section, this is not a necessary feature of rebates.

International reference pricing

3.169 One potential argument against the use of rebates stems from the fact that UK pharmaceutical prices are used as an international benchmark, according to which other countries set their own prices. If UK pharmaceutical prices reflect their true

38 In communication document (Comm (2003) 383)
therapeutic value, it would be efficient to broadcast them as clearly as possible to other countries that refer to UK prices when setting their own. The use of rebates may distort the transparency of this price signal.

3.170 However, this argument only applies if rebates are not transparent. Nothing in the current argument suggests this needs to be the case. It would be perfectly feasible to be transparent about both value-based prices and list prices, preserving the signalling benefit of value-reflective prices.

Conclusion

3.171 There are several reasons for allowing more flexible pricing structures than at present. By better reflecting the value of drugs, non-linear prices can help align the incentives of manufacturers and the NHS and reduce socially inefficient expenditure. In the presence of parallel trade they can also help ensure mutually beneficial deals for payers, manufacturers and therefore patients.

Design issue four: setting the level of prices / size of budget

3.172 The discussion so far has focused on relative prices (how to price one product relative to a substitute), when to negotiate prices and how to design price structures. There remains the question of how to set the overall level of prices for drugs that have been ranked in terms of their comparative usefulness or, alternatively, how to set the overall budget available for drug expenditure.

3.173 This design issue takes up this question. It first considers the two alternative approaches – fixing prices or fixing the budget – and then discusses some of the factors that could inform changes in the level of prices over time.

3.174 It should first be noted that the maximum cost / QALY threshold for all healthcare interventions could in principle be derived on a technocratic basis from the overall level of the NHS budget, which is one conception of what NICE attempts to do.39 There would be no need to have a policy view or to hold negotiations on drug expenditure or the overall level of drug prices – the only political decision that would need to be made would be to set the overall level of the NHS budget.

3.175 However, this does not reflect the current political environment in which the scheme operates. If Government wanted to make a higher (or lower) contribution to the global costs of R&D, for example, it would not feel constrained to do so only through increasing or decreasing the size of the NHS budget. The periodic negotiations through the PPRS about the overall level of prices demonstrate the keen interest –

from both industry and Government – in the level and trend of drug expenditure.\textsuperscript{40} The following discussion assumes that the current political debate on the level of drug expenditure will continue, but considers how that debate could best be accommodated within a value-based approach to pricing.

**Fixed price or fixed budget?**

3.176 There are two broad approaches by which drug price levels can be determined. Either prices can be fixed in advance and the budget determined ex post or (less commonly) the drugs budget can be fixed in advance and prices determined ex post. These different approaches can be termed ‘fixed price’ and ‘fixed budget’ methods.

3.177 A fixed price approach makes a fixed payment for each unit of output delivered by a company. Under a value-based approach to pricing, a fixed (maximum) price would be paid for each unit of incremental value delivered by a drug. The concept discussed earlier in this chapter of a maximum acceptable ICER – expressed in terms of a cost per incremental QALY- is an example of a fixed price approach. Under this approach, the budget is derived each year according to volumes prescribed and the price assigned to each drug.

3.178 Fixed budget methods set the drugs budget in advance and derive prices actually paid ex post, at the end of the budgetary year. The simplest way of doing this would be to require payments to be made between the NHS and individual companies at the end of the year to deliver the amount of expenditure fixed in advance. If, for example, the budget was underspent, the NHS would make a payment at the end of the year, which would be distributed to companies on a pro rata basis. If the budget was overspent, companies would be required to make a payment to the NHS, again in accordance with revenues received in the course of the year.

3.179 Fixed price approaches are more common around the world. The current approach to pricing in the UK would fall into this category, for example. There are some examples of fixed budget approaches, however. New Zealand is perhaps the clearest example, as the drugs budget is fixed each year and Pharmac negotiates various deals (such as price-volume arrangements) with suppliers on all medicines so as not to breach it. There is a statutory requirement not to exceed the budget and in practice expenditure is consistently slightly below the maximum each year.

3.180 France uses a hybrid of both methods. Annual drugs budgets are voted by parliament, suggesting that the overarching principle is fixed-pot. But in practice the regime relies on a fixed-payment approach, setting the prices of many drugs in a reasonably formulaic way according to an assessment of their incremental benefits

\textsuperscript{40} This partly reflects the fact that it is difficult, given current information constraints, to arrive at robust estimates of the appropriate threshold from the overall level of NHS expenditure. As this situation changes in the future, it is conceivable that the current focus on the drugs component of expenditure will reduce.
over close therapeutic substitutes, with the result that the drugs budget often overruns. A case study of France appears at Annexe K.

3.181 The two options are perhaps best assessed in terms of their effects on the allocation of risks between companies and the NHS. A fixed budget approach would help the NHS manage financial risks, by fixing a major component of expenditure. For industry, this approach would also create certainty over aggregate expenditure. Individual companies, however, would be exposed to the sorts of risks to which the broader NHS is currently exposed. For example, their revenues would be reduced (rather than NHS expenditure increased) by the introduction (by a rival company) of a major, new life saving treatment onto the market, while their revenues would increase (as opposed to NHS expenditure falling) if the large selling drug of a competitor went off patent.

3.182 Since fixed budget arrangements contain total expenditure, they also have the potential to increase competitive pressures between suppliers. If manufacturers of branded drugs were rewarded from a single, fixed budget according to the share of health benefits their products provided, drugs for different conditions would compete more explicitly for public funding. This may in turn change the terms of the debate about how pharmaceutical products are paid for by the NHS.

3.183 Decisions by bodies such as NICE would become less contentious, as they would be called upon to determine what proportion of the fixed budget companies would receive. Companies would have greater incentives to challenge favourable assessments given to competitors. The NHS would have fewer incentives than at present to apply volume controls to restrict expenditure, since under a fixed budget pricing scheme all drugs would be funded but the question would be at what price.41

3.184 These outcomes are potentially very attractive from an NHS perspective. The disadvantage of the approach is that hypothecating drugs expenditure in this way would restrict the flexibility of PCTs to shift resources from drug expenditure to other types of expenditure (such as that on elective care in hospitals) and vice versa. Therefore it would dampen any competitive constraints drug and non-drug interventions impose on each other.

3.185 We also detected little appetite for a fixed budget approach among most of the companies we spoke to42 although this is perhaps in part due to the fact that countries that have adopted variants of the fixed budget approach have tended also to have secured low prices – New Zealand being an obvious example. In principle, of

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41 As Annexe A discusses, while under current arrangements NAS are freely priced ex ante, the NHS employs a number of demand-side controls in an attempt to restrict expenditure, including rationing or withholding them entirely in some cases.

42 An exception was a suggestion put to us by several companies that resources for drugs that have received NICE approvals should be hypothecated within PCTs for use only on those drugs.
course, a fixed budget approach would be consistent with any overall level of expenditure.

3.186 We think either approach – fixed prices or fixed budget - could be made to work in the UK. We think there is particular merit in considering the fixed budget approach, for the reasons discussed above. We note, however, that the approach would represent a greater departure from current arrangements and that the experience of drug budgets in the UK in the past suggests that keeping to a fixed budget can be difficult to achieve in practice. While we believe the approach set out above would be perfectly possible to implement, it would perhaps require a wider ranging reform of NHS funding arrangements and may only be a long term option.

3.187 Therefore, in the rest of this annexe and the options for reform discussed within it, we proceed on the basis that the UK continues to adopt a fixed price approach. This would mean that the NHS budget would still bear the risks of drug entry and exit (for example, new drugs coming onto the market and being taken up in large numbers or major drugs going off patent). However, we believe the rebate arrangements proposed above, under which payments could vary with total prescribing volumes rather than being constant across all usage, would at least insulate NHS from some types of volume risks – those that arise out of a drug being prescribed in indications for which it is not cost effective.

3.188 Under a value-based approach to pricing, a fixed price approach would imply adopting a maximum cost per incremental QALY for all drugs. The next section discusses the factors that should be taken into account in establishing the level of this threshold.

Factors determining the level of prices

3.189 This section gives some consideration to how the level of the maximum cost / QALY threshold should be set. The same considerations could apply to determining the appropriate level of the drugs budget under a fixed budget approach. It is not for the OFT to decide the correct level of the threshold nor to recommend the size of the total drugs bill but have given some considerations as to how these values might be set periodically.

3.190 As noted, this discussion will assume a fixed price (as opposed to fixed budget) approach is adopted. In the context of value-based pricing, to derive a price requires a value per QALY. The value per QALY used will drive the level of prices and hence (in the absence of other constraints) the UK’s expenditure on drugs.

3.191 Broadly, we can see two alternative approaches to determining a value per QALY:

- the first, which might be termed a bottom up approach, is to establish a value per QALY directly from information such as surveys, comparisons with other public investments and other forms of microeconomic data
the second, which might be termed a top down approach, is to determine an appropriate value for the drugs budget and then to calculate the value per QALY implied by this level of expenditure.

3.192 Possible data sources under the bottom up approach include questionnaire results, evidence on decisions taken by people when taking decisions involving risks to health and similar valuations used by other public authorities. Questionnaires could assess patients’ willingness to pay for better health, and an overall value per QALY could be based on patients’ estimated average willingness to pay (a similar approach was taken at one time to determining the value that electricity users lost when their electricity supplies were cut off).43

3.193 In addition, estimates of the cost / QALY threshold consistent with maximising health outcomes from the overall NHS budget will clearly be very important parameters in any decision over the threshold employed.44 Estimates of values per QALY already exist and are used, with various qualifications, by HTA bodies in the UK and abroad, including NICE (which uses a range for the value per QALY in determining cost effectiveness). A pragmatic approach for any new scheme would be to retain the existing cost / QALY threshold used by NICE and revise it to take into account inflation and other external parameters.

3.194 Turning to the top down approach, the drugs budget could, similarly, be determined on the basis of previous year’s expenditure plus a given rate of growth. A possible alternative, suggested to us, could be to base the budget on a direct estimate of the UK’s fair contribution to pharmaceuticals R&D. Under this approach, the value per QALY would be set at the level which equates the estimated surplus of price over production and distribution cost for all prescribed drugs with the UK’s fair contribution to pharmaceuticals R&D.

3.195 Under this approach, estimates of production and distribution cost for each drug could be based on the generic price (for drugs where there is a competitive generic market), or on the price of a comparable generic (for drugs where there is a drug with similar costs and a competitive generic market) or on the price in a low cost country (for other drugs). The UK’s fair contribution to pharmaceuticals R&D might be based on a broad estimate, for example total worldwide R&D expenditure multiplied by the UK’s share of world GDP.45 This approach would also require

43 Under the arrangements in place after UK electricity privatisation, electricity generators’ incentive to invest in new capacity was based on the value of lost load (VOLL), which was computed from survey evidence and subsequently increased in line with inflation.
44 However, as noted above, we do not anticipate that they will provide the only answer, at least in the short term.
45 The simple logic behind this is that the world pharmaceutical industry requires sufficient surplus to continue investing in R&D at the present rate, and that a fair UK share is equal to the UK’s share of world GDP. It might be argued that current R&D is not necessarily the same as the level of surplus that remunerates previous investment in R&D at the cost of capital. If necessary, allowance could be made for this through a broad brush adjustment.
forward estimates of prescribed volumes of each drug or group of drugs, but this might be based on current volumes with allowance for growth.

3.196 These approaches are not mutually exclusive and in practice, both could be used to set the appropriate cost / QALY threshold. As elaborated upon in Chapter 7, we think that the appropriate level of the threshold could be debated, on the basis of the above factors, between industry and Government every five years or so under a reworked, value-based PPRS.

Design issue five: institutions and the operation of pricing schemes

3.197 The final design principle is concerned with the question of how to ensure that a well-designed system works smoothly in practice. This will depend crucially on the working relationship and relative bargaining positions of the NHS and the pharmaceutical industry.

3.198 For a theoretically sound system to work smoothly in practice, a number of demands must be placed on the institutions that administer it. Broadly, those institutions need to:

- be able to work well. They should have clear mandates, deliverable with proportionate resources. They should be insulated from political concerns
- be seen to work well. They should be perceived as credible, fair and consistent by the NHS, the industry and the general public, and
- be backed by legal authority or a strong bargaining position. A pricing body may be fit-for-purpose and popular but without authority and it may not achieve its goals in practice.

3.199 The following discussion focuses on value-based pricing and considers how the institutions of a value-based pricing scheme might be set up to meet these demands and why, in our opinion, the NHS contains working institutions (and resources that could be harnessed for them) that could do so.

Being able to work well

3.200 Fit for purpose institutions would have well defined roles within a pricing scheme meeting as many as possible of the high-level design objectives laid out at the beginning of this discussion. As much as any other factor, the institutional framework and the resources available to implement it will affect the ability of a scheme to meet these objectives.

3.201 In the context of value-based pricing, some countries, such as Australia and a number in Europe, have separate authorities for therapeutic assessment and pricing. Having two bodies with clear mandates can expedite the listing process by dividing it into well ordered technocratic procedures. If it were thought desirable to have clinical assessments and price negotiations carried out by separate bodies, they would need
to work together closely to achieve the objective of securing speed of access to market

3.202 To meet the challenges of value-based pricing the institutions administering it could require substantial resources. In the UK, the cost effectiveness bodies NICE, SMC and AWMSG are natural candidates to take on the therapeutic assessment component of a value-based scheme. Between them, they provide a world class HTA resource. Overall resources may need to be increased, however. We consider these resource requirements of our proposals in Chapter 6.

3.203 As discussed in Annexe B, we also believe that there are certain respects in which current institutional arrangements for NICE, SMC and AWMSG could be developed to help implementation of any future value-based pricing scheme.

3.204 For example, allowing for earlier engagement between the cost effectiveness bodies and companies (that is, at the phase III trials stage) will give companies a better opportunity to produce the sort of information that is needed to make a compelling case for the cost effectiveness of the drug. The recent Cooksey review has called for moves in the direction of earlier engagement and we welcome these proposals.

3.205 Second, there is a need to make the best use of available resources, implying a greater level of coordination between these bodies than at present. Many companies feel that having to make cost effectiveness submissions to multiple bodies is not an efficient use of resources, particularly given the increasing overlap between SMC assessments and NICE STA appraisals. We recognise that this raises complex issues of sovereignty: the existence of multiple bodies represents a legitimate desire to have guidance and guidelines produced at a devolved level. Pricing decisions are not devolved however, which implies that, in producing cost effectiveness assessments as an input into a UK pricing decision, there will need to be greater coordination between the bodies.

3.206 We discuss specific mechanisms for facilitating such greater coordination in Chapter 7.

Being seen to work well

3.207 It would be vital for the institutions of a value-based pricing scheme to enjoy credibility with all stakeholders so as not to meet constant opposition and be compromised in their ability to function.

3.208 Stakeholder interactions would be most frequent with pharmaceutical manufacturers, whose goodwill would be critical. In any value-based system, there will be 'winners' and 'losers' among individual drugs. Companies would only accept this when decisions were clearly reasoned and issued by authorities with a reputation for fairness in the application of rules, and appropriate flexibility.
3.209 The institutions of a value-based pricing scheme could also face challenges from political pressures. Political pressures might be broadly defined to include any demands of government, the public, the industry or the NHS that do not relate to the rational objectives of a pricing scheme. The political climate around drugs can be difficult. Decisions by NICE, for example, to reject a product for use in the NHS on cost effectiveness grounds are widely reported in the press and sometimes condemned by interested parties with little regard to the reasoning offered.

3.210 The institutions of a value-based pricing scheme could experience similar pressures from these quarters but also others – including the NHS and patients. Even with efficient pricing, public healthcare budgets would remain limited by available taxpayers’ funds and access to drugs could sometimes be constrained.

3.211 The institutions would need to be able to demonstrate their ability to withstand pressures engage in opportunistic behaviour, in order to provide strong incentives to invest in valuable drugs in the future. In economic terms, they would face a commitment-credibility problem, discussed in the box below. One solution would be for an independent pricing body to be established. This would require legislation to implement and time to build up the right capacity within the institution. Therefore, as discussed in Chapter 7, we would consider it a long term option only.

**Box 3.6: Institutional independence as a commitment mechanism**

A buyer in a market is said to have ‘buyer power’ if it is able to influence market outcomes such as the market price. In the case of the market for pharmaceuticals, the NHS has buyer power as it is one of the biggest purchasers of drugs in the world and other countries peg their prices to those in the UK. The NHS may use its buyer power to acquire pharmaceuticals at a lower price, and in doing so reduces manufacturers’ profits. In the static market, the NHS always has the incentive to acquire pharmaceuticals at the lowest possible prices by using its buyer power.

However, the exercise of buyer power may have repercussions on firms’ incentives to invest in R&D. In order that firms undertake R&D investments or make large sunk costs (as is the case in the pharmaceutical industry) there needs to be the possibility of high profits for effective drugs.

In order to provide adequate incentives to invest in R&D, the NHS may therefore want to commit to prices for effective drugs that allow companies sufficient profits (thus reducing the extent to which it exercises its buyer power). However, since the NHS has the incentive to renege on these prices and use its buyer power in the short run, its commitment to these prices may not be credible. If this is the case, then R&D investment will be discouraged.

A possible solution would be if prices could be set through long term enforceable contracts between the companies and the NHS. However, due to the nature of pharmaceutical investments (principally the uncertainty involved) some discretion in pricing will always be necessary. This will most likely preclude the possibility of enforceable contracts. A further possibility is therefore to assign pricing responsibility to an independent body, with statutory objectives to consider both the short and long run, in order to ‘constrain the discretion’ of the public purchaser. Analogous approaches have been used in the utilities and financial sectors.
Utility markets are typified by large sunk costs and marginal costs that are low and decreasing in output. However, due to the large investments that need to be made, firms will need the incentives of positive profits to continue making them on an ongoing basis. The regulator thus faces the problem of credibly committing to prices high enough to encourage investments (as it has the incentive to renege on them once sunk costs have been incurred).

This problem is also analogous to the ‘time-inconsistency’ problem in monetary policy. This problem stems from the government’s two conflicting objectives of increasing output and maintaining stable prices. In this case, the government may not be able to credibly commit to a policy of a low inflation because of its incentive to pursue expansionary policy in the short term. Price-setters and wage-setters in the economy are aware of this incentive and will adjust their inflationary expectations accordingly, thereby causing inflation.

The solution adopted by Governments to both problems is to create independent bodies with clear objectives (for example, to target inflation). This approach has been successful in creating stability and instilling greater confidence in the long run (to investors in the case of utility regulators sectors and the broader economy in the case of the independent monetary authorities). Recently, perhaps inspired by these models, both principal political parties have made proposals for giving greater autonomy and independence to the whole NHS, proposing that it be run more independently of ministerial supervision with the establishment of an NHS board.

The creation of an independent drugs pricing body would be consistent with this broader trend towards the use of constrained discretion in policy implementation. In chapter 7 we discuss such an option, which we would consider to be a potentially attractive institutional arrangement for the long term.

3.212 Equity and fairness to patients would be an important principle to observe under any reformed pricing scheme. Difficult issues include, for example, whether an ‘ultra orphan’ drug treating an extremely rare condition should be awarded a very high price such as to divert substantial resources from other drugs. These are stark questions but forums already exist for debating society’s views on them, such as the Citizens’ Council set up by NICE in England.

3.213 Another important credential of institutions that would be seen to work well would be their ability to function flexibly in the face of uncertainty. Any pricing scheme must face unpredictable developments (such as fundamental changes in science) requiring a forward-thinking outlook. New medical technologies may work in uncertain ways and have effects in the population that could be difficult to predict even with the best available information. For the judgement of clinical-evaluation and pricing authorities to be accepted in such cases it would have to be backed by considerable expertise and some degree of popular consensus. This could mean consulting with companies, the NHS and patients on major decisions.

3.214 Institutional arrangements set out in Chapter 7 include provision for appropriate consultation with both patient groups and industry bodies.

46 Very many existing drugs in common use are only partially or even poorly understood. Examples include a number of painkillers, anti-inflammatory agents, drugs for asthma and many more.
Being backed by a strong bargaining position

3.215 All public drug pricing schemes are essentially bargaining relationships because no government can legally compel pharmaceutical manufacturers to supply. Companies have the ultimate threat of not supplying a drug when an agreement cannot be reached on price. A company may rationally follow up on its threat and sacrifice profits in a country – for instance if accepting a low price would harm the company’s price and revenues in other markets by the action of international reference pricing. A company may also wish to acquire a reputation for being willing to withhold supply, so as to strengthen its bargaining position in future negotiations.

3.216 Like companies, pricing authorities’ negotiating positions also need to be backed up with credible threats. The main mechanisms are the provision of guidance and control over reimbursement status.

Guidance

3.217 The issuance of negative guidance is the principal ‘threat’ underlying the decisions made by NICE, SMC and AWMSG. A drawback with guidance in particular is that it can be hard to enforce, whereupon it becomes an empty threat. Annexe B, which explores the role of the national cost effectiveness bodies, investigates adherence within the NHS to guidance issued by NICE and SMC. The overall picture is varied but implementation can be poor in some contexts.

3.218 In relation to local guidance, there are issues relating to both implementation and quality. These are issues being covered in an ongoing study by the National Audit Office into value for money in primary care.47 The NAO is interested in the various drivers of value for money, including the methods used by PCTs to encourage GPs and other practitioners to follow best-practice advice. The NAO has identified several PCTs that it considers to have effective medicines management policies but is aware of others that are less successful. The NAO report will be published in the first half of 2007.

Reimbursement restrictions and withdrawal

3.219 By far the most common (and arguably the most powerful) bargaining mechanism available to pricing and reimbursement authorities is the ability to restrict, refuse or withdraw reimbursement status for a drug. The UK, unusually, does not link pricing and reimbursement in this way.48

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47 The NAO study team and the OFT have collaborated on pieces of analysis common to the assessment of value for money in primary care and the wider issues raised by the PPRS. For example, the NAO and OFT jointly commissioned a survey of GPs to assess their awareness of branded drug prices and other issues. The survey is analysed in Annexe C of this report.

48 There are mechanisms that formally restrict prescribing in the UK – mainly the grey list of the Drug Tariff. However, these have fallen into disuse.
3.220 One approach is to list a drug at the agreed price but restrict reimbursement (for example, requiring doctors to obtain special authorisation to prescribe). These approaches are commonly used around the world, for example in Australia and Spain.

3.221 A further approach is to require patients to pay a share of the price of a product the authority considers to be of questionable cost effectiveness. Public health services in many countries charge patients co-payments that are proportional to the total cost of drugs – and proportions can be increased for drugs that the authorities consider dubiously cost effective. Germany and Australia provide examples of systems in which patients may have to make high co-payments to obtain the drug of their choice if the relevant authority considers a more cost effective comparator to be available.

3.222 This approach can in principle help the bargaining position of the payer, since the threat of restricting reimbursement might be seen as more credible than that of withdrawing reimbursement altogether. This approach could not be applied in the UK, since there is no co-payment system here (beyond the flat-rate prescription charge that is not levied on most scripts).

3.223 It should be noted, however, that, while a useful instrument to the public purchaser, co-payment systems are not necessary to implement value-based approaches to pricing. Sweden is an example of a country that implements value-based pricing, but simply withdraws reimbursement for a product if the manufacturer is not prepared to accept the maximum price set. Moreover, in other countries such as the Netherlands patients are highly reluctant to make co-payments and thus the effect of a manufacturer setting the price of a new medicine above reimbursement value is similar to the effect of withdrawing reimbursement (in that very few patients get the benefit of the new medicine).

3.224 The fallback threat of any pricing authority faced with an application for what it considers to be an untenably high price is to withhold reimbursement altogether. We would regard this as the most credible threat that the NHS could make in the absence of a co-payment system and in the light of difficulties with guidance. It would of course be a last resort option: the threat not to reimburse could not be used lightly due to the welfare implications of denying patients access to medicines, particularly for unique drugs. This fact would put a degree of pressure on the institutions of a value-based pricing scheme to be both credible and fair so as to avoid having to choose whether to follow up on the threat.

3.225 With these key provisos in mind, we think the threat of refusing reimbursement is an important component of any fully effective pricing scheme and is accordingly a component of the second and third options for reform discussed below – ex post and ex ante value-based pricing. For reasons discussed above, it is most likely to be credible in the conduct of ex ante assessments.
Statutory approaches

3.226 It is worth noting that there are some rare examples of systems that rely on statute alone to underpin pricing decisions (that is, that do no relate pricing and reimbursement). Canada’s PMPRB adopts such an approach (see Annexe K).

3.227 In the UK, provision exists for a statutory scheme to be imposed by the Secretary of State, and it seems that adherence to the current, voluntary, PPRS is in part underpinned by the threat of imposing this statutory scheme. In Chapter 7, we consider the prospects for a future voluntary PPRS founded on value-based principles.

Conclusion

3.228 We conclude from the first design principle, on the measurement of therapeutic value, that although there may be challenges in assessing the cost effectiveness of medicines the issues cannot be avoided. Public health purchasers must achieve value for money because they cannot afford to spend public funds on medicines that are not cost effective. They should also send signals to encourage investment in useful new drugs, as patients will depend on their continued supply in the future. At present, as argued in Annexe M of this report that quantifies some price inefficiencies under the PPRS, substantial NHS resources are consumed by prescribing of certain expensive branded drugs despite the availability of close therapeutic substitutes at much lower cost.

3.229 Branded drugs should be valued in the light of the availability of relevant comparators. This should include generics if they are the cost effective alternative in any particular case. We believe it would be inappropriate to flat-price a brand with similar chemicals in a way that ignored incremental benefits - the rewards paid to incremental innovation should be proportional in value added terms to those paid to breakthrough treatments.

3.230 We conclude from the second design principle on the timing of price negotiation that, while for some drugs it is possible to appraise effectiveness accurately using trials data available at launch for others a clear picture of clinical usefulness may take years to emerge. This could motivate conducting both ex ante and ex post assessments to handle different products. The choice between ex ante and ex post controls also affects the bargaining position of pharmaceutical companies and payers.

3.231 We conclude from the third design principle on the structure of prices that it should be feasible to remunerate drugs on the basis of therapeutic benefits in different indications and subgroups without establishing an unworkable system of multiple NHS list prices. Instead, rebates could reward drugs for added value but not for prescribing beyond beneficial uses. This should align the incentives of manufacturers with those of the NHS to a greater extent than at present. We also suggested
options for handling the international implications of any change in price structure, through effects on parallel trade and international reference pricing.

3.232 We conclude from the fourth design principle that it is possible to fix either prices or the drugs budget ex ante. Both approaches have their particular merits, although in the majority of countries it is prices that are fixed and total drug expenditure that expands or contracts according to entry, exit and volumes prescribed.

3.233 We conclude from the fifth design principle that institutional design is key. Institutions must work well and be seen to work well, inspiring confidence in key stakeholders. They must underpinned by a strong bargaining position but also incorporate adequate appeals mechanisms and arrangements for consultation.
4 EVALUATION OF OPTIONS FOR REFORM: OFF-PATENT BRANDS

Introduction

4.1 This chapter explores options to reform the pricing of branded drugs for which the patent has expired, which are currently priced under the PPRS. It first summarises problems identified in other parts of the report, before recommending changes to current pricing and margin arrangements. Finally transitional arrangements are considered.

4.2 In the 2005 PPRS, it was stated that 'standard' branded generics (that is, non-originator brands) would, subject to public consultation, no longer be covered by the PPRS and would be transferred to the new arrangements for the reimbursement of generics. This consultation was put on hold pending the outcomes of the present study. Our recommendations cover both originator and non-originator off-patent brands.

Summary of Problems

Value for money

4.3 The most fundamental concern we have with current pricing arrangements for off-patent brands is that they do not deliver value for money for the NHS. Generic pricing arrangements (under the Category M scheme) have helped ensure that competition between generic manufacturers delivers savings to the NHS. In contrast, off-patent brands – whether originator or not – are priced under PPRS price and profit controls and, in most cases, are many times more expensive than their generic equivalents. In Annexe M, we provide a range of estimates for savings that could be produced if off-patent brands with equivalent generic products were reimbursed at the price of their generic equivalent.

4.4 Considering generics with Category M equivalent generics only and excluding modified release products, we estimate that savings to the NHS would exceed £60 million per year from a change in reimbursement regime. All of the drugs considered in the analysis are fully bioequivalent (that is, consist of drugs of the same chemical

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49 When prescribed by brand name. As explained in Annexe A, a brand dispensed to meet a generic prescription is remunerated as a generic unless the pharmacy can demonstrate no generics are available.
50 Formally known as 'Scheme M' but referred to in this chapter as 'Category M' arrangements, referring to the listing of drugs on the Drug Tariff.
51 As discussed later in this chapter, we recommend that off-patent originator brands be priced at a 25 per cent premium to the equivalent generic. Savings from such a move would fall in the range £64 million to £83 million for 2005. We are only proposing that the reimbursement regime be changed for drugs with a category M equivalent. Other drugs will be reimbursed under the arrangements for on-patent brands discussed in the next chapter.
form and strength). Therefore, very significant price disparities cannot be justified on value for money grounds – one of the fundamental objectives set out above.

**Price Modulation**

4.5 As discussed in Annexe A, generics compete with brands in two types of market.52 The first type of market centres on competition to secure prescriptions from prescribers in primary and secondary care. In these types of markets, generics compete with therapeutic substitutes and bioequivalent products (off-patent brands) on the basis of clinical efficacy and price (reimbursement price in primary care and transaction price for hospitals).

4.6 The second – downstream – market concerns competition to supply pharmacies for the purposes of dispensing against a generic prescription. In these markets, generics manufacturers compete with other generics manufacturers and with the manufacturer(s) of the equivalent off-patent brand(s), on the basis of transaction price and margin to the pharmacy.

4.7 As discussed in Annexe J, the price modulation provisions of the PPRS have the potential to distort competition in both of these types of markets, by giving companies strong incentives to concentrate price reductions on drugs for which volume is likely to increase in response to a reduction in price (in other words, for which demand is price sensitive).

**Competition to secure prescriptions**

4.8 In relation to the first type of market, in general, prescribers’ demand is relatively insensitive to price changes, as demonstrated in our survey of GPs. Nevertheless, there may be circumstances where price does affect prescribing decisions and there is consequently either price competition between one or more brands and generics, or brand-on-brand competition. This situation is more likely in relation to off-patent brands – that is, where a number of different brands of an off-patent drug are available.53

4.9 In these circumstances, modulation creates the incentive for a multi-product company to increase the price of products which are relatively price insensitive and reduce the price, possibly to below marginal cost, of products which are relatively price sensitive. This would be to the advantage of companies with many products

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52 Here, as elsewhere in the report, ‘market’ is to be understood in general terms, as descriptive of the nature of competition between companies to supply a particular component of demand. We are not making a statement as to the relevant market in a Competition Act or merger case, which can only be defined on a case by case basis in relation to the particular question being addressed.

53 It should be recalled that price reductions cannot be included in modulation proposals where the patent/SPC has expired within one year before, or will expire within two years after, the date of modulation (six months and one year respectively for modulation at the time of a price cut such as 1 January 2005).
with differing price sensitivity, but is to the disadvantage of the NHS (which experiences higher costs), smaller branded suppliers (which find it more difficult to modulate because of their smaller product range) and generic suppliers (who lose sales to the brands subject to price cuts).

4.10 Modulation may also increase the incentive to reduce prices of branded products ahead of patent expiry in order to discourage generic entry (because the price cuts can be funded by price increases on other price insensitive drugs). This is most likely for products with relatively small markets where entry is relatively costly for generic suppliers.

Competition to supply pharmacies

4.11 Within the second type of market, manufacturers sometimes supply branded drugs to pharmacies at a discounted price for the purposes of dispensing against generic prescriptions (‘brand equalisation deals’). Some firms have previously attempted to include brand equalisation volumes meeting generic prescriptions in their price modulation returns. Not only would this practice cost the NHS money (since it would not gain from the price cut on brand equalisation volumes), it would also provide the manufacturer in question with a significant competitive advantage against generic manufacturers. However, under the 2005 PPRS, brand equalisation volumes meeting generic prescriptions have been explicitly excluded from modulation volumes and hence we do not consider the issue further here.

Margin differences between brands and generics

4.12 As discussed in Annexe A, currently very different methods are used to set the reimbursement prices of brands (PPRS) and generics (a variety of mechanisms but predominantly through Category M). These methods allow pharmacies to secure much higher margins on generics rather than brands, which can give branded manufacturers competing with generics a strong source of competitive advantage in markets to secure GPs' prescriptions.

Generic reimbursement

4.13 Reimbursement prices for Category M generics are linked to generic manufacturer transaction prices but, as part of the 2005 pharmacy contract for England, DH agrees that pharmacies retain a total profit margin of £500 million (known as the retained profit margin). Category M reimbursement prices are set quarterly in such a way that pharmacies continue to earn the £500 million retained profit margin.

4.14 On many generics, notably Category M, margins earned by pharmacies are substantial. Our rough estimates (see Annexe A) suggest an average margin on generics of 28 to 35 per cent. However, we understand that margins on some generics, in particular some Category M drugs, are much higher—sometimes over 50 per cent.
Branded reimbursement

4.15 On domestically-supplied branded drugs (on- or off-patent), pharmacies typically earn a low margin. This reflects a typical discount on list price from manufacturers to wholesalers of 12.5 per cent and wholesalers’ margin of around two per cent, giving a pharmacy purchase price about 10.5 per cent below list price, offset by DH reimbursing at 9.2 per cent average clawback\(^{54}\) on list prices.

4.16 It should be noted here that a branded manufacturer enjoys an effective monopoly position in the market for supplying the pharmacy to dispense against off-patent branded prescriptions.\(^{55}\) However, as far as we are aware, there is no rule that specifically requires manufacturers to sell on terms that enable the pharmacy to purchase at less than reimbursement price. The 12.5 per cent discount referred to above is a convention rather than a rule. In principle, therefore, there is a possibility that a branded manufacturer might sell a particular drug to the wholesaler / pharmacy at a price that would cause the pharmacy to incur a loss.\(^{56}\)

4.17 Our understanding is that, were this to happen, pharmacies in aggregate (although not necessarily each individual pharmacy) would recover the resulting loss through higher margins on Category M products, but the NHS would end up paying more as a result of the higher Category M margin. Therefore the potential result of a branded manufacturer reducing its discount on list prices is increased income for the manufacturer and increased cost to the NHS. We discuss this issue further in the options for reform section of this chapter.

Competition effects of margin differences

4.18 These significant differences in pharmacy margins between off-patent brands and their generic equivalents have the potential to distort competition between branded manufacturers and generics in markets for securing prescriptions. This is because, under current arrangements, manufacturers of off-patent brands can market their products to PCTs and prescribers as cheaper than the generic and yet still sell to the pharmacy at a higher price than that of the generic.

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\(^{54}\) Products with certain characteristics are exempt from clawback. The average across all products (including these exempt products) is currently 9.2 per cent (see Annex A).

\(^{55}\) Ignoring parallel imports, which tend not to be significant in the relatively low volume off-patent brand sector.

\(^{56}\) That is, at a price exceeding the pharmacy reimbursement price less clawback. This applies to both on-patent and off-patent brands.
4.19 The more brands compete with generics in this way, the more significant the effect of margin differences will become. In the long run, they risk undermining competition from generics and costing the NHS money, since the lower margins pharmacies earn on off-patent branded prescriptions will result in higher margins on remaining generic prescriptions (in order to attain the £500 million retained profit margin agreed in the pharmacy contract).

4.20 We have heard that originator brands have started to exploit margin differences by setting off patent brand list prices below reimbursement prices for generics. In addition, certain non-originator brands have been employing this strategy for a number of years, as discussed in the next section.

**Margin arbitrage**

4.21 A particular example of the effects of significant differences in margins for brands and generics can be seen in what we call ‘margin arbitrage’ activity. Margin differences create an opportunity for companies (which we call ‘margin arbitrageurs’) to profit by purchasing a generic drug at the market price and supplying it to the NHS as a branded generic. This requires a prescription to be issued for the branded generic, and prescribers are motivated to do this by the margin arbitrageur setting a list price below the comparable generic price. The brand can still be sold to the pharmacy at a price that allows the arbitrageur to cover its costs and make a profit because the brand is making a far lower contribution to overall pharmacy margins than the generic.

4.22 We understand that margin arbitrageurs market their branded generics to PCTs, whose prescribing advisers persuade prescribers to prescribe the branded generic rather than the true generic. We have noted elsewhere in this report that PCTs have limited ability to influence prescribing decisions, but their effectiveness is greater where there is no countervailing marketing activity from companies (as is the case with generics).
4.23 The immediate effect of this practice is that the PCT saves the difference between the reimbursement price of the branded generic and the Category M price but pharmacies get a smaller profit margin. However, as noted, DH adjusts Category M margins so that pharmacies continue to earn the £500 million retained profit margin. Providing monitoring arrangements accurately capture the margin earned by pharmacies, the effect of margin arbitrage activity will be to increase reimbursement costs to the NHS (and thus to PCTs in aggregate) to cover the costs incurred by and profits made by the margin arbitrageurs. Thus, although each individual PCT has an incentive to encourage prescribing of the branded generic, the end result is higher aggregate reimbursement costs for PCTs taken together.

4.24 Table 4.1 illustrates this effect. The branded generic price is set ten per cent below the Category M price, so the PCT makes savings of £0.30, but the loss in pharmacy margin triggers margin adjustment of £2.00, resulting in a total net cost to the NHS of £1.70.

<table>
<thead>
<tr>
<th></th>
<th>True generic</th>
<th>Branded generic</th>
<th>Savings from branded generic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement price (after clawback*)</td>
<td>3.00</td>
<td>2.70</td>
<td>0.30</td>
</tr>
<tr>
<td>Pharmacy purchase price</td>
<td>1.00</td>
<td>2.70</td>
<td></td>
</tr>
<tr>
<td>Contribution to £500m pharmacy retained profit margin</td>
<td>2.00</td>
<td>0.00</td>
<td>-2.00</td>
</tr>
<tr>
<td>Total savings to NHS</td>
<td></td>
<td></td>
<td>-1.70</td>
</tr>
</tbody>
</table>

*Assumes average clawback of 10 per cent.

Source: OFT calculations

4.25 We do not have accurate estimates of the current costs of margin arbitrage activity. But even if the costs are fairly small at present, there are grounds for concern that the practice could increase in future (for instance as PCTs realise that they will lose out if they do not encourage prescribing of margin arbitrageurs’ branded generics).

Summary

4.26 We have two concerns about the actual and potential exploitation of margin differences between brands and generics:

- it distorts competition between branded and generic suppliers since branded suppliers can get a higher income while charging the customer a lower price for the bioequivalent product, and
- it leads to the NHS having to pay more for the same drugs.

4.27 This adverse effect on the NHS is compounded if price modulation enables the branded supplier to set price reductions on brands competing in this way with generics against increases in prices on other brands with inelastic demand. We were told that that one margin arbitrageur had accumulated substantial headroom under
the price control as it had modulated down its prices to match generic price reductions. In principle this headroom could be used to increase prices of other products with inelastic demand, for instance if the margin arbitrageur was taken over.

Summary

4.28 The problems we have identified are:

- in many cases the NHS has to pay substantially more for branded products than bioequivalent products from generic suppliers
- branded suppliers can exploit margin differences to set a list price such that the reimbursement price for the brand is below the reimbursement price for generics while the income to the branded supplier is higher than to the generic supplier and the ultimate cost to the NHS is also higher, and
- PPRS rules on modulation potentially distort competition between brands and generics.

4.29 We now turn to consider options to address these problems.

Options for reform and discussion

4.30 In principle, the problems identified above could be solved by requiring pharmacies to dispense all approved off-patent drugs generically. Some other countries have adopted this approach – known as 'generic substitution'.

4.31 However, to adopt such an approach in the UK would represent a major move in the direction of constraining prescriber autonomy. It would also require a lengthy process of renegotiation of the pharmacy contract and very careful design of the incentives facing pharmacies to ensure that they are aligned with the needs of patients. It is noteworthy that one country that has implemented generic substitution by pharmacies – Sweden – has an entirely publicly owned pharmacy network, with no financial incentives to make margins on dispensing.

4.32 Such wholesale behavioural and structural reform of the NHS is outside the remit of this study into pricing and reimbursement. In the remainder of this section, we assess potential options for reform to pricing and reimbursement arrangements to address the problems identified.

4.33 We assess several options for reform of reimbursement arrangements that might address the issues outlined above. We assess them against the objectives laid out in chapter two: principally whether they deliver short-run and dynamic efficiency and are stable. The principal options and their relative merits are discussed below and assessed against each other and the status quo. The options are:

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57 See Annexe K for further details.
• Option 1: Exclude all off-patent brands from price modulation returns
• Option 2: Reimburse pharmacies for dispensing against a prescription for a standard branded generic at the lesser of the Drug Tariff price of the comparable generic or the list price of the branded generic
• Option 3: Reimburse pharmacies for dispensing against a prescription for all off-patent brands (originator brands as well as branded generics) at the Category M generic price, so long as the drug has a Category M equivalent. Allow a maximum 25 per cent premium for originator brands
• Option 4: As for Option 3 but with additional steps to remove incentives to exploit margin differences by passing the costs of margin arbitrage through to individual PCTs via the financial settlement.

Option 1

4.34 Option 1 would address, in an incremental fashion, the potential distortions to competition between off-patent brands and generics arising out of price modulation. It would not, however, have a significant impact on value for money for the NHS.

Option 2

4.35 Option 2 is, in essence, the option on which DH consulted in 2005 and 2006. Two important components of the proposal are that it would only cover non-originator brands (standard branded generics) and that the reimbursement price would be set at the lower of the comparable generic or the list price of the branded generic. In a Regulatory Impact Assessment (RIA) for the proposal, DH estimated the savings from such a change to be ‘some £10 million a year’.58

Option 3

4.36 Option 3 differs from Option 2 in three respects.

4.37 First, the proposal is restricted to brands with Category M generic equivalents (rather than applying to any generic equivalent). This is partly on grounds of tractability and ease of transition (as it would focus on an easily definable group of drugs accounting for the majority of expenditure implications, as shown above). More importantly, however, restricting the proposals to Category M drugs provides a mechanism by which in the future when drugs go off patent, generics have a chance to enter the market and foment competition before the price falls. This is important for the stability and sustainability of proposed arrangements.

4.38 Second, the proposal is that the off-patent brand reimbursement price should be set at that of the generic comparator, rather at the lower of the brand price and the

58 Reimbursement of 'standard' branded generic medicines: A further consultation, DH, 2005.
generic comparator. Assuming the price of the generic comparator is set through the broadly competitive Category M price, we see no reason for setting the brand price below this. Furthermore, this measure will help address adverse competition effects arising from margin differences, as discussed below.

4.39 Third, the proposal includes both originator and non-originator brands. A central design principle, discussed in the previous chapter, is that price should be value-reflective to promote static and dynamic efficiency. This is a key factor in considering options for reform in the next chapter. In our view, there is no argument for excluding off-patent originator brands from these principles. Indeed the arguments are if anything stronger when applied to off-patent brands, since under current arrangements there are some extreme examples of prices not reflecting value to patients (for example, twenty fold differences in price for chemically identical products).

4.40 However, it could be argued that, if originator brands were reimbursed at the same price as generics, GPs might prefer to continue to prescribe the brand after patent expiry as this is what their patients are familiar with. Therefore, in order to maintain the impetus for generic prescribing, there is a case for reimbursing originator brands at a small premium over the generic reimbursement price. As discussed below, we recommend allowing a maximum premium of 25 per cent over the generic price.

4.41 Option 3 could in principle address margin-related distortions to competition—because, if brands are reimbursed at the same price as generics, PCTs no longer have a financial incentive to encourage prescribing of brands. However, Option 3 does not address the margin issue at source. Under Option 3, branded suppliers could in principle continue to exploit margin differences, by offering PCTs a side payment, for example, instead of—as at present—offering them a lower reimbursement price.

Option 4

4.42 Margin-related distortions to competition arise because pharmacies earn a higher margin on Category M generics than on brands. They could be removed by equalising the effective margin on generics and brands. In the long run, we think this would best be achieved by continuing the move in the current pharmacy contract to remunerate pharmacies through fees for service rather than through the Category M margin. Option 4 provides a more immediate approach, which would involve passing the loss of margin arising from prescribing an off-patent brand (instead of a Category M generic) through to PCTs in their financial settlement.

4.43 The following information would be needed to estimate the reduced pharmacy margin and allocate it to individual PCTs: prescribing of relevant brands by PCT (available through PPA), margins on Category M (already known to DH) and margins on brands (currently being collected by DH). It appears therefore that adequate information might exist to pass through to PCTs the additional cost of prescribing brands instead of Category M generics.
4.44 Under Option 4 margin differences could be passed through to PCTs as follows. We take the illustrative example of a Category M drug, for which the reimbursement price is £6 (the same as the reimbursement price of the equivalent off-patent brand under the reforms proposed here).\textsuperscript{59} Assuming pharmacies purchase from generic suppliers at an average of £4 and from the branded manufacturer at £6, the PCT would be charged £6 for the generic prescription and £8 for the branded prescription (to make good the loss of £2 to the global retained profit margin).

4.45 Option 4 would clearly remove any incentive to prescribe brands in order to avoid contributing to the retained profit margin. However, it is perhaps overburdensome compared to Option 3, which, by reimbursing brands at no less than the generic reimbursement price, should achieve the same result.

**Preferred option**

4.46 Option 3 is our preferred option, although Option 4 could be considered if significant exploitation of margin differences via side payments emerged.

**Savings from Option 3**

4.47 As shown in the table below, we estimate a total of around \textbf{£64 million in savings could be generated each year if all off-patent drugs with category M equivalents were reimbursed at generic list prices plus 25 per cent}. As mentioned above, savings under our recommendation, to apply a premium only to originator brands and not other branded generics, would be slightly higher than this figure. The table also shows the savings that would be generated if all off-patent brands were remunerated at the prices of equivalent generics without applying the 25 per cent premium. Savings under our recommendation would fall between the two estimates – that is, between £64 million and £83 million. As discussed in Annexe M, the calculations are based on 2005 data (and do not take into account any savings from removing exploitation of margin differences).

\textsuperscript{59} For ease of exposition, we ignore the 25 per cent premium for originator brands and wholesaler margins in this example. This does not affect conclusions.
Table 4.2 – Savings from reimbursing off-patent brands at Category M generic prices in 2005 (£ millions)

<table>
<thead>
<tr>
<th>Country†</th>
<th>Category M equivalent plus 25%*</th>
<th>Category M equivalent (no premium)</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td>34.7m</td>
<td>44.9m</td>
</tr>
<tr>
<td>Scotland</td>
<td>15.4m</td>
<td>20.2m</td>
</tr>
<tr>
<td>Wales</td>
<td>2.7m</td>
<td>3.2m</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>11.0m</td>
<td>14.6m</td>
</tr>
<tr>
<td>Total</td>
<td>63.8m</td>
<td>82.9m</td>
</tr>
</tbody>
</table>

Source: OFT calculation based on PCA and Drug Tariff data for the UK. Savings per product represent the higher of branded price less generic price and zero. Hence, savings do not include the effect of branded prescriptions in reducing pharmacy margin and consequently increasing generic margin.

† Outside England PCA data sometimes codes branded drugs as generics. We have made adjustments so as not to underestimate savings but in some cases it is most appropriate to quote a range. The lower range has been quoted in the table.

* To take a conservative view, we did not calculate potential savings from remunerating modified release formulations of drugs, where available, at the price of generics of the standard-release chemical.

Source: OFT calculations based on PCA and Drug Tariff data for the UK.

Impetus for generic prescribing and entry under Option 3

4.48 An important aspect of these proposals is that they would retain – and in some important respects improve - incentives for generic prescribing and generic entry. This is an important feature of any revised system, since as discussed in Annexe A, generic prescribing and pricing has delivered significant benefits to the NHS in recent years. We consider first likely effects on prescribing behaviour and second on the entry of generic manufacturers (that is, on markets to supply pharmacies).

Generic prescribing

4.49 In relation to generic prescribing, as discussed in Annexe A, this is largely driven by GPs' training (to prescribe by chemical name whether the drug is on- or off-patent) rather than sensitivity to the price of generics. An indication of this is that, with some notable exceptions, generic prescribing rates are high before a drug goes off patent and do not noticeably increase when generics enter.

4.50 For those drugs for which incentives for generic prescribing are affected by price, we believe our proposals will improve incentives to prescribe generically. First, by reimbursing brands at no lower than the price of the equivalent generic, they largely address the concern that under current arrangements brand manufacturers can exploit margin differences to gain a competitive advantage over generic suppliers. Second, by removing off-patent brands from price modulation, they remove the potential advantage current provisions give large multi-product companies in competing with generic (and smaller branded) suppliers.

4.51 Our recommendations would clearly reduce the price disparity between some brands and their generic equivalents – this is in large part the rationale for the recommended reform. However, we do not think this in itself will reduce the impetus for generic
prescribing, since our proposals would allow originator brands to be reimbursed at a maximum 25 per cent above the generic price. While much lower than many current premiums, this approach has the advantage of being transparent to prescribers, in contrast to current price disparities, which can be very wide but exhibit significant variation and as a result are not always known to prescribers. Annexe C, for example, suggests there are widespread misconceptions about the prices of off-patent branded products.

Generic entry

4.52 It is important to maintain competition in the generic market, and consequently to ensure that there is sufficient incentive for generic manufacturers to enter the market. Our proposals would not reduce the incentive for generic manufacturers to enter and sustain supply.

4.53 First, our proposals only affect drugs with a Category M price. At the time of entry of the first generic manufacturer, there is no Category M price and thus our proposals involve no change from the current position. Therefore, to the extent to which initial generic entry is driven by high brand prices, this would remain the case under our proposals. (For drugs in Category C, the reimbursement price for generics is based on the price of a brand and again would be unaffected by our recommendations.)

4.54 Second, after initial entry, the Category M generic price is, in almost all cases, determined by competition between generic suppliers and not by the price of the originator brand. Under our proposals, there is no reason to expect the competitive generic price (and hence the anticipated profits from entry by a generic manufacturer) to be lower than under the present system.

4.55 In the small number of cases where there is only one generic manufacturer supplying a Category M priced drug, the generic price is likely to be constrained by potential entry by other generic manufacturers. Under the terms of Scheme M, it is also formally constrained to be no higher than the price of the brand at the time of patent expiry. Neither of these two constraints is affected by our proposals.

4.56 It is only if, in any individual case, the current price of the originator brand provides the binding constraint on generic pricing on an ongoing basis that our proposals might have a material effect on generic entry, by making this constraint more binding. Under such – rare – circumstances, a lower price of the originator brand might reduce the expected profits from entry of a single generic manufacturer. In general the other constraints mentioned – in particular competition from other generics manufacturers - are likely to be much more important and this is not therefore likely to have a significant effect in practice.

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60 Table 5.2 of Annexe A shows that more than 75 per cent of the value of generic supply is accounted for by drugs where there are four or more generic suppliers.
Summary of recommendation

4.57 To sum up, we propose that for drugs where there is a Category M price, standard branded generics should be reimbursed in line with the Category M price, while originator brands should be priced up to a maximum of 25 per cent above the Category M price. Drugs that do not have a Category M equivalent would not be affected by this proposal and would be treated in the same way as on-patent brands, pricing arrangements for which are considered in the next chapter.

Implementation issues

4.58 There is a number of specific issues in the implementation of our recommendation that need to be addressed. These are discussed below.

Full bioequivalence

4.59 The first issue to be addressed is which drugs should remain under the PPRS when their patent expires, and which should be reimbursed under Category M. The key principle here is that the drugs should have fully equivalent therapeutic effects. This is defined in Annexe M but in broad terms, the requirements are that the two products should have the same pharmaceutical form, the same active substance and be bioequivalent, as determined by MHRA. To establish bioequivalence, studies must show that after administration two products have essentially the same effects with respect to both efficacy and safety.

4.60 Not all off-patent brands have exact generic equivalents. This is the case, for example, with certain off-patent modified release products where MHRA regulations do not allow generic supply but a number of brands are available. These drugs would continue to be reimbursed under Category C of the Drug Tariff under our proposed arrangements. In our estimate of savings, we have, accordingly, omitted all modified release products.

Constraints on branded list prices

4.61 Under current arrangements, most brands are reimbursed at list price less clawback of an average ten per cent. We noted above that under these arrangements, a problem could arise if a branded supplier reduced its wholesaler discount to below the customary 12.5 per cent. The pharmacy could be in the position of making a loss on the individual transaction, and the NHS would end up paying more as a result of the higher Category M margin.

4.62 This possibility applies to on- and off-patent brands and is therefore not specific to our proposed reforms. However, since under our proposals pharmacy reimbursement for branded prescriptions would no longer be a systematic function of the

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61 We presume that manufacturers are unable to sell to wholesalers at prices above their own list prices.
manufacturer’s list price, the risk to which the pharmacy is exposed may be greater (since branded suppliers might set their list price higher than the reimbursement price).

4.63 To avoid this eventuality, it would therefore be necessary under our proposals to limit the list price that can be charged by branded suppliers. The appropriate limit depends on the position regarding clawback. The current position in England and Wales is that clawback is applied at the same rate to both generic and branded reimbursement. In these circumstances we would recommend limiting the list price to no more than the reimbursement price before clawback. In practice, since the Category M reimbursement price will fluctuate from quarter to quarter, we recommend that the manufacturer’s list price be restricted to no more than last quarter’s reimbursement price before clawback.

4.64 Two points should be noted in relation to this proposal. First, manufacturers could still sell to wholesalers at a price higher than the customary 12.5 per cent discount. The only way to address this problem more fully, short of regulating the transaction price, would be to reduce the level of pharmacy clawback and the list price accordingly, an option we consider in the concluding section of this chapter. Second, even under these proposed arrangements, transactions prices secured by branded manufacturers would still be significantly higher than those for generic manufacturers.

Payments in lieu of price changes

4.65 For various reasons, patent/SPC protection expires at different times in different countries. Consequently, we recognise that setting the reimbursement price for the originator brand in line with the Category M price even with a 25 per cent premium could lead to parallel exports from the UK, potentially leading to the manufacturer losing revenues in countries to which they are exported.

4.66 To help companies deal with this, we would suggest they be given the option of making a payment to the NHS in lieu of changing the list price of their products. Under this approach, the reimbursement price for the originator brand could remain at its level before patent/SPC expiry62 if the supplier of the originator brand agreed to make periodic repayments to the NHS equal to the difference between this price and the relevant Category M reimbursement price plus 25 per cent. This would prevent originator brands entering the UK supply chain at very low prices with associated risk of parallel exports to countries where patent/SPC protection is still in force. It would only apply if the supplier of the originator brand agreed to make the repayments.

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62 We would envisage that the supplier of the originator brand could reduce its price below this level but not increase it.
Stability of branded supply

4.67 In any scheme, stability of supply is paramount. One risk to be considered in this respect is the possibility that, in response to the alteration of pricing arrangements, originator companies may threaten to withhold the supply of brands. As long as a generic equivalent is readily available, which will be the case for all branded drugs moving to generic reimbursement arrangements, this threat will be less credible – and less harmful to the NHS – as prescribers can switch to the generic equivalent. Moreover, we believe a variety of features of the proposals we have made should maintain the incentive to continue to supply the originator brand:

- the ability to make repayments in lieu of a price change
- the 25 per cent higher reimbursement price for originator brands, and
- the lower margins pharmacies earn on branded products (allowing branded manufacturers a higher share of revenues than for generic products).

Generic pricing mechanisms

4.68 As noted in Annexe A, quarterly Category M prices for some products have been relatively volatile. There are three main sources of the volatility seen in Category M prices. They relate to:

- supply side issues (for example a decision of a manufacturer to sell large quantities of 'short-dated' stock rapidly by significantly reducing the price)
- recalibration (DH recalibration of the tariff to maintain the agreed level of purchase profit for community pharmacies)
- teething problems following on from the creation of Scheme M (for example, we heard that some companies inadvertently submitted inaccurate data at the beginning of the scheme’s operation).

4.69 Significant volatility in prices may be a problem for PCTs, as it potentially makes it more difficult for them to manage their drugs budgets effectively. However, brands’ share of drugs subject to Category M pricing would be relatively modest (even though large enough in absolute terms to generate savings of over £60 million) and any additional problems for PCTs should be of limited scale.

4.70 Further, we note that other factors should reduce the recent volatility of generics prices. Recalibration is within DH’s control and we understand that it has undertaken not to recalibrate the Tariff as frequently in the future. The significance of teething problems should also be expected to decline over time, as companies become more familiar with the Category M arrangements, which have now been in place since 1 April 2005.

4.71 A related issue is that originator brand manufacturers are increasingly seeking to supply the generics market through brand equalisation deals. But Category M prices, under Schemes M and W, are set following quarterly surveys of generic
manufacturers and wholesalers. Consequently Category M prices do not reflect the prices at which originator brand manufacturers are supplying the market through brand equalisation deals. In order to remove a potential distortion to the price setting process, it may be desirable to extend the information gathering process to include all supplies by branded manufacturers, and to calculate separately branded manufacturers’ implied average net selling prices for drugs dispensed generically as distinct from their prices for drugs dispensed as a brand. This would then give DH the option of taking into account the prices for supply against generic prescriptions implied by brand equalisation in setting Category M prices.

Treatment in price and profit controls

4.72 As regards the price control, we have already suggested that the relevant brands (those where our proposal is to constrain prices on the basis of Category M prices) should be excluded from modulation. It would, moreover, be sensible to remove these brands from the price control altogether—as their reimbursement prices are constrained by Category M generic prices it is unnecessary for them to be subject to a second price constraint.

4.73 As regards the profit control, one possibility would be again to exclude the relevant brands. However, this might involve some additional burden for companies (for instance in cost allocation) and would in our view be unnecessary. An alternative would therefore be to leave the relevant brands within the profit calculation for the profit control. This would have the effect of reducing profit margins (brands remunerated at prices linked to generics are likely to have below average profit margins) and hence overall profits: this would be to companies’ advantage but this is not in itself a significant concern since, as discussed in the next chapter and Annexe H, the profit control has not been binding for most countries in recent years.

Conclusion

4.74 For originator brands for which there is a bioequivalent generic supply subject to Category M pricing, we recommend that pharmacies should be reimbursed at the Category M generic price plus a maximum of 25 per cent. Or, if suppliers wished, pharmacies could continue to be reimbursed at a price up to that prevailing before patent/SPC protection as long as the supplier agreed to repay to the NHS the difference between this price and the branded price.

4.75 For brands other than the originator brand (standard branded generics) for which there is a Category M equivalent, we recommend that pharmacies should be reimbursed at the Category M generic price.

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63 This could be done, for example, by calculating a manufacturer’s total net revenue for each relevant off-patent drug, subtracting its notional net revenue from branded prescriptions (volume times price on normal terms) and dividing by its volume meeting generic prescriptions. Revenue would be net of discounts and distribution costs.
4.76 In both cases, **suppliers should be precluded from setting an excessive list price.** 
Under current clawback arrangements, this would involve restricting the list price to no more than the previous quarter’s before-clawback reimbursement price.

4.77 **Brands affected by these proposals would be excluded from the PPRS price control,** in particular its modulation provisions.

4.78 If margin arbitrage behaviour persists, then further steps to prevent exploitation of margin differences could be considered (for example by passing through to individual PCTs the loss of pharmacy margin due to prescribing a brand rather than an equivalent generic). In the long run, however, we think the most logical solution would be to continue the move in the current Pharmacy Contract to remunerate pharmacies through fees for service rather than on the Category M margin.

4.79 Regarding concerns about the ability of manufacturers to charge higher than standard transaction prices with the effect of reducing pharmacies’ margins, if these persist in the future, a further long term option would be to reduce the level of clawback and require branded suppliers to make a compensating reduction in list prices.64 This would reduce the risk of pharmacies making a loss on dispensing any individual brand, while retaining the incentives of pharmacies in aggregate to secure competitive prices.65

4.80 Off-patent brands for which there is no Category M equivalent product would be reimbursed under the same arrangements as on-patent brands. These are discussed in the next chapter.

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64 Other than for products already meeting the DH requirements for the zero discount list.
65 Individual pharmacy reimbursement could remain linked to their monthly total volumes dispensed. So, for example, if manufacturers’ list prices were reduced by 10 per cent, clawback could also be reduced by 10 percentage points, while the transaction prices of manufacturers and wholesalers to pharmacies would remain unchanged. Adjustments for individual pharmacies (currently ranging between 11.5 and 5.63 per cent clawback) would then range from clawback of 1.5 per cent to extra reimbursement of 4.37 per cent. Individual pharmacies’ reimbursement would consequently remain unchanged.
5 EVALUATION OF OPTIONS FOR REFORM: ON-PATENT BRANDS

5.1 In this section we propose four concrete options for reform of pricing of on-patent brands that draw on our conclusions from the preceding discussion of design principles. They reflect the high-level objectives for a rational pricing scheme that were set out at the beginning of this annexe but also more practical issues arising from the discussion of the design issues. Few people would oppose any of the high-level objectives but any workable reform to the PPRS would involve compromises between them. The purpose of working through the design issues was to reflect on such compromises and to identify where we feel the balance of arguments lie.

5.2 The first option we consider would involve retaining the core instruments of the PPRS, but amending them to eliminate some of the problems identified. Options two and three would involve replacing the PPRS profit cap and price cuts with value-based mechanisms. Option four considers removing the PPRS altogether and instead having prices set under local tendering arrangements.

Option one: incremental reform to existing PPRS controls

5.3 In this section, we consider how far incremental reform to the existing PPRS price and profit control could meet the objectives set out in Chapter 2. We have already recommended (in Chapter 4) that, where generics are subject to category M pricing arrangements, off-patent brands should be excluded from the PPRS. Therefore, in this section, we consider what further changes could be made to improve the existing price and profit controls, while retaining their fundamental characteristic of being imposed at a company level, rather than individual drug level.

Overview

5.4 In this sub-section, we summarise briefly our findings on the existing controls and set out the possibilities for incremental reform. The next two sub-sections consider, in greater detail, two options for reforming the profit control.

Profit control

5.5 As regards the PPRS profit control, as discussed in Annexe H, our principal concern was that it essentially remunerates on the basis of inputs (costs) rather than outputs (useful drugs), yet – crucially – there is little systematic link between the costs and outputs of innovative activity in the pharmaceutical sector – through skill, ingenuity and perhaps some luck different firms will enjoy very different levels of success in producing useful drugs from a given level of expenditure on R&D.

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66 Recall that economic efficiency – short-run and dynamic efficiency – are the most important and most closely reflect the current stated objectives of the PPRS.
5.6 In practice, we found that it does not constrain the profits of most existing member companies but may potentially have adverse effects in deterring entry and/or rapid expansion by research intensive small companies focused on the UK.67

5.7 We have considered two possible reforms to the profit control:

- some companies suggested to us that a more binding profit control should replace the price control which currently constrains prices. We have therefore considered whether and how the profit control could be tightened
- second, we have considered more modest changes to the existing profit control to address the potential adverse effect on smaller UK-based research-intensive companies.

These two possible reforms are discussed in detail below.

Price cuts and modulation

5.8 As regards the price cuts, as discussed in Annexe J, our finding was that they do deliver savings in primary care, but that the level to which prices are constrained is arbitrary as it is not linked to the therapeutic value of drugs to patients. We also found that the arrangements for averaging price increases and decreases (modulation) have the potential to distort competition (see Annexe J).

5.9 We believe there is limited potential for incremental change to address these problems (beyond the changes that would arise from removing off-patent brands from price modulation). This is partly because the arbitrariness is inherent to the current system of negotiated price cuts and control at company, rather than individual drug, level.

5.10 The potential distortion to competition could in principle be addressed by removing companies’ freedom to modulate prices but this would substantially reduce their flexibility, in particular to respond to parallel imports. Under the current framework, this would in turn make companies less willing to accept price cuts and hence may result in higher prices. We have also given some thought to the method of averaging prices used in modulation calculations. At present DH measures delivery of the price control using current volume weights. Using base weights might reduce the potential distortion of competition68 but would create other problems, for example an incentive to increase the price of products for which demand is growing relatively rapidly.

Therefore, were company-level controls to remain in place, we would not be in

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67 We did not identify AFR companies with these characteristics that are currently disadvantaged in this way in practice. But the design of the scheme is a potential constraint on entry / expansion by such companies in the future.

68 Modulation creates an incentive for companies to reduce the price of products with elastic demand (that is, those facing competition) and increase the price of products facing inelastic demand. This incentive is greater with current volume weighting because volume increases as the price of products with elastic demand decreases (and hence current volume of such products is greater than volume prior to the price cut).
favour of removing price modulation, beyond the removal of off-patent brands from modulation as discussed in the last chapter.

Price increases

5.11 On a related aspect, the PPRS at present only allows a company that is constrained by the price control and has profits above the minimum under the profit control, to increase prices through modulation. This means that such a company cannot obtain a price increase on a particular drug without reducing other prices, even if the avoidable costs of continuing to supply that drug exceed its revenue from the NHS. In these circumstances, it could be profitable for the company either to discontinue supply or to sell the drug on to another company which had headroom under the price control (or whose profits are below the minimum or would fall below the minimum as a result of such a transfer).

5.12 In order to address this issue, it was suggested to us that there should be a formal process for companies to propose an increase in the price of specific products. We agree it would be desirable to introduce a mechanism for DH to have discretion to allow a price increase where drugs generate valuable patient benefits but price has fallen below the avoidable costs of supplying the drug to the NHS. We would not expect this to affect many drugs (the obvious examples would be older drugs already subject to three or more price cuts in successive PPRS agreements) and thus we would not expect it to have major effects on NHS costs. **Were current controls to be retained, we would be in favour of this proposal.**

Threshold for exemption from the PPRS

5.13 It was also suggested to us by certain companies that the minimum sales threshold should be increased from £1 million for the price control to £50 million. This would benefit smaller companies with few products, which are potentially disadvantaged by modulation under the price control.

5.14 However, we believe such a large increase in the threshold would create other distortions. For example it would create a strong incentive for exploitation by other companies, for example through larger companies setting up a number of associate companies, each of which had sales of less than £50 million, in order to avoid the price cut. Overall, this option would create a risk of significant increases in the cost of drugs to the NHS without commensurate benefit to patients. **We would therefore not be in favour of this proposal, were current controls to be retained.**

Procedural reforms

5.15 Two reforms to the negotiating process were suggested by certain companies. First, it was suggested that the negotiations should take place earlier in the financial year, with more lead time before implementation of any changes, to give companies more time to adjust financial plans in line with any new agreement. Second, it was suggested that smaller companies should be represented at negotiations with the DH.
We have not considered procedural matters in detail but these suggestions may have merit, and we consider it would be desirable for DH to consider them, to the extent practicable, in any future round of PPRS negotiations.\textsuperscript{69}

**Tightening the profit control**

5.16 As noted above, several companies have suggested to us that they would be in favour of taking price cuts out of the PPRS, if necessary replacing them with a more binding profit control. While such proposals have not included any degree of detail, this section considers the feasibility of this option, by working through what, in our views, it would entail in practice.

5.17 Tightening the profit control would involve altering the basis of the control so that it constrains companies to earn no more than the cost of capital on their investments. This implies narrowing substantially the margin of tolerance so that it just reflects uncertainty about profits during the year. More importantly, major changes would be required to bring PPRS profits into line with the economic concept of profits. These fall into two main areas: first, treatment of companies’ internal costs arising outside the UK, and, second, accounting for R&D. We consider these in turn, and then consider whether a tighter profit control should be based on actual costs or efficient costs.

**Costs arising outside the UK**

5.18 The costs arising outside the UK are principally cost of goods sold (COGS) and R&D. We concentrate here on COGS and consider R&D below.

5.19 Currently, where COGS arises outside the UK, the PPRS relies on transfer prices from corporation tax returns and, in most cases a default cost breakdown. As set out in Annexe H, this gives rise to a number of problems:

- first, the default breakdown leads to understatement of PPRS profits against target because too low a proportion of transfer price payments are attributed to R&D (which is a capped item of expenditure) and too high a proportion to cost of goods sold (which is not capped)
- second, and most importantly, most companies use resale-minus transfer prices, which introduces a circularity into the determination of profits. Under this approach, the PPRS cannot constrain profits (the difference between sales value and costs) because costs are based on transfer prices which are themselves derived from sales value. A profit control based on the current PPRS approach to

\textsuperscript{69} Clearly, one issue of importance – under any of the options for reform considered in this chapter that retained a broad PPRS-style agreement – is what should happened should companies disagree over which industry body should represent them. It is not obvious that negotiating multiple agreements with different groups of companies would be feasible.
transfer pricing cannot therefore be binding for the majority of companies, which use resale-minus transfer prices.

5.20 A separate point is that the rate of corporation tax is 30 per cent and an approach that is appropriate for that tax rate is not necessarily robust for a binding profit control. A binding profit control is equivalent to imposing a tax at a rate of 100 per cent and would consequently require a different type and level of monitoring.

5.21 The problems with transfer pricing might be avoided if companies provided information on the actual manufacturing and other direct costs they incur in producing drugs and getting them to the UK. Such costs tend to vary, at least in the long run, with the volume produced and, where necessary, it would appear reasonable to allocate such costs to the UK according to the UK’s proportion of volume. Since the UK’s share of volume is likely to vary between drugs, this would have to be done on a drug-by-drug basis. DH or independent auditors would need to verify the costs were accurate.

5.22 However, companies show no willingness to provide information about costs outside the UK. The reasons given by companies for not providing a cost breakdown include that US legislation prevents this information being provided and that the UK company does not know the breakdown of costs from overseas affiliates. Currently, in the few cases where a cost breakdown of transfer prices is provided, the auditors merely state an opinion that there is ‘a reasonable level of assurance’ that the breakdown applies. This is insufficient for a binding profit control, which would require careful monitoring and verification of overseas costs.

5.23 It is therefore doubtful that companies would provide costs, outside the UK and allow them to be verified by DH. It might also be difficult to obtain costs outside the UK as part of a statutory scheme, as this could give rise to claims of extra-territoriality. Additionally, verifying companies’ costs outside the UK would be a very costly and time-consuming exercise.

R&D

5.24 The current PPRS treatment is to include R&D as an item of current (rather than capital) expenditure, subject to a maximum allowance which depends on sales value and the number of in-patent active substances. Companies' allowances do not reflect the individual characteristics of its drugs. Additionally, both the R&D allowance and the profit target impact differently on different size of firms. These disadvantages would be more serious if the profit control were tightened so that it became profitable for companies to manipulate the allowance to their advantage.

5.25 An alternative would be to treat R&D as an item of capital expenditure, reflecting its economic characteristics. R&D would then be capitalised and depreciated like other assets. We have given some thought to how this might be done. Broadly, there are two main approaches that might be followed:
• a ‘successful efforts’ approach capitalises development (but not research) expenditure but includes only successful development expenditure. Unsuccessful development expenditure would be written off at the point it is recognised as unsuccessful. We understand this approach is now used by some companies in their commercial accounts
• a ‘full cost’ approach potentially capitalises all R&D: we discuss below how this might be done.

5.26 We consider each of these and then the issues involved in attributing R&D to the UK.

5.27 The successful efforts approach has the advantage that it is used by oil and gas companies, and now by some pharmaceutical companies, and hence may not be completely unfamiliar to accountants and industry executives. It also has the merit of rewarding successful R&D more than unsuccessful R&D. However, in the pharmaceutical sector, uncertainty is such that some unsuccessful development is inevitable. Excluding research and unsuccessful development expenditure from the capital employed on which companies earn a rate of return means that capital employed is less than the economic value of what companies have invested.70

5.28 In order to ensure that companies get a fair return on what they have invested and have an incentive to continue investing in R&D, the target return on R&D capital would need to be above the cost of capital.71 But this would bias R&D decisions towards relatively low risk projects as these would have a higher chance of success and hence a higher chance of being included in capital but would still earn a rate of return based on average risk.

5.29 A second issue with the successful efforts approach is that it may be difficult to verify when developments become unsuccessful: companies would have an incentive to delay admitting that expenditure was unsuccessful in order increase the capital on which they earn a rate of return.

5.30 A ‘full cost’ approach would aim to approximate the economic value of a company’s R&D capital. A possible way of doing this would be broadly as follows:
• R&D in each year would be classified according to type (for example, research, phase 1 trials etc)
• R&D would then be compounded forward at the cost of capital to the expected date of marketing approval (based on the average time expected to be taken for each type of R&D)

70 Data in Di Masi et al (2003) suggest that about one third of life cycle R&D expenditure is research or preclinical development, which presumably could not be capitalised, and another third is unsuccessful clinical development expenditure, which would be written off. This would suggest a ‘successful efforts’ approach includes only around one third of the economic value of R&D capital.
71 There could be a different (lower) target rate of return on other capital.
compounded R&D would be included in capital from the expected date of marketing approval (but not before)

R&D capital would then be depreciated according to some average of economic depreciation rates\(^{72}\) for drugs. Since the bulk of cash inflows for drugs tend to occur towards the end of the patent period, this might be very different from straight-line depreciation through the patent period.

Under this approach, each company’s capital would reflect what it had actually spent on R&D, and its profit target would be equal to its capital employed (including R&D) times cost of capital. This approach would have the merit of treating companies fairly and reducing or eliminating biases associated with differences between the target rate of profit and the cost of capital. But it would remunerate R&D spending rather than the value of the drugs developed and would appear relatively unfamiliar to accountants and industry executives.

Whichever method is used for capitalising R&D, it would be complex and expensive to implement. Moreover, there are a number of potential problems with applying estimated R&D capital and depreciation in the PPRS profit control.

R&D expenditure is incurred throughout the world by global pharmaceuticals companies and therefore there may be similar issues with costs arising outside the UK to those outlined above in regard to COGS: companies might be reluctant to provide, or allow independent verification of, information on costs arising outside the UK.

it is unclear whether companies would have sufficient historical information to calculate R&D capital values for existing drugs, as R&D expenditure would be needed going back many years into the past.

R&D costs are both fixed (non-varying with output volume) and sunk (irrecoverable once incurred) and the allocation of global R&D costs to the NHS is far from straightforward (see Annexe H). Allocating costs to the NHS in proportion to its share of volume is not necessarily appropriate if the NHS has a different willingness to pay from the average for all users of the drug.

Actual costs versus efficient costs

Ideally, a profit control would be based on the efficient level of costs rather than the level that companies actually incur. Basing profits on efficient costs means that companies retain the incentive to control costs. Unfortunately, it is difficult if not impossible to know the efficient level of costs, particularly in a sector such as pharmaceuticals, in which the drugs produced by companies differ markedly.

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\(^{72}\) The economic depreciation rate for a particular drug may be defined as the rate of decline in present value of future cash flows. Grabowski et al (2002) shows average cash flows over the product life cycle from which economic depreciation rates might be calculated.
There would appear to be four main alternative approaches that might be adopted in a profit control, each of which, however, has its own difficulties:

- determine profits using actual costs. This gives companies no incentive to control costs as higher costs lead to lower profits. The lack of incentive to control costs means that costs most likely would be higher than otherwise and this would potentially offset any effect of a tighter profit control in restraining prices.

- determine profits using actual costs, subject to DH agreeing that costs are reasonable. This is the approach currently used in the PPRS for cost categories which are not subject to allowances (for example, general and administrative costs). Currently, however, most companies’ profits fall within the margin of tolerance and they have little incentive to challenge DH’s profits assessment. This would not be the case with a tighter profit control: companies would have the incentive to challenge everything and this could lead to a spiralling of administration costs and unmanageable burden for the arbitration panel.

- determine profits using a broad allowance, as is currently the case for R&D, marketing and information costs. Again, however, it is more difficult to rely on broad allowances with a tighter profit control, as such allowances cannot accurately reflect the individual circumstances of each individual company. If the allowance is too low, companies will have to spend above the allowance with the consequence that their profits are constrained to a level that is too low and their incentive to invest is reduced. If the allowance is too high, the control will fail to constrain profits adequately and prices will be too high to the detriment of the NHS.

- determine profits on the basis of projections using evidence of companies’ relative efficiency. This approach is used by UK utility regulators, such as OFWAT and Ofgem, but it is complex and resource intensive to implement. Moreover, unlike utilities, pharmaceutical companies each have their own individual portfolio of drugs which makes efficiency comparisons between companies much more difficult.

Summary and conclusions

Tightening the profit control so as to reduce reliance on price cuts would involve a number of problems:

- unless modulated to reflect some measure of the value of the drugs produced by a company (a possibility we consider at the end of this section) a profit cap suffers from the fundamental problem that it provides weak incentives to invest in the most useful drugs.

- a profit control based on the current PPRS approach to transfer pricing cannot be binding for most companies because they have the freedom to use, and most do actually use, resale-minus transfer prices. Any binding profit control would require companies to provide, and DH or independent auditors to verify, data on
costs incurred outside the UK. This would be very complex and burdensome both for companies and DH

- broad allowances do not reflect the individual circumstances of each company, and identifying an ‘efficient’ level of costs is extremely difficult in the pharmaceutical sector, since each firm has a very different portfolio of projects. It therefore seems likely that more reliance would have to be placed than at present on actual costs rather than allowances. This would reduce companies’ incentive to control costs and may lead to increases in costs and prices.

- capitalising and depreciating R&D potentially reflects each company’s circumstances but it is unclear how R&D capital and depreciation should be allocated to the UK. Furthermore each of the main approaches to capitalising R&D involves incentive drawbacks: capitalising only successful R&D requires a target rate of return above the cost of capital, creating an incentive to over-invest in low-risk assets, while capitalising all R&D fails to reward successful rather than unsuccessful R&D.

5.35 Overall, we think the case for a more binding profit control substituting for price controls is weak as it would be very complex and burdensome to implement. Compared to the current PPRS it may even have an adverse effect on incentives for cost control and would not necessarily provide better investment incentives.

Addressing the potential bias against small UK-based companies

5.36 The current PPRS profit control does not significantly constrain companies’ prices but potentially has adverse effects in deterring entry and/or rapid expansion by research intensive small companies focused on the UK. One possibility would be to drop the profit control, but if DH and ABPI wish to retain it, we consider it should be amended to remove the potentially detrimental effects on smaller UK-based R&D-intensive companies.

5.37 In this context, a number of suggestions were made to us by companies and industry bodies:

- address the disparity between target return for ROC and ROS companies
- allow some smoothing of profits for relevant small companies, for example by allowing losses to be carried forward
- increase the R&D allowance for emerging bioscience companies
- extend the definition of new products for relevant small companies to include new versions of existing molecules as well as new chemical entities (this would increase the number of products qualifying for the R&D allowance)
- reduce the lower margin of tolerance for relevant small companies (this would make it easier to obtain a price increase).
5.38 In general, we think it preferable for incremental reforms to remove the disadvantages facing relevant companies rather than try to introduce offsetting advantages. Reform also needs to be focused on the relevant companies and be reasonably easy to implement. Consequently, we concentrate on the first three of these suggestions (the fourth is not focused on research-intensive companies, while it is unclear how relevant companies could be identified for the fifth). We also think that the transfer pricing arrangements need to be addressed.

5.39 The most appropriate incremental reforms would therefore include:

- amending the target profit and transfer pricing rules so that different types of companies are treated more equally. This would involve all companies having a target based both on sales and capital. We expand on this below
- allowing some smoothing of profits for young companies. Under this proposal, young companies (for example those which had launched their first product anywhere in the world within the last ten years), showing excess PPRS profits would be allowed to carry forward excess profits for a period of say five years. They would only be required to make a repayment or reduce prices if they earned cumulative excess profits over the period
- allowing a higher level of R&D allowance for companies with high R&D intensity. Under this proposal, R&D-intensive companies (those with a global R&D to sales ratio above their existing R&D allowance) could have their R&D allowance increased to their actual ratio of global R&D to sales. A rapidly expanding company with one or two in-patent active substances and a global R&D to sales ratio of 30 per cent would be allowed to include R&D costs equal to 30 per cent of sales, as compared to between 20 per cent and 23 per cent at present. This would apply to the calculation of maximum profits but not minimum profits, that is, it would not enable additional price increases. It might be sensible also to limit this to young companies, for example those which had launched their first product anywhere in the world within the last ten years.

Amending target profit and transfer pricing rules

5.40 We now expand on the first bullet point in the previous paragraph. The position of rapidly expanding R&D-intensive companies focused on the UK could be improved by addressing the relative treatment of ROS and ROC companies and bringing the scheme rules somewhat more in line with economic logic (without fundamental change and substantial additional information requirements).

5.41 This would involve two things. First, all companies would be allowed a target profit level consisting of a percentage of sales plus a percentage of capital employed. This would give all firms a target return on sales (broadly intended, together with the R&D allowance, to remunerate investment in R&D) and firms with capital employed would receive additional target profit in line with their cost of capital employed (which we estimate at about ten per cent, see Annex H).
Second, the treatment of transfer price payments would be amended to be consistent with the above. The treatment of imports from affiliates is a major problem for any profit-based control but, in the absence of detailed global cost information, we see no alternative to the existing approach based on transfer prices used for tax purposes. However, the transfer price approach could be modified so that the breakdown of transfer price payments is realistic and consistent with other aspects of the profit control.

As discussed in Annexe H, the current transfer price breakdown attributes too high a proportion of transfer price payments to COGS and too low a proportion to R&D. It would seem more reasonable to attribute 50 per cent (instead of 59 per cent) to COGS and 30 per cent (instead of 21 per cent) to R&D leaving 20 per cent attributed to profit, as at present. Companies where COGS accounts for more than 50 per cent of transfer prices would still be able to submit a company specific breakdown.

At present, transfer price profit is added to target profit (ROS companies) or capitalised (ROC companies)\(^7\). In order to remove the element of double counting, our proposed treatment would be that only the surplus of the transfer price profit percentage over the target profit rate should be capitalised. So, for example, if target profit is 12.5 per cent of sales value, 7.5 per cent (20 per cent - 12.5 per cent) of transfer price payments would be capitalised, and if target profit is 20 per cent of sales value none of the transfer price payments are capitalised.

Conclusion on option one

To sum up:

- **the case for attempting to replace the price control with a more binding profit control is weak.** We do not think a binding control is feasible for the majority of companies that use resale minus transfer prices, without a very resource-intensive process of attempting to audit data on costs incurred outside the UK. Still less would it be possible to identify an 'efficient' level of costs under such a scheme. If a scheme were binding, it would therefore suffer from the fundamental incentive problems of giving poor incentives for efficient and effective expenditure

- **we would be in favour of dropping the profit control altogether, but if it is retained, its potential adverse effects on smaller research intensive companies focused on the UK could be addressed.** This could be done through modifying the profit target, increasing the R&D allowance for highly research intensive companies and smoothing profits for young companies

- **a formal mechanism could be introduced to allow price increases on drugs where the avoidable cost of supplying the NHS exceeds NHS revenue.**

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\(^7\) The effect is the same in both cases.
5.46 These changes would not however address our main concerns with the existing PPRS, in particular they would not provide a mechanism for linking prices to the value of patient benefits.

5.47 In principle, notions of therapeutic value could be grafted on to current PPRS controls. For example, one suggestion we received was that the rate of return earned by companies should be linked in some way to the therapeutic value of a company’s products. This would be at best a very indirect way of attempting to set value-based prices and, given the problems with the profit control identified above, would almost certainly not be binding for most companies.

5.48 Alternatively, the level of the price cut could be amended to reflect therapeutic value. This has strong similarities with elements of Option two in particular (except that we envisage that it would apply at the product level rather than the company level). We discuss this option next.

**Option two: ex post value-based pricing**

**Overview**

5.49 This option would be based on a series of ex post reviews of the value of medicines to replace the PPRS profit cap and price cuts. It would retain many of the other features of the scheme, such as freedom of pricing up front. Whether a PPRS-style agreement that incorporates these components could be negotiated in practice depends on whether the agreement of all companies concerned could be secured. If this is not the case, then a statutory scheme could be imposed under the NHS Act 2006 (which replaces and reproduced the relevant provisions of the 1999 Health Act). In the following discussion, we present the option as it would be implemented under a PPRS-style agreement. The main substance of the recommendations would be the same under a statutory scheme.74

5.50 Manufacturers would retain freedom of price setting for new active substances (NASs) at launch. However, the list prices of all on-patent branded drugs would be reset according to analyses of cost effectiveness during price reviews occurring at roughly five-year intervals, with the first review of each product falling at most five years after launch.75 Five years is the maximum duration for which NASs currently earn revenues at launch prices before a PPRS price cut is imposed. The system proposed here matches that calendar but replaces today’s price cuts across all products in a company’s portfolio with value-based measures aimed at specific drugs.

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74 The same considerations apply to option 3 in the next section.

75 A modified PPRS would continue to apply to NHS list prices (used to reimburse community pharmacies) as at present. Hospitals may continue to negotiate commercial discounts to list prices. However, as explained below, this option would only apply to on-patent brands. Off-patent brands were discussed in Chapter 4.
5.51 We envisage that the cost effectiveness assessments informing price reviews would be carried out by NICE, SMC and AWMSG, which already contain much expertise in health technology assessment. From 2010, they would provide this analysis as a coordinated input into the pricing and reimbursement decision of DH.

5.52 In the medium term, a new, UK-wide Commission on the Value of Medicines would be created, comprised of representatives of NICE, SMC and AWMSG and other key NHS stakeholders that would provide analysis on the cost effectiveness of medicines as an input into the pricing and reimbursement decision of the Secretary of State (in practice a unit within DH). Price decisions would be accompanied by guidance, to explain them to clinicians and budget holders, and encourage appropriate usage.

5.53 In the long term, this body could evolve into an independent institution, taking pricing and reimbursement decisions autonomously. This would require primary legislation to achieve.

5.54 This option does not involve ex ante price reviews. Existing arrangements for ex ante assessments would be retained, under which SMC and NICE (through the STA process) review the cost effectiveness of drugs and issue guidance to prescribers on their use.

5.55 Under this approach the PPRS could in principle continue working to its present calendar of renegotiations every five years, providing a forum for the principles informing new arrangements to be debated between government and industry. The details of the scheme would of course be very different: provisions relating to price modulation and the assessment of profitability would, for example, be replaced by considerations such as the appropriate level of the cost effectiveness threshold. But industry / government dialogue, an aspect of current PPRS arrangements that many companies value, could be retained.

Option two in practice

5.56 Reviews would establish maximum prices of individual on-patent branded drugs at a level fixed to reflect the availability and type of therapeutic substitutes. When a brand’s patent expired it would be reimbursed in relation to the price of a Category M generic once a Category M equivalent was available, as discussed in Chapter 4.

5.57 Many types of drug may command high prices under these arrangements, for example a breakthrough therapy for a previously untreated condition or a drug that would significantly improve the level of patient care provided by existing (perhaps more invasive or inconvenient) non-drug interventions. Drugs launched in areas where several cheap medicines already provide high-quality care would receive less

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76 See Chapter 6. The split of responsibilities is prevalent in many countries, such as Australia, and can enable greater focus on each task.
favourable prices unless compelling advantages over existing treatments could be demonstrated.

5.58 As discussed in Chapter 3, the leading principle applied during reviews would be to set the maximum prices of all on-patent brands in a therapeutic area with reference to an appropriate comparator (such as a benchmark generic, where available). The benchmark for each on-patent product would be chosen to be the best available clinical substitute. The price threshold of a brand would be further constrained by the price (and also the relative clinical effectiveness) of brands that have preceded it on the market. The price of an on-patent brand would exceed the cost of its benchmark product in proportion to the improvement in therapeutic efficacy delivered.77 The rationale for this general approach is set out in Chapter 3.

5.59 Where no drug comparator was available, brands could be priced with regard to a next-best non-drug treatment. In some cases where not even that exists – that is for breakthrough drugs – the maximum price would be defined taking account of every unit of value delivered relative to a placebo. The price may be high, but that is consistent with giving strong incentives to invest in drugs that have a major impact on patients’ lives.

5.60 To price branded drugs with reference to therapeutic substitutes, reviews would evaluate all products in a class at the same time. Therapeutic classes can be defined in various ways, though a natural starting point in many cases could be to consider Paragraphs of the British National Formulary (BNF).78 Since there are around 350 Paragraphs in the BNF this could call for 70 or so reviews per year on a five-yearly cycle.79 We propos that, while all drugs would be reviewed over a five year period (for example, over the five year term of a value-based PPRS) there would not necessarily be gaps of exactly five years between the reviews of any individual drug. Precise timing of group reviews will be function of various factors such as new entry, new clinical data or patent expiry of substitutes.

5.61 Not all reviews would be complex, since some represent very low levels of expenditure. Others contain only a few off-patent products that would revert to generic prices under this arrangement and would not need to be reviewed at all.

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77 As noted elsewhere in this annexe, a moderate ‘brand premium’ over the competitive generic price could be negotiated to capture potential ‘value in variety’ – namely the possibility that different drugs may have different benefits for certain types of patient in ways that have not been demonstrated in RCTs and formal cost effectiveness analysis.

78 BNF Paragraphs are roughly equivalent to ATC3 classifications operated by the WHO and EPhMRA. See Annexe A for details. Clinicians may sometimes consider groups of drugs substitutable in practice to be wider or narrower than this. For example, sustained-release morphine resides in a Sub Paragraph with other drugs that are not appropriate substitutes and that may need to be treated separately. By contrast, the statins are a BNF Section.

79 Hence under this option, individual drugs would experience price reviews at the same frequency as they currently undergo price cuts but different drugs would be on separate cycles, rather than all on the same cycle as today.
5.62 Regarding more complex reviews – in major drug classes containing a number of on- and off-patent products of varying degrees of innovativeness – one aspect that would need to be considered carefully is timing. In a market expected to undergo an event that would change the assessment of cost effectiveness of all products in it – such as a major chemical going off patent or a new product launch – it would make sense to time a review for one to two years afterwards so as to capture the impact. A short wait would give time for generics prices to stabilise as a point of comparison, in the case of a patent expiry, or for clinical practice to fill out the evidence on the safety and efficacy of a new product launch. The timing of reviews could be discussed during periodic renegotiations of a value-based PPRS.

**Mechanics**

5.63 Under this option for reform of the PPRS, the average drug would go through two value-based price reviews during its patent life, before reverting to generics pricing mechanisms.\(^80\) The following applies to prices set during a first review, typically five years post-launch. Subsequent reviews would generally be simpler.

**The cost effectiveness threshold**

5.64 A maximum Incremental Cost Effectiveness Threshold (ICER) would be set for all drugs.\(^81\) Therefore the price of a branded drug could not exceed the level at which its ICER (relative to the benchmark product) reaches this threshold. The manufacturer could price below this threshold. However, once the product has been sold to the NHS at a given price, that price could not subsequently increase until the next review takes place. This is primarily in the interests of budgetary stability for the NHS.

5.65 It could be felt desirable to evaluate the non-patient benefits of drugs and allow those to justify higher prices. Such benefits or cost savings could be assessed using current methods. Whether and how to include them in the process could be one of the high-level questions about a value-based PPRS to be agreed during periodic renegotiations of the scheme.

**Price structure**

5.66 Value-based prices would take account of the relative therapeutic benefits of drugs in different indications and patient subgroups, so as to reward products for the value they actually deliver and provide incentives for efficient marketing. However, it would not be practicable to operate several reimbursement prices for one drug since keeping track of prescribing by indication/subgroup would require data that are not currently available in the NHS and could create a substantial administrative burden.

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\(^{80}\) Assuming the average drug is launched with less than 15 years of patent life left. One source puts the average patent life remaining post launch at 12 years.

\(^{81}\) The level of the maximum ICER would be a matter of debate for the government and the pharmaceutical industry and could be reviewed in periodic renegotiations of a reformed PPRS. As discussed in Chapter 3.
As discussed in Chapter 3, there is a number of possible solutions:

- set a single maximum price for the drug that ensured that it fell below the relevant cost effectiveness threshold in all licensed indications and subgroups
- issue guidance to prescribers on the cost effective use of the drug, and
- negotiate non-linear price structures, including price-volume agreements and rebates, which seek to ensure that in aggregate the NHS secures value for money from the use of the drug.

All of these approaches could be accommodated within Option 2 (and Option 3 below).

Informational and analytical requirements

A pricing authority would be able to employ today’s analytical tools in setting the maximum price of a drug. Probabilistic models of a drug’s effect on the progression of the condition treated are currently used to determine whether a course of therapy costs on average less than the threshold amount per incremental QALY delivered in specific indications or patient subgroups, taking into account that some cases are more severe than others and call for more prescribing. The same models can be used to determine which price would, on average, cost the NHS a given amount per incremental QALY.

Incremental QALYs would be measured across different indications and subgroups, implying several theoretical prices for the same drug. As regards the assessment of the incremental QALYs delivered by a drug in each of the indications and subgroups where it might be prescribed, there are a number of factors to consider. Different forms, salts, metabolites, isomers or modified-release variants of a chemical may add value for some patients but not others. Typically, however, it would not be worth trying to judge the value of different strengths because it is very common to have to titrate drugs differently for individual patients. Today, many drugs are flat-priced across strengths so as not to add economic concerns to the dosage decision. It seems reasonable to retain this feature.

In view of potential data limitations, it would not be appropriate to take an entirely formulaic approach to value-based pricing. Expert judgement should ensure proportional decisions. Involving industry and patient groups in high-level questions such as whether and how to remunerate non-patient benefits should also help build a consensual system in which negative (low price) decisions would be well understood.

The same generic benchmark may not be appropriate for all brands in a therapeutic class if some have licensed indications that the benchmark does not. It may therefore be necessary to have subsidiary benchmarks for some drugs.
As observed above during the discussion of design principles, any modification to the PPRS such as that proposed here would require volumes of information of different types to assess the therapeutic value of drugs in their various applications.

Formal links would need to be established between a pricing authority and many bodies in the NHS to ensure that the most relevant information could be fed through to pricing decisions. Depending on the type of drug being assessed – for example whether it is for an acute versus a chronic condition, whether treatment endpoints tend to be mortality-based or not, or whether the drug is usually administered in hospitals or the community – hospital consultants, prescribing advisors from primary care or academics may be able to provide the most useful insights. In order to be able to work with so much information a pricing authority would need sufficient expertise and credibility to make final decisions in cases of doubt or ambiguity.

Institutions and bargaining

To avoid challenges to decisions, assessment and pricing institutions would need characteristics discussed in Chapter 3 of this annexe, broadly: credibility, fairness and independence.

Compared with options that include some form of ex ante assessment (such as Option three), the bargaining position of the payer would be weaker under this approach. This is because the ultimate sanction of any payer – that of withdrawing reimbursement – would be a less credible threat, as it is more difficult to withdraw reimbursement for a product currently being prescribed (due to patient habituation) than to refuse it for new products. It may therefore be necessary to resort to statutory provisions to ensure maximum prices are adhered to in practice.83

Assessment of Option two

This section briefly summarises some of the advantages and disadvantages of Option two. The key advantages of a value-based approach to pricing are discussed at some length elsewhere in the report (in particular Chapter 3), so we do not dwell on them at length here.

Short run and dynamic efficiency

In short, we think the approach to the assessment of value set out here would both help secure value for money and give good incentives to invest. In particular, this system offers relatively high initial rewards to all brands in a breakthrough class if they offer major improvements in treatment. Once generics begin to enter the market, both existing brands and new launches will only be able to achieve high

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83 Powers to do so are provided for under the Health Act. However, such an approach is unusual internationally. Canada – through the PMPRB - provides an example of a system in which statutory controls on prices are imposed.
rewards where it can be shown that they offer significant therapeutic benefit over the alternatives.

5.78 In the long run, companies will therefore have greater incentives to invest in areas of unmet demand, without being unduly penalised for launching a drug slightly later than the first mover due to chance factors in the development process.

5.79 This approach would also allow for the use of more complex prices. As noted, given the possibility that a drug will have widely varying cost effectiveness over different indications and patient subgroups, the benefits to society from the use of a drug are usually non-linear (typically diminishing with larger volumes). The use of complex prices including rebates can help to reflect this, and align to a greater extent (than under a single price applicable to all volumes) the interests of manufacturers and the NHS. Incentives to engage in unproductive marketing expenditure will be reduced.

Workability

5.80 A potential concern with undertaking regular reviews of this kind is that such an undertaking would be impracticable due to information and resource constraints. However, we do not believe this would be the case in practice.

5.81 This system would result in a workload of 70 or so class reviews per year. However, some of these reviews would be simple (for example, reviews of small classes of drugs containing off-patent products), and others could be timed flexibly to reflect factors effecting the workload, such as the incidence of new launches, patent expiry events, etc. While an increase in the workload of the cost effectiveness bodies would be called for, the increase in costs would be dwarfed by efficiency savings. Chapter 6 sets out in some detail resource estimates.

5.82 QALYs should provide a robust basis for estimates. They are an established convention and directly measure what society cares about, namely how drugs differentially extend and improve people’s lives. Although the use of QALYs has its limitations, the process of converting the results of clinical trials into a pragmatic outcome measurement involves the application of common sense. As discussed in chapter 3, the maximum cost / QALY threshold could be negotiated on a periodic basis between government and industry and would be relatively simple to apply.

5.83 With appropriate institutional arrangements, wider consultation would help to ensure that decisions are proportionate, and that a value-based PPRS would be an accountable and legally defensible use of public resources. Involving industry and patient groups in high-level questions, such as whether and how to remunerate non-patient benefits, could help build a consensual system in which negative (low price) decisions would be well understood.

5.84 To avoid challenges to decisions, assessment and pricing institutions would need to display credibility, fairness and independence. Proposed institutional arrangements are discussed in Chapter 7.
Comparison with ex ante approaches

5.85 Option two retains the benefit manufacturers enjoy under the current PPRS of ensuring rapid access to the market for pharmaceutical products. Most manufacturers therefore seemed to prefer it to ex ante approaches to pricing. However, the major disadvantage is that, relative to the ex ante approach, it delays value-based prices—and therefore the short and long run advantages discussed above. For market segments in which cost effectiveness assessments have a major impact on uptake, it could potentially delay the uptake of cost effective products. In short, the usage of drugs could be distorted if value-based prices turned out to be substantially different from prices set at launch.

5.86 Another potential disadvantage to companies is that, although five years is a reasonable time for efficacy data to become available for many drugs, a purely ex post system provides no way for the payer and manufacturers to agree at launch which data may be most useful to assess different types of drug. The payer may therefore be called upon to interpret available data as best possible, and there is no guarantee that this would best serve all products.

Option three: ex ante value-based pricing

Overview

5.87 This option involves modifications to Option two to address some of the problems identified above. It relies on the same principles of value-based pricing as before but moves further away from the current PPRS by restricting manufacturers’ freedom of pricing for NASs at launch.

5.88 In place of free pricing, this option involves a rapid upfront negotiation of price. Companies would have the option of pursuing either a fast track pricing decision (that is, a maximum price agreed for their product) or, where sufficient information was not available, to take an informed view of negotiating a risk sharing agreement with the relevant authority (see Chapter 6 for a discussion of institutions.) Risk-sharing contracts would set provisional prices at launch and review them at preset intervals in the light of data that both manufacturers and the NHS would generate in the interim. If the data were clear at the time of launch that the drug is not cost effective (for example, the drug is clearly dominated and the company shows no willingness to reduce price) then reimbursement would be refused.

5.89 Although some of the mechanics of pricing differ, the concepts employed would be the same as those under Option two, with branded drugs being assessed, at the level of indications and patient subgroups, for the incremental therapeutic benefits provided relative to a comparator.

5.90 Drugs for which ex ante pricing might be particularly attractive include many medicines prescribed for small groups of patients in hospital settings – such as an increasing number of modern cancer therapies targeted at specific genetic types –
clinical trials available at launch may give a reasonably accurate picture of true clinical efficacy. The controlled conditions of trials, where patients are treated under constant supervision and followed up closely, resemble those in which some hospital drugs are used in practice. Drugs for acute conditions, in which final endpoints are observed over a relatively short period of time, would be natural candidates for such an approach. In such cases it would not be difficult principle to negotiate a value-reflective price at launch. Welfare gains from avoiding slow uptake (such as 'NICE blight' under today’s system) would be large.

5.91 However, manufacturers have stressed to us that ex ante price assessments may not be practicable for all drugs, at least not without substantial delays, which motivates the risk-sharing approach for certain products. For example, the efficacy of a drug for a widespread, chronic condition that is usually managed in primary care may not become clear for several years, before the drug is taken by a large population of patients with different circumstances. Negotiating a value-based price for such a drug using only regulatory data could be more difficult than for a medicine treating an acute condition. Such products would be natural candidates for a risk-sharing approach.

5.92 Prices set by the fast track ex ante process would still be subject to ex post reviews, to take account of such factors as a comparator product going off patent. Such reviews would be essentially identical to those carried out under Option two above. For drugs where risk sharing would be called for, an initial price would be agreed with the manufacturer. Within a range agreed with the cost effectiveness body, the manufacturer would choose the price. A contract would then be written between the Health Departments (or a pricing institution on behalf of them) and the manufacturer to agree:

- what data would be needed to inform a subsequent value-based price (extra trials, observation of clinical practice, further evidence on pharmacological mechanism, etc)
- how the manufacturer, NHS and/or other bodies could be expected to provide such data at reasonable cost
- how any subsequent price would depend on the data provided, by applying the same principles as in Option two (see below)
- when price changes would be implemented
- how repayments would be made between manufacturers and the NHS if launch prices turned out to be higher or lower than value-based prices.

84 The range would be set to reflect the extent of uncertainty regarding a treatment’s efficacy. Thus the upper bound price would highest realistic expectations of benefits delivered by the product. Were the initial price unconstrained under a risk sharing contract, this would give perverse incentives to pursue this option rather than the fast track ex ante approach, even if full information on a drug’s efficacy were at launch.
After any price change following a risk-sharing review, a reconciliation payment would be made between the manufacturer concerned and the Department of Health to compensate for the difference with the initial price over the period between launch and the review. Thus if the agreed launch price was lower than the reviewed level manufacturers would receive compensation for the difference over prescribed volumes in the interim. High interim prices would trigger repayments from companies to government. Reconciliation is intended to make the system as flexible as possible for manufacturers while avoiding perverse incentives to pursue risk sharing rather than the fast track ex ante approach.

We would stress that risk sharing is one possible approach under this option. As discussed below, we recognise that there may be circumstances in which agreeing a contract on these terms is not feasible.

Option three in practice

Fast track ex ante pricing

Whenever data available during the licensing process of a new chemical entity can, with reasonable accuracy, predict efficacy in clinical practice, both manufacturers and the NHS can gain from setting value-based prices at launch. To secure value for money in the longer term, it would still be appropriate to review prices set ex ante after a major comparator lost patent protection. The prospect of such reviews would not unduly constrain the development of innovative drugs, because truly innovative products tend to appear in new therapeutic areas, with generics following after a decade or more.

Many types of drug are used either in hospital settings or in acute treatments in primary care, with the result that the data available from pre-launch trials predicts efficacy in clinical use quite closely (because in practice there is little time and/or scope for factors other than the drug to be responsible for observed therapeutic effects). Examples of such drugs include many treatments for cancer and other serious conditions where mortality is high, drugs used in surgery (for example to suppress immune response to implants and transplants, or certain cardiovascular drugs used only in connection with hospital procedures), and drugs for a wide range of common conditions where efficacy is quickly apparent, such as sleeping disorders or nausea.

As discussed in Annexe B, there is evidence to suggest that positive recommendations increase uptake of drugs, particularly in hospitals. This suggests that for such drugs there would be a real benefit - for patients and companies - in securing an early-stage assessment. It is worth noting that those companies that did express a preference for some form of ex ante assessment tended to be those that operated predominantly in the secondary care sector, where NICE guidance may have the greatest impact.
Risk sharing

5.98 Under this option, a contract could be established for any product where clarity about a value-based price was lacking at launch. Cases where clarity would be lacking include:

- as discussed above, drugs for chronic conditions where efficacy is best assessed over the time or breadth of use following launch
- drugs where the technology or relevance to disease progression are not well understood and further studies could be required
- drugs in classes where new products are known to be in late-stage development and close to launch, or where a major product is about to lose patent protection – and hence where the cost effectiveness of any launch price could change substantially within a short period.

5.99 These examples are not exhaustive and there may be other situations in which drugs would benefit from risk-sharing contracts rather than upfront value-based pricing.

5.100 The data required to establish value over the duration of a risk-sharing contract would vary according to the case. For a new drug for a major chronic condition, observational data from a representative cross-section of primary care use over several years might be most informative (though less data may be needed if the drug were launched into a well established area containing existing products with similar modes of action). For a new launch in a class where a major competitor was about to go off patent and become a benchmark generic treatment, a head-to-head study would help establish relative therapeutic benefits to inform a price for the new brand once generic prices of the future benchmark had stabilised.

Principles and practicalities

Ex ante fast track assessment

5.101 As noted, one of the major concerns of industry concerning an ex ante pricing decision is that it would lead to the sort of delays in gaining reimbursement that have historically been seen in several countries that have adopted this approach. To avoid this happening, it is very important that the assessments should be strictly managed to a fast track timetable.

5.102 There is relevant experience to draw on here. SMC appraisals take four months whereas the new NICE STA process takes an average of six months, including the time given to companies to prepare their submissions. Some STA appraisals have been produced within a very short space of time of the licence having been granted.

Much simpler contracts could be written for drugs where value-based prices are clear ex ante, to provide ways of handling uncertain developments. For instance, in the contract for an innovative new cancer drug, priced ex ante reflecting clear outcomes data, it would be useful to provide for an ad-hoc review to be triggered by the launch of a competing product in future.
5.103 With earlier engagement between companies and cost effectiveness bodies, it should be possible to reach decisions on most drugs swiftly. Where there is genuine doubt about outcomes, the option to pursue a risk sharing contract would avoid the need for a stand off (and hence protracted negotiations) between companies and the NHS.

Risk sharing

5.104 The only previous experience with risk-sharing arrangements at a national level in the UK has been with beta interferon and glatiramer for multiple sclerosis. Following a negative decision from NICE in 2002, the Department of Health in England and manufacturers concerned developed a scheme under which clinical evidence would be collected over ten years and prices reduced if the drugs proved to be less effective than claimed. Although similar in principle to what is suggested here, the design of the MS scheme has been criticised in some quarters. Some of the issues are discussed in the box below. The lesson is that risk-sharing arrangements need to be designed carefully. However, the experience with MS is not overly pessimistic for risk sharing in general because MS is a particularly challenging area in which to assess the efficacy of drugs by any means. The box also discusses a pilot scheme implemented at a local level in England, which dealt with the statins for cholesterol.

Box 5.1: Previous experience with risk sharing in the UK

Multiple sclerosis

The government’s risk-sharing scheme for beta interferon and glatiramer wrestles with a difficult problem. Because multiple sclerosis develops over twenty or more years, no double-blind randomised controlled trials of modern drugs are available. Therefore it was decided to estimate the efficacy of beta interferon and glatiramer by comparing ongoing studies of the drugs with longer-term data on the progression of MS from a cohort of untreated Canadian patients followed during the 1970s and 80s.

BMJ (2003) points out numerous biases that can arise in this artificial recreation of trial conditions. Because much of the ‘placebo’ data is from the old Canadian study, and because patients recruited during the present scheme are mostly given beta interferon or glatiramer, comparisons are not randomised. The circumstances of UK patients today (environmental factors, genetics, etc) are different from those of the Canadian patients from the 1970s and may affect treatment outcomes as much as the drugs under investigation. Assessment is further confounded because multiple sclerosis remains poorly understood.

To properly assess beta interferon and glatiramer, a long-term trial starting in the present day would be required, comparing the drugs either to placebo or head-to-head against therapeutic substitutes such as azathioprine. Under a risk-sharing arrangement, this could mean that the manufacturers of beta interferon may not be fully compensated for twenty years if the drug were introduced at a reasonable price but emerged as a breakthrough therapy. This is the most difficult situation conceivable for a risk-sharing scheme.

Risk sharing may be much easier for some other drugs. In Annexe M of this report we

consider a number of areas where drugs are priced inefficiently under the PPRS as currently constituted. A new launch in any of the therapeutic areas discussed in Annexe M might be amenable to risk-sharing arrangements. Medicines such as proton pump inhibitors for dyspepsia or antiplatelets used in the management of coronary heart disease are either used for relatively short durations or treat conditions with clear clinical endpoints.

Statins

In 1999, North Staffordshire Health Authority, Parke-Davis (now Pfizer) and Keele University collaborated on an ‘outcomes guarantee’ for atorvastatin.87 At the time, North Staffordshire was a low user of statins but cardiovascular disease was a local priority and the HA was keen to disseminate best practice. The scheme was seen as an opportunity to work openly with a pharmaceutical manufacturer to spread the burden of providing useful product information to GPs. It was also aimed at protecting the health service from paying for a drug that did not work – had it turned out to be less effective than claimed or inappropriately prescribed.

Under the terms of the scheme, the list price of atorvastatin set under the PPRS remained unchanged but Parke-Davis/Pfizer committed to reimburse the HA if atorvastatin proved to be less effective than an agreed target in a studied population of patients who were treated to a predefined algorithm (that stated atorvastatin must be used as a first-line therapy, required patients to have clearly documented cholesterol, and made other conditions).

To measure the efficacy of atorvastatin, a matrix was derived from the results of clinical trials, which predicted the percentage of patients treated under the scheme who would be expected to reach target low density lipoprotein (LDL) concentrations at various doses of atorvastatin, depending on their baseline LDL. It was, however, recognized that patients not complying with prescriptions may not reach the target through no fault of the drug. Hence the scheme allowed for non-compliance by 20 per cent of patients before requiring the manufacturer to pay reimbursements.

An example scheme for the future

Under the present option for reform of the PPRS a candidate for an early risk-sharing scheme might be rosuvastatin. But the terms a scheme would ideally differ from those of the atorvastatin scheme detailed above.

Even more than atorvastatin, rosuvastatin has been shown to lower low-density lipoprotein (LDL) cholesterol aggressively. However, although the link between elevated LDL and heart disease is well established, it remains to be seen if very low LDL levels, which could be achieved by rosuvastatin, lead to fewer cardiac events such as strokes or heart attacks either in broad populations or patient subgroups. To date, there have been no large-scale mortality studies involving rosuvastatin.

Ideally a risk-sharing contract would make premium prices for rosuvastatin contingent on clear evidence of reduction in mortality and morbidity. Data could be obtained from observation of clinical practice over three or more years.

5.105 Challenges for implementation are real and will in many cases mean that risk sharing approaches are not appropriate. Nevertheless, we believe that risk sharing is a potentially promising approach for the future for drugs where there is a plausible but

unproven value proposition and there are reasonable prospects of data being available in the medium term to make a more thorough determination.

5.106 In France similar agreements are sometimes used, including when a manufacturer disagrees with the public authorities over the therapeutic assessment of a drug. In such cases, a company is permitted to charge a higher price than would otherwise be granted, on condition of sponsoring an empirical evaluation of the drug’s clinical benefits and lodging an upfront deposit from which compensation is deducted if the evaluation fails to confirm the company’s claims. This approach is often applied to orphan drugs.

5.107 The pricing principles applied under this option for reform of the PPRS would be the same as laid out in Option two since risk sharing is simply a tool designed to elicit information and smooth prices and uptake.

**Mechanics**

5.108 The same considerations would apply to the assessment of value under this option as under Option two.

5.109 For drugs that are most suited to risk-sharing contracts the prospects of them being evaluated at launch as delivering high clinical benefits with reasonable certainty would be low and any value-based price would reflect that. Hence the prospect of a flexible launch price and value-based ex post reconciliation under a risk sharing scheme should be attractive to companies with products suited to the approach.

5.110 Important practical questions to be resolved with risk sharing concern how reviews would be handled. The two principle issues are how reconciliations might be made and how reviews and reconciliations might affect manufacturers’ incentives.

5.111 A danger with reviews concerns the possible reaction of manufacturers when prices would be required to fall from high launch levels. As explained in Chapter 3, the most credible threat that any UK pricing regime can make to a supplier when negotiating prices is to withhold reimbursement entirely. Threats of increasing patient co-payments are not available in the UK and negative guidance has been shown to be only inconsistently taken up. But the threat of withholding reimbursement would lose force quickly once a drug was in use because patients are not easily withdrawn or switched from treatments. Hence there is a possibility that a supplier could enjoy sufficient bargaining power during a risk-sharing review to be able to force up a prices from a value-based level.

5.112 Various measures could be put in place to counter this eventuality. One would be to require manufacturers subject to risk-sharing schemes to pay deposits (into an escrow account) returnable pending cooperation with a price review, following an appeal process if an initial decision was contested. Such an approach has been used in France in relation to orphan drugs. Another possibility would be for existing and possibly future legal powers to be used to fix maximum prices unilaterally.
Institutions that could administer this option for reform of the PPRS, and the legal powers that would underpin them, are discussed in Chapter 7.

5.113 The other main question with reviews is how reconciliations would be paid. In principle this could be done by a central body administering the scheme on behalf of primary care organisations around the NHS, whose financial allocations would be adjusted accordingly.

5.114 On the subject of the structure of payments it is important to note that any of the approaches, discussed in Chapter 3, could apply here. For example, for drugs where arriving at a single value-based price is particularly difficult due to very different clinical benefits being delivered in different indications or patient subgroups (for example clopidogrel or the A2RAs which provide significant incremental benefits to patients experiencing the dry cough on an ACE inhibitor but not to others), a single value-based price could be applied and annual repayments made to reflect estimates of relevant clinical volumes.

Institutions and bargaining

5.115 Ex ante assessment would give greater bargaining power to the payer than Option two, primarily because of the option of refusing reimbursement to a new treatment before it comes on to the market. Therefore the need to have assessments carried out by credible, fair and independent institutions is all the greater. This issue is taken up in Chapter 7. The balance of bargaining power in a risk sharing contract is dependent on the particular terms of the contract, as discussed above.

Assessment of option three

5.116 Since the core principles of value-based pricing applied under this option would be the same as under Option two they are not repeated. Only the incremental features of this option are assessed, such as up front assessments and the possibility of using risk-sharing contracts. Although risk sharing would be very challenging for some drugs it could be practical for certain others.

5.117 The main advantage of this option relative to Option 2 is that the benefits of more value-reflective prices will be felt by the NHS at all stages in a drug’s commercialisation and, for positive assessments, it should help ensure predictable uptake for manufacturers. Benefits in terms of value for money and improved investment incentives would be enhanced. As noted, the onus on institutions carrying out assessments to be competent, fair and to carry out their assessments rapidly would be greater, but if this can be achieved the outcome should be mutually beneficial for the NHS and innovative companies alike.

5.118 A further important advantage is that, unlike Option two, it provides manufacturers with strong incentives to generate information on the cost effectiveness of a product up front.
Perhaps the most novel feature of the option is the facility to negotiate risk sharing contracts. We should note that these would only be used in a limited number of cases – where there is genuine doubt about the efficacy of a drug and reasonable expectations that uncertainty can be addressed within a reasonable timescale.

Risk sharing arrangements can help coordinate the expectations of the payer and manufacturers, allowing for more predictable uptake for manufacturers, and predictable health gains for a given expenditure for the NHS for drugs for which otherwise an agreement may not be able to be reached. There, however, a question as to whether the use of contracts would be overly burdensome to agree and audit, given the information and resource constraints.

While these challenges are real – and will in some cases mean that risk sharing approaches are not suitable – in many cases contract terms should be fairly obvious. For many drugs, NICE decisions already show a keen awareness of the issues and questions to be addressed – the problem is usually missing data.

For drugs used extensively in primary care, initiatives already exist to collate observational data (such as NHS disease networks or the General Practice Research Database, GPRD). For drugs that are experimental or poorly understood, it is reasonable for manufacturers to share the burden of investigating the efficacy and rationale of their product with the NHS. There would clearly be greater costs relating to the funding of large head-to-head trials. Reform of clinical trials has been considered by the Cooksey review, as discussed in Chapter 6.

The question remains outstanding as to whether negotiations over the exact terms of contracts would be protracted, for example due to costs of providing data. There is potential for debate over a number of variables, such as the comparators, patient groups/indications, endpoints and methods of assessment under contracts. A pragmatic approach would be to negotiate these elements for individual products or classes, giving each a chance to make its case for pricing.

However, due to the complexity of the decision, we would expect risk sharing contracts to take longer to agree than fast track ex ante assessments. In relation to the latter, as noted above, the NHS already assesses drugs in a timely fashion pre-launch and the SMC assesses all drugs concomitantly with the licensing process. The new NICE Single Technology Appraisal (STA) process is more involved but has completed within a few weeks or less the licensing for a number of cancer drugs as of late 2006.

**Option four: local price negotiations**

**Overview**

The previous options have considered reforms to the PPRS that would retain the scheme but either modify the profit cap and price cuts, in the case of Option one, or
replace those mechanisms with more value-based alternatives in the case of Options two and three. The remaining alternative we consider is to remove the PPRS entirely.

5.126 Removing the PPRS was explored in discussions during the 1990s, including the 1998/99 negotiations that preceded the 1999 scheme. These discussions led to a joint assessment by the DH and ABPI of the scope, pace of change and practical impact of competition in the supply and use of branded medicines for the NHS. This assessment was unable to find evidence of consistent volume responses to price changes, suggesting that—in the absence of other measures —pharmaceutical companies would not have strong incentives to constrain the list prices charged for branded drugs. We do not believe the position has changed significantly since then (see Annexe J).

5.127 This evidence, and the significant evidence of cost ineffective prescribing, persuade us that there is a continued need for instruments to ensure that the NHS obtains value for money in its purchases. As noted elsewhere in this report, we view this desire on the part of a customer to secure value for money as a necessary feature of competition, and not as a form of regulation. Consequently, we do not regard removing a national level demand side instrument such as the PPRS as in itself a deregulatory measure. Those who have called for ‘deregulation’ appear to be calling for price negotiations at a more local level to substitute for national level instruments.

5.128 We therefore felt it was important to explore what sort of outcomes might be produced through local-level instruments substituting for national level instruments. Thus, in this section we consider an option for reform involving primary care organisations (PCOs) negotiating primary care prices with the suppliers of branded drugs. We recognise that, since this represents the most radical of the reform options, our considerations of its outcomes are necessarily more speculative.

5.129 The prices negotiated under this option depend in the first instance on the potential for PCOs to play off one supplier against one or more others, and hence on the number of substitutes (drugs with similar therapeutic effects) for any particular drug. If a drug has no substitutes, PCOs would have little or no scope to negotiate discounts on list prices. Under this option, then, prices paid by PCOs for drugs with no substitutes would continue to be determined by list prices. By contrast, where a drug does have substitutes, PCOs potentially have scope to negotiate discounts on list prices.

5.130 For PCOs to be able to negotiate effectively with drug manufacturer, two basic requirements need to be fulfilled:

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88 The health service is no different. In every country we examined in our international case studies – including the United States – we found that payers negotiated strongly with companies over the prices they pay.
• first, PCOs themselves must have the incentive to negotiate lower prices—higher expenditure must not simply result in a higher payment from the Government (sometimes known as a hard budget constraint)
• second, in order to be able to play off manufacturers against each other, PCOs must be able to influence prescribing behaviour.

5.131 The first requirement is met to a greater extent under the current NHS structure than in the past. Budgetary pressures are increasing on PCO managers (who can in principle be dismissed through failing to meet financial targets), although it is not true to say that they face a genuinely hard budget constraint. There is much more doubt about the second criterion. As summarised earlier in this discussion, the various prescribing (volume) controls employed by the NHS can be ineffective in their immediate aims of controlling usage.89

5.132 PCOs do seek to influence prescribing through their prescribing advisers. We note however that prescribers may be subject to other conflicting influences, for instance the effects of marketing by pharmaceutical companies in relation to on-patent patent brands. The ability of PCOs to offer financial incentives to primary care practices has even been subject to legal challenge. A detailed description of PCO – prescriber relations is set out in Annexe A.

Mechanics

5.133 In primary care, patients obtain medicines from pharmacies, which are then reimbursed the cost of the medicine by the NHS. At present this reimbursement price is standard throughout the UK and is equal to manufacturer’s list price less clawback. Under this option, each PCO would seek to negotiate a reimbursement price below list price for each drug.

5.134 It would be difficult and costly, if not impossible, for each PCO to reimburse pharmacies at its own negotiated price as this would require separate supply chains for each PCO. Moreover, parallel trade would be likely between different PCO areas, with pharmacies purchasing at a price determined by the lowest negotiated price and earning profits equal to the difference between this price and the price at which they were reimbursed by their patients’ PCO.

5.135 A more practical option is therefore for pharmacies to continue to be reimbursed at a price linked to UK list price, and manufacturers to make periodic repayments to PCOs, representing the difference between pharmacy reimbursement price and negotiated price. Negotiations would therefore be over the discount on list price. It was suggested to us that repayments from manufacturers to PCOs might involve

89 The main difficulty is that such controls mainly take the form of guidance, but varying sources of guidance can conflict and prescribers may face other incentives working in the opposite direction. For example, under the QOF GPs have financial incentives to prescribe drugs that have not been expressly recommended by NICE guidance. Such incentives can override efforts by PCOs to contain usage.
legal problems. If the legal problems are insurmountable, this option would seem to be unworkable (since PCO-specific reimbursement is impractical).

5.136 In principle, negotiated discounts might be made public, or might remain known only to the negotiating parties. If discounts were disclosed, each PCO would tend to become aware of discounts negotiated by others. Discounts for different PCOs might then be expected to converge towards a similar level. Moreover, manufacturers would also tend to become aware of discounts offered by manufacturers of substitute drugs, reducing the incentive to offer discounts in the first place. Disclosure of discounts therefore tends to undermine the bargaining process: the most effective negotiations would require discounts to remain only to the negotiating parties.

5.137 Unlike most purchasers of goods and services (including hospitals), PCOs are unable to negotiate directly on the volume of primary care drugs that they are going to purchase (because they do not control primary care prescribing decisions). Nor do they have the power to refuse to reimburse particular drugs. However, to the extent that PCOs have influence over prescribers, they may be able to negotiate over preferred status with manufacturers of a group of substitutable drugs: the manufacturer offering the lowest price drug would be recommended by the PCO to its primary care prescribers. The attractiveness of preferred status to manufacturers, and hence a PCO’s negotiating power, would depend on how far its prescribers followed its recommendations.

5.138 In some areas, there are already moves being taken negotiation with manufacturers over the cost of drugs for primary care. In particular, a system (STEPS) covering both hospital and primary care purchases is being introduced in Northern Ireland. Manufacturers of drugs for which there are therapeutic substitutes are invited to tender and on the basis of a range of clinical and cost criteria a short list of drugs is chosen. This approach has already been adopted to statins in Northern Ireland, with usage targets applied in primary care for prescribing preferred statins.  

5.139 Prescribers receive financial rewards through prescribing incentive schemes to encourage compliance with targets. The choice of preferred drugs reflects prices, combined with an assessment by stakeholders, in primary and secondary care, of the therapeutic benefits of the statins on the market. However, while the approach has apparently been successful in achieving a consensus with the prescribing community about the most effective statins, it appears unlikely that this process will put real pressure on prices unless it is adopted more broadly across the UK. This is because the price manufacturers are asked to submit as part of the tender process is the list price and it is unlikely that they will be willing to reduce it (thus losing revenues across the UK) in order to obtain preferred prescribing status within a (comparatively) small population of prescribers.

90 The targets are that 70 per cent of statin prescriptions should be for simvastatin and atorvastatin, and that 70 per cent of total prescriptions for these two statins should be simvastatin.
5.140 Hospitals have been procuring branded drugs independently, and at prices often quite different to list prices, for a number of years, though latterly regional and national bodies have helped coordinate their efforts. Despite the differences between primary care and hospitals (in particular the stronger control of hospitals over prescribing decisions, and hence their stronger negotiating position), it may be useful to consider hospital experience in purchasing drugs. This is summarised in Box 5.3. It is conceivable that similar developments might also occur in primary care under this option.

**Box 5.3: Experience in the UK hospital sector**

In England, the NHS Purchasing and Supplies Agency (PASA) arranges National Framework Agreements for the purchase of generics\(^91\) and has begun overseeing a number of pre-existing regional Pharmacy Service Groups that procure branded drugs. PSGs employ variable approaches. Some concentrate on securing volume discounts for specific branded drugs whilst others put out therapeutic tenders in broad disease areas to which all suppliers (manufacturers, wholesalers or parallel importers) of therapeutically substitutable medicines are invited to bid.

Arrangements elsewhere in the UK are quite similar. In Wales, the All-Wales Drugs Contracting Committee organises centralised tenders for both branded and generic drugs, though Welsh hospitals also make some purchases unilaterally. In Scotland, the Scottish Pharmacologists Group and National Procurement Organisation together award national contracts for generic drugs, whilst branded medicines are jointly procured by regional groups of hospitals. In Northern Ireland, the Regional Supplies Service contracts on behalf of hospitals for a large number of drugs, both branded and generic.

As a result of these arrangements, prices obtained on the same branded drug can vary substantially by locality (hospital, consortium, etc) and product. Substantial discounts to PPRS list prices can be obtained if a contract is negotiated by a strong team, for a large volume, or if the product concerned is available from many suppliers or subject to competition from therapeutically substitutable drugs.\(^92\) In other cases contract rates can be at negligible discounts to PPRS list prices, for example when negotiations are less successful or when hospitals are forced purchasers of specialist medications without therapeutic substitutes.

We analysed the discounts that hospitals obtained on list prices and found that discounts were smaller where there was no other drug in the same BNG paragraph. This supports the intuition that purchasers can negotiate bigger discounts where substitute drugs are available.

Note: Hospital purchasing is described further in Annexe A

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\(^{91}\) National Framework Agreements are not legally binding contracts but, rather, negotiated templates of terms and conditions serving as the basis for local contracts. They do quote national prices.

\(^{92}\) Another driver behind discounts is that hospital markets can be 'strategic' for drug manufacturers. Hospitals sometimes initiate treatments requiring lengthy follow-on prescribing in primary care and for which GPs may be reluctant to alter patients’ prescriptions. Manufacturers can perceive gains from offering hospitals low prices on drugs as a ‘loss-leader’. This driver would not affect local procurement in primary care.
Outcomes

5.141 The level of prices under this option compared to other options depends on the negotiating power of PCOs. This depends on two main factors:
- the extent to which drugs have substitutes with therapeutically similar effects
- the extent to which PCOs can influence prescribing decisions.

5.142 Where a drug has no close substitutes, PCOs would have little scope for negotiating discounts on list prices. List prices at the time of launch of such drugs would potentially be constrained, as at present, by factors such as assessments by HTA bodies (NICE, SMC and AWMSG) and parallel trade. However, in the absence of the PPRS price cuts, list prices might not decline after launch, indeed they might increase. Thus prices of drugs without close substitutes would most likely be higher than at present, or under other options.

5.143 Most drugs, particularly those prescribed in significant quantities in primary care, do have therapeutic substitutes, but the prices resulting under this option will depend on the extent to which PCOs can influence prescribing decisions. The actual outcomes are extremely difficult to predict, and are likely to differ between PCOs, but we would stress three points:
- In most, if not all, cases there is a practical limit to the therapeutic substitutability of different drugs. Hence, even if PCOs have high influence over prescribers, non-preferred drugs will continue to be prescribed for some patients (for example, patients for whom they are more suitable than the preferred drug). Each PCO’s non-preferred drugs would by definition not be obtained on preferential terms and prices would most likely be higher than under other options.
- If PCOs have little influence over prescribing decisions, they will have little ability to negotiate discounts and prices overall would most likely be higher than under other options. Key in this respect is the fact that PCOs do not have the power to refuse or withdraw reimbursement status for a drug, which, as noted in Chapter 3, can be an important tool in negotiations.
- If, however, PCOs could effectively influence prescribing decisions, they might be able to negotiate substantial discounts and prices overall might be lower than under other options. However, there is no reason why the resulting price would be in line with therapeutic value.

5.144 As a result of this latter point, negotiated prices might not be consistent with the UK making a reasonable contribution to companies’ return from successful research and development. For illustrative purposes, it is useful to consider the extreme case, where two or more pharmaceuticals companies successfully develop drugs with similar large therapeutic benefits but a PCO effectively plays them off against each other in negotiations. The result could be that the reimbursement price is reduced towards marginal cost and the companies obtain little return on their investment in
R&D (because the company that is successful in the negotiations gets a price not far above marginal cost and the unsuccessful companies get low volume).

5.145 PCOs themselves have incentives to improve health in their area and their interest is in purchasing drugs at the lowest price: they can not be expected to pay higher prices just to reward pharmaceutical companies for their R&D. In general, the interests of more localised decision makers tend to be less aligned with long run incentives to invest and more with short run costs. There are good reasons for this since the population represents a very small proportion of global demand (all of which stands to gain from investment in drugs) so the temptation to 'free ride' is greater. Various countries we have considered in our case studies seem to confirm this view.

5.146 A further potential cost to companies would be the increased transactions costs of multiple negotiations with localised decision markers. Further, the complexities of cost effectiveness assessment are such that there are considerable economies of scale. Diluting available resources over many different actors is not likely to represent the best use of these resources for the NHS.

**Assessment of Option four**

5.147 This option would require PCOs to negotiate prices with manufacturers. It consequently represents a comparatively decentralised solution, with drug prices resulting from direct negotiations rather than arbitrary rules or administrative procedures.

5.148 However, there is uncertainty both about whether this option could be implemented in practice (it would require each PCO to negotiate secret repayments with manufacturers) and about the outcome if it can be implemented.

5.149 Price levels would depend on PCOs' bargaining strength which depends on their influence over prescribing decisions and is highly uncertain.

- if PCOs have little influence over prescribing decisions, prices are likely to be higher than under other options to the detriment of the NHS
- if PCOs have a lot of influence, effective negotiation could push prices very low, but such prices might be below the level that provides a reasonable return on R&D investments by pharmaceutical companies.

5.150 We note that there is considerable uncertainty regarding outcomes under this approach. In the future, with a significantly reorganised NHS, it may become more attractive. But this would require major change in the institutions of the NHS and is not a near term prospect.
6 **RECOMMENDATIONS: ON-PATENT BRANDS**

6.1 Each of the value-based approaches - Options two and three - for reforming the PPRS presented above has particular strengths and weaknesses. However, in our opinion the best long-term arrangement for the UK would be Option three: to replace PPRS profit controls and price cuts with an ex ante value-based approach to pricing. Under this approach, if, at the time of launch, trials data supported the value proposition of the company, a fast track pricing decision would be reached. Where sufficient information is not available at the time of launch, but there is a prospect of it being developed after a period of use in clinical practice, a risk sharing contract could be agreed.

6.2 We recognise, however, that this would require several years to implement. Therefore we suggest that an appropriate transitional arrangement would be to conduct ex post value-based reviews (Option two) in selected high-priority areas.

**Overview**

6.3 We consider Option four to be the most speculative of the options for reforming the PPRS. There is uncertainty both about whether this option could be implemented in practice and about the outcome if it could be implemented. Price levels would depend on PCOs’ bargaining strength which depends on their influence over prescribing decisions and is highly uncertain. If PCOs had little influence over prescribing decisions, prices would be higher than under other options to the detriment of the NHS. To be feasible, the option would require considerable organisational change and is not a near term prospect.

6.4 In relation to Option one, we have considered a range of potential options for modifying the existing instruments of the PPRS. We considered that there is limited potential for incremental change to company level price cuts (beyond the changes that would arise from removing off-patent brands from price modulation).

6.5 We think the case for replacing price cuts with a more binding profit control is weak. We do not think a binding control is feasible for the majority of companies that use resale minus transfer prices, without a very resource-intensive process of attempting to audit data on costs incurred outside the UK. Still less would it be possible to identify an ‘efficient’ level of costs under such a scheme. If profit controls were more binding, the scheme would therefore be more likely suffer from the fundamental incentive problems associated with profit caps (namely, encouraging companies to inflate costs).

6.6 Despite its limitations, the PPRS is sometimes said to have the advantage of stability. This, it is argued, helps companies plan investments (such as R&D activity) at a broad level even if the incentives at the level of individual products are not optimally aligned. The OFT agrees that a stable regulatory environment is an important factor
in investment decisions for a global industry. But we do not assume that the PPRS as currently constituted guarantees such stability in the future.

6.7 An important aspect of the PPRS that seems incompatible with stability is the increased emphasis on one-off price cuts at the start of each new scheme. The trajectory of the price cuts has been rising – from three percent in 1993, to four-and-a-half percent in 1999 and seven percent in 2005. Moreover, price cuts necessarily have an element of arbitrariness since they apply to all branded drugs irrespective of therapeutic value, and are not obviously related to external parameters.

6.8 Since companies have freedom to set prices initially, the more price cuts become a regular feature of PPRS, the more firms are likely to anticipate them in setting initial prices (at the optimal price plus anticipated percentage price cut) particularly towards the end of a given PPRS period. If this continues, price setting risks becoming a strategic game in which firms attempt to guess the level of forthcoming price cuts and DH attempts to double guess this effect in setting the level of price cuts. We do not consider this to be a sustainable model of pricing for the future.

6.9 In short, incremental changes to existing controls would not address our main concerns with the existing PPRS – that neither the profit control nor the price cuts account for the therapeutic value of the drugs they affect. As shown in Annexe J of this report, under current arrangements, drugs that are clinically substitutable sometimes have widely divergent prices. This does not represent value for money. Further, failing to reflect relative clinical benefits in prices could also distort manufacturers’ incentives to invest.

6.10 Other aspects of UK pharmaceuticals policy, such as the creation of NICE, SMC and AWMSG in part compensate for the fact that the PPRS is not value-reflective. While these bodies are regarded as highly expert in the assessment of clinical and cost effectiveness and have made a major contribution since their creation, we believe that the restricted remit they have been given limits the extent to which they can ensure resources are used cost effectively. These restrictions relate, in brief, to: the inability to use cost effectiveness analysis to inform price setting directly; the uneven implementation of guidance93; the fact that not all drugs are assessed; and the fact that existing drugs are not always subject to the same level of assessment as new drugs. These considerations are set out in detail in Annexe B. Our Options 2 and 3 are aimed at relaxing these restrictions.

6.11 In short, we believe there is a compelling case for adopting a value-based approach to pricing within the PPRS, as the best available means of delivering the high-level objectives of the scheme of securing value for money for the NHS whilst providing appropriate incentives for manufacturers to invest in beneficial drugs in the future.

93 For negative recommendations, this partly reflects the inability of the bodies to deny or withdraw reimbursement status.
Many stakeholders have agreed that value-based pricing is attractive in principle but have expressed concerns that it would be costly and difficult to implement in practice. They have also highlighted the key importance of institutional design, given the central role any pricing body would have under such an approach. In the remainder of this annexe, we address both concerns.

First, in the rest of this chapter, we attempt to provide a high-level indication of the benefits that might be expected to accrue from value-based pricing and compare those with the costs of implementation. In the final chapter, we set out proposals for how new and existing institutions could implement our proposed Options two and three in the short, medium and long term.

Costs and benefits of value-based pricing

Value-based pricing can have positive short-run and long-run effects. In this section we explore these effects in greater detail, considering first how inefficient prices can distort company investment decisions (long-run effects) and second how they can undermine value for money and exacerbate rationing in the NHS (short-run effects). We believe these inefficiencies could in part be addressed by adopting a value-based approach to pricing.

The following discussion seeks to capture the order of magnitude of possible costs and benefits of value-based reforms to the PPRS, rather than providing a detailed account. It bears noting, however, that the potential benefits are very large – in financial terms in both the short and long run, and in clinical terms over the medium-to-long run. Benefits are of a different order of magnitude altogether to the costs.

Benefits

The most immediate benefits of adopting value-based mechanisms within the PPRS are set out in Annexe M. They are potential efficiency savings from adjusting the current prices of certain on-patent branded medicines to be more in line with their clinical benefits relative to close therapeutic substitutes available generically. Possible efficiencies run to over £500 million per year. These efficiency savings, which could under an alternative scheme be reallocated to improve access for patients to new and existing drugs, provide an initial indication of some of the gains that could be achieved through value-based pricing.

Substantial further gains may be available over the longer term because setting prices to reflect incremental therapeutic benefits delivered beyond existing medicines would influence manufacturers’ incentives to invest in areas of unmet clinical need. As discussed below, the influence of UK prices on the investment decisions of the global pharmaceutical industry should not be dismissed since the UK affects prices and demand in many other countries through the mechanism of international reference pricing.
6.18 The two tables below summarise savings from the initial exercise to quantify the benefits of value-based pricing conducted in Annexe M. The first shows potential savings on branded drugs where we believe that all current prescribing volumes would be fairly reimbursed at prices near to the cost of closely substitutable generics.

6.19 The second table shows savings on a class of branded drugs where we believe that only some current prescribing should be reimbursed at significantly lower prices than today in order to reflect clinical benefits delivered beyond next-best comparator medicines.

6.20 As discussed in Annexe M, in order to generate the savings shown in both tables we conducted an extensive review of publicly available information on the relative therapeutic efficacy of each branded product (or class) and generic comparator shown. It is assumed that no formally published clinical trials of these products in use have demonstrated clear clinical superiority. We also took advice from a panel of clinicians, pharmacists and pharmacologists to test our views. In relation to the drugs in Table 6.1, we concluded that there is little evidence of clinical superiority for the brands. The products in Table 6.2 do provide significant incremental benefits beyond alternative chemicals available generically in some indications or subgroups.

6.21 In all savings calculations we propose that the brands considered might be remunerated at a rate 50 per cent above current generic prices (the 'brand premium'). This is in recognition of potential clinical benefits that have not been formally demonstrated through RCTs and formal cost effectiveness analysis.

Table 6.1: Savings from reimbursement changes, 2005 volumes

<table>
<thead>
<tr>
<th>Product</th>
<th>Comparator</th>
<th>Generic price plus 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>Simvastatin</td>
<td>£352.00m</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Simvastatin</td>
<td>£28.01m</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>Omeprazole</td>
<td>£91.50m</td>
</tr>
<tr>
<td>Levocetirizine, Escitalopram</td>
<td>Citalopram, Cetirizine</td>
<td>£28.30m</td>
</tr>
<tr>
<td>Cardura XL&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Doxazosin</td>
<td>£10.90m</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>£510.71m</strong></td>
</tr>
</tbody>
</table>

6.22 Savings in Table 6.1 are calculated on the total UK primary care prescribing volumes across all presentations of each brand shown (all branded chemicals in the class in the case of the PPIs). For each branded product, savings are estimated for each

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<sup>5</sup> It should be stressed that the object of this exercise is to provide only an initial indication of some of the gains that could be achieved through adopting a value-based approach to pricing. We stress that the results from this exercise should not be considered as guidance to prescribers. All views are those of the OFT and do not override the conclusions of other expert bodies following a detailed review of the available evidence, including NICE, the SMC, NHS Quality Improvement Scotland and the All-Wales Medicines Strategy Group. In particular, this annexe does not alter the obligations of Primary Care Trusts in England to provide funding for treatments consistent with guidance issued by NICE.
presentation by multiplying 2005 volumes\textsuperscript{95} by the difference between the current list price and an eighteen-month average of the generic (Category M) price, up-rated by 50 per cent, of the equivalent dose of the comparator. Average prices are used for comparator drugs because UK generics prices can exhibit some volatility month by month. We recognise in relation to atorvastatin – which represents a high proportion of potential savings – that efforts have been made to reduce prescribing rates in 2006. Therefore we might expect current volumes – and potential savings – to be somewhat lower than those shown here.

<table>
<thead>
<tr>
<th>Product</th>
<th>Comparator</th>
<th>Volume</th>
<th>Generic price plus 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2RAs</td>
<td>Generic ACE Inhibitor</td>
<td>60% of 2005 total UK prescribing volumes</td>
<td>£64.0m</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>£64.0m</strong></td>
</tr>
</tbody>
</table>

6.23 The approach in Table 6.2 is the same as above except that savings are calculated on only 60 per cent of total primary care prescribing for the angiotensin II receptor antagonists (A2RAs). This is because, as set out in Annexe M, current prices for these products seem to be value-reflective in some patients but not others. In our view, these products represent potential strong candidates for price / volume or rebate agreements, since the current linear price structure arguably gives companies the wrong incentives to incur marketing expenditure.

6.24 It must also be noted that we would not expect gains estimated on the basis of prescribing volumes observed in 2005 to persist indefinitely. The products considered in this assessment will go off patent in a few years. We would argue that, in the absence of a value-based approach to pricing, there is a greater possibility of drugs continuing to be prescribed in the future at prices that do not reflect their value, but it is difficult to speculate on medium term outcomes at this point.

6.25 As set out in Annexe M, even assuming a reduction in the prescribing of atorvastatin in 2006, there are potential savings of more than £500m a year in the near future.

\textsuperscript{95} Volumes used in these calculations are taken from Prescription Cost Analysis (PCA) data. PCA data records volumes dispensed by community pharmacies and reimbursed by the NHS in units (for example, tablets and capsules) rather than packs. By contrast, price sources like the BNF and UK Drug Tariffs quote the cost of packs (usually 28 units where tablets or capsules are concerned). Our approach was to divide prices listed on a per-pack basis by 28 to convert them to a per-unit basis, before multiplying the price difference \([\text{target drug} - \text{comparator drug}, \text{up-rated as relevant}]\) by the volumes of the target drug to obtain savings. Sometimes drugs are available in other pack sizes (such as 56) where the price per unit is different from packs of 28. In such cases it would be impossible to predict future expenditure as we do without making assumptions about the pack sizes likely to be dispensed. However, this is not an issue for most drugs considered in this annexe, which in primary care are only available in packs of 28. Note: Savings are not calculated for a number of presentations of branded PPIs for which there is no generic equivalent. These include special forms of some of the chemicals (such as injections or dispersible tablets) and combination products (usually a PPI plus an antibacterial).
resulting from the products above and a number of other areas of inefficient expenditure where we have not published savings in this indicative exercise. Even a fraction of these savings from our preliminary exercise dwarf the likely extra financial costs of setting up institutions to run a reformed PPRS which, as discussed below, should be under ten million pounds a year even under the most resource intensive approach.

6.26 However, the implications of value-based pricing are wider than this simple comparison of immediate costs and savings would suggest. The savings could be reinvested in improving access for patients to drugs and other healthcare interventions and improving the supply of useful drugs in the future. We take up these issues below.

Short-run benefits – value for money and patient access to healthcare

6.27 When the prices of prescription medicines do not reflect their relative therapeutic benefits the NHS may obtain poor value for money in the short run. This is a problem because the UK drugs bill is around 12 per cent of the total NHS budget, so obtaining poor value for money on some drugs can mean inefficiently diverting limited resources from other drugs and non-drug interventions.

6.28 Box 6.1 below investigates the question of how expenditure on some drugs might constrain healthcare budgets that could be put to other uses – and exacerbate problems of rationing in the NHS. But it is important to stress that implementing value-based prices should not simply achieve savings on the drugs bill to be spent on other interventions. Savings on poor value drugs might also release resources for other valuable, but high-cost, medicines.

Box 6.1: The effects of inefficient drug prices on access to healthcare

The resources available to the NHS for expenditure on drugs and other healthcare interventions are limited. This implies that, if the price of a treatment is out of line with its relative therapeutic value, the NHS is not making the best use of its funding to improve patients' health. More value-reflective prices would achieve a better outcome for patients, allowing wider access to therapies on a timely basis. The precise mechanisms by which resources are allocated in the NHS and access to treatments may be restricted are complex, and discussed in some detail in Annexe A.

It should be noted that drugs budgets are not fixed. Primary care organisations\(^\text{97}\) receive needs-based funding which they have discretion to allocate to a number of uses, including primary care prescribing and hospital commissioning, according to local requirements. We

\(^{96}\) As explained in Annexe M, in order to publish savings estimates for drugs we had to undertake detailed analysis of the clinical evidence before inviting comments from companies concerned and their lawyers. It was not feasible to undertake this process for all areas of potentially inefficient expenditure that are subject to debate within the NHS.

\(^{97}\) Primary Care Trusts (PCTs) in England and ('Local' or ‘Area’) Health Boards in Wales, Scotland and Northern Ireland. Often in the text we use the shorthand ‘PCT’ to refer to primary care organisations across the UK because the acronym ‘PCO’ has a historical connotation in England.
have heard from PCTs that, in attempts to balance their budgets, they sometimes respond to high drug prices by rationing access to other forms of healthcare. Such rationing can affect commissioning of simple elective procedures in hospitals (such as hip operations or cataract removals, which may either be cut or have waiting lists extended) as well as services directly provided by PCTs.

For many drugs prescribed in primary care, a high price will not necessarily result directly in curtailed use. The fact that some of the drugs reviewed in this annexe enjoy very high prescribing rates despite doubts over their cost effectiveness demonstrates this. Furthermore, evidence provided in Annexes C and A shows that GPs are not generally sensitive to (or at times aware of) the prices of some of the largest-selling drugs in the UK. The situation may be different for prescribers in hospitals, who are more likely to be sensitive to prices.

There are some categories of drugs where rationing does take place on cost grounds. For example, it is likely that access to ‘high-cost’ drugs (meaning high cost per patient rather than by total expenditure) may be directly curtailed as a result of inefficiently high prices. PCTs have mechanisms for restricting access to certain high-cost drugs (in some cases requiring approval of prescribing decisions on an individual basis or only agreeing to fund a certain level of prescribing over a given period). As drugs become increasingly tailored to smaller patient groups and specific genetic profiles, this rationing of access to expensive therapies may become a more significant issue in the future. To help ease access it will be necessary to address the prices of less cost effective treatments that are nonetheless prescribed in very large volumes.

For other drugs, the means by which PCTs are able to constrain expenditure are likely to vary by locality. These approaches, including the use of prescribing advisers and financial incentives to affect prescriber behaviour, are discussed in Annex A.

While PCTs’ ability to constrain expenditure varies significantly, there is some evidence to suggest that this behaviour has, in aggregate, had a material impact on patients’ access to drugs. An example of restricted access is provided by the anti-TNFα therapies for inflammatory arthritis. In March 2002, NICE approved the use of the ‘anti-TNFs’ for people with severe rheumatoid arthritis for whom alternative treatments had failed. But a survey in 2005 by the British Society for Rheumatology found that a third of rheumatologists consulted were prevented from prescribing anti-TNFs in accordance with NICE guidance by PCTs, usually citing resource constraints.

At a more general level, in August 2006 the King’s Fund published a report highlighting large variations in the amount different PCTs in England spend on three major disease areas in which drugs are a central part of treatment: cancer, heart disease and mental health. In each area the difference in expenditure between low-spending and high-spending PCTs was around eight-fold. The report observes that PCTs are allocated funds by the Department of Health on the basis of local health and demographic needs so it is natural to observe some variations in expenditure. Heart disease, for instance, might be more prevalent in one PCT population than another. But even after adjusting for needs, the report observes that a high-spending PCT can devote four times more resources to cancer, heart disease or mental health than a low-spending peer.

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98 The survey was conducted jointly by the BSR and the Arthritis and Musculoskeletal Alliance (ARMA). See http://www.rheumatology.org.uk/public_affairs/armabsrtnfsurvey/
These differences in needs-adjusted expenditure could reflect many factors. High-spending PCTs may face local needs or costs that are not taken into account accurately enough by the resource allocation formula. Or they might achieve better health outcomes than are required by the government’s National Service Frameworks for major diseases, perhaps reflecting the preferences of local populations. But variations are also consistent with PCTs restricting access to drugs on expenditure grounds.

While practice varies between PCTs, many companies have suggested to us that the mechanisms they employ can be fairly blunt and focus more on reducing cost in the short term rather than achieving value for money. This is one of the motivations for using cost effectiveness assessment to inform price directly – to give local decision makers greater assurances that drugs prescribed are cost effective at prevailing prices and to avoid the need for using volume controls to contain expenditure.

**Long-run effects – investment incentives**

6.29 If the prices of drugs reflect their value to patients and broader society companies will be given efficient incentives to invest in pharmaceuticals in the future. These issues are addressed in greater detail in Box 6.2, which reviews some therapeutic areas in which there is unmet demand, shows the importance of UK prices in global demand and hence demonstrates how a value-based approach to pricing could improve incentives to invest in these and other priority areas.

**Box 6.2: Potential gains from value-based pricing in the long term**

When the prices of medicines do not reflect relative therapeutic benefits the investment incentives of firms can be distorted. Specifically, companies may not face strong incentives to invest in drugs that are most beneficial to society and may conversely be encouraged to spend large sums developing products that offer scant improvements to patients over existing alternatives. This can be bad for public health in the long term, leaving patients without effective treatments to combat their diseases.

The World Health Organisation has identified many ’pharmaceutical gaps’ in serious conditions where it is not profitable for private sector companies to research effective treatments.100 Some examples of missing medicines according to the WHO are:

- An effective treatment for acute stroke;
- New antibiotics to replace older products rendered ineffective by overuse (and associated microbial resistance);
- Antidepressants with proven efficacy in children and the elderly;
- Effective antibacterials for a number of conditions prevalent in developing countries including: malaria, tuberculosis, leishmaniasis and trypanosomiasis;
- Technologies to complement drugs in many areas, such as a heat-stable formulation of insulin or better diagnostic tools for Alzheimer’s (for insights into how the onset of

the condition differs from the usual process of ageing, which could improve understanding of the current generation of controversial drugs where efficacy is debated).

The recent Cooksey review of the UK health research funding also identified several priority therapeutic areas that are likely to present increasing health challenges in the UK, such as cancer, mental health, diabetes, asthma and arthritis.

Against this backdrop of need, the drugs that generate the biggest revenues globally tend to be for conditions that are chronic, non-fatal (at least for many patients for a long time) and for which there are several substitute therapies with similar characteristics and efficacy. Examples of such conditions include dyspepsia and high cholesterol. Commentators sometimes call these sorts of pharmaceuticals 'me-too' drugs. We do not think it is useful or accurate to divide drugs crudely into 'innovative' versus 'me-too' categories. Many innovations are incremental in nature, bringing benefits to patient groups that may be poorly served by existing drugs. Such benefits can take the form of more effective treatments or reduced side effects and it is key to securing value for money that any such incremental benefits be reflected in prices.

The concern we address in this report is that, for some drugs we review in Annexe M, relative price differences do not appear to reflect relative incremental benefits. To the extent to which this is true, prices will be out of line with value and will not give helpful incentives to companies to invest in drugs in the future.

Value-based prices might bring huge gains over time to the extent to which they could drive investment in areas of clinical need. Such gains are clearly difficult to quantify, however, since we do not know today what drugs could be produced tomorrow under helpful incentives. We also recognise that improving investment incentives depends on many variables, not least how pricing regimes around the world interact with countries' science and industrial policies. As well as pricing, other factors in the profitability of drug development include the cost of R&D, which is determined by the regulatory process in leading markets, notably the US and Europe. In the UK the Cooksey review has considered how costs of development could be reduced, and public funds better targeted, so as to improve success prospects for new medicines in some therapeutic areas.

But price is undoubtedly a central concern in getting investment incentives right. UK prices are particularly important in this regard. Annexe D of this report investigates the effect of UK prices on the incentives of global firms to invest in new drugs. Although the UK is a small market in terms of prescription volumes, it exerts a disproportionately strong influence on global prices due to the fact that public health services in many other countries follow the UK's lead in pricing new drugs. Countries accounting for around 25 per cent of world pharmaceuticals sales reference the price of a proportion of their products to prices in the UK.

**Resource implications of reforms**

6.30 Several companies indicated to us that they see merit in the principle of value-based pricing, but were concerned at the resource implications of any move in this direction. It is clearly right that reform only be implemented if the benefits outweigh the costs. Accordingly, in this section we consider the likely costs to the public and private purse of implementing a value-based approach to pricing.
To be conservative, we attempt to estimate the costs of the most resource-intensive, long term option that we consider in Chapter 7 – namely, the creation of a separate body charged carrying out both ex ante reviews for all new active substances and ex post reviews covering the all BNF paragraphs over a five year period. In practice, the resource implications would likely be much less than this. In a transitional period, for example, only a handful of reviews would be carried out.

**Public Resources**

Within the NHS great resource is available to administer both the transitional and long-term options for reform that we propose. NHS personnel involved in healthcare evaluation are among the most experienced in the world. However, we believe that this expertise should be coordinated to a greater extent than at present, to make best use of existing resources at a devolved and local level.

**Resources of existing cost effectiveness bodies**

NICE, SMC and AWMSG are natural candidates for conducting the cost effectiveness analysis required to implement value-based pricing. As set out in Annexe B, they represent a combined resource and expertise that is almost certainly unmatched in any other country. NICE’s assessments in particular are considered a gold standard for technology appraisals around the world. But improvements could be made. In particular, the bodies need to coordinate to a greater extent than at present on medicines HTAs, addressing the current situation in which certain drugs are assessed ex ante both through an SMC appraisal and though a NICE STA.

The institutional proposals we set out are designed to make best use of existing resources through greater coordination while also recognising the proper distinction between devolved and national responsibilities. The box below sets out a broad brush estimate of the additional resources these bodies would require to implement our proposals.

**Box 6.3: Existing resources of cost effectiveness bodies**

This box considers the resources which NICE, SMC and AWMSG currently use to conduct work of a very similar nature to the economic modelling that would be required under our proposed reforms to the PPRS. We consider in Chapter 7 below, on the implementation of reforms, how these and other bodies, as well as clinicians from around the NHS, could work within a new scheme. At this point we merely compare resources employed today with those that might be required in future health technology assessments (HTA).

**Current workload and resources**

At present, NICE in its STA and MTA processes conducts around 30 Technology Appraisals per year. This figure slightly overstates the level of medicines appraisals because it includes other appraisals such as those of medical devices. The AWMSG has historically undertaken around ten drug reviews per year, generally in areas not scheduled for a NICE appraisal. In 2006, however, AWMSG announced plans to more than double its work programme. The SMC assesses all drugs launched in Scotland, though in less detail than a typical NICE appraisal. In
the past four years of its work, SMC has increased the number of reviews carried out each year: in 2005, 87 reviews were undertaken. Many of these were reviews of new strengths or new indications of existing drugs rather than new drug reviews. Among all the bodies, NICE publishes the most thorough analyses that can take up to 14 months (but often less) for MTAs. The shorter STA process is closely coordinated with the final stages of licensing and lasts only six months.

The capacity to carry out drug reviews varies between the cost effective bodies. AWMSG has about 14 voting members and 10 non-voting members and employs few staff in cost effectiveness evaluation. The SMC employs about 60 full-time staff. In addition it has around 100 decision-making members and draws upon the advice of a clinical panel of over 200 experts. NICE employs a total of 235 staff. Within NICE, the Centre for Health Technology Evaluation and parts of the various other directorates are involved in the process of pharmaceutical cost effectiveness appraisal and implementation.

NICE publishes the most detailed annual report of its accounts and has a budget of just over £30 million. Similar detailed accounts for SMC or AWMSG were not available. NICE employs 41 people directly in the Centre for Health Technology Evaluation. The budget for the Centre is just under £3 million, producing a direct cost per Technology Appraisal of about £100,000. However, to include a contribution to other directorates and corporate overheads, we have uprated this estimate to £150,000 per appraisal. Thus the HTA budget to review the current level of 30 appraisals, including a provision for overheads, amounts to approximately £4.5 million or £150,000 per appraisal. These estimates are generous compared to the costs of drug appraisals carried out in other countries (see Box 6.5), but this reflects the fact that NICE’s appraisal process is more in-depth and rigorous than in many other countries.

**Future workload and resources**

Under a value based approach to inform pricing decisions, the current level of health technology assessment would need to be scaled up. Our assessment of the future cost implications considers the most expensive option – that of conducting ex ante reviews for all New Active Substances (NAS) and ex post reviews covering all drug classes over a five year period. Therefore the estimate represents an upper bound estimate of resource implications, only likely to be incurred in the long run.

On a five-yearly cycle, this option would require up to 90 appraisals on an annual basis of either specific drugs or closely related groups. This covers both ex ante reviews for drugs newly introduced to the market and ex post reviews for existing drugs. The breakdown of the 90 appraisals is as follows: 20 ex ante reviews and 70 ex post reviews. The estimate of ex ante reviews required each year is based on the current number of new active substances introduced to the UK market.\(^{101}\) The level of 70 ex post reviews is based on information from the BNF. The BNF consists of around 350 paragraphs and is a comprehensive directory of drug classes. Covering all paragraphs over a five year period would require 70 reviews a year. However, reviews will be of varying intensity. Some paragraphs contain very low levels of expenditure or may consist solely of generic products. The reviews conducted to date by NICE have tended to focus on difficult or contentious areas. Fewer resources would be needed for less problematic drugs. Further, the fact that reviews in some areas have already been completed would reduce the

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\(^{101}\) Academic research suggests that 20 NAS per year is also close to the historical average. See (Jeffreys DB, Leakey D, Lewis JA, Payne S, Rawlins MD (1998). ‘New active substances authorised in the United Kingdom between 1972 and 1994’, British Journal of Clinical Pharmacology, 45:151-156.)
amount of resources needed because assessment could draw on analysis already carried out. Therefore we assume that for the 40 additional ex post reviews required to be carried out per year, the required resource will be half that for the 30 current reviews, or £75,000.

Summing up, a rough estimate of required annual resources would be 20 ex ante and 30 ‘resource-intensive’ ex post reviews at £150,000 each and 40 less resource-intensive reviews at £75,000, for a total of £10.5 million. This would be allocated among the three bodies in accordance with their workload. This compares with NICE’s current expenditure on HTAs of £4.5 million per year.

In total, the option would represent an increase in expenditure among the existing bodies of less than £6 million. It should be noted that we have not taken into account, in producing this estimate of additional resources, the fact that the existing resources of SMC in particular would make a significant contribution to the workload, since we do not have budgetary information on SMC.

Our estimate is conservative because it does not account for economies of scale and scope. This may mean that the incremental costs of HTA required by our reforms could be lower than our initial estimate – or at least not significantly higher if unpredictable factors are allowed for.

Other bodies in the UK

6.35 Under the medium term approach set out in Chapter 7, a separate pricing unit within DH would carry out the pricing reviews on the basis of a cost effectiveness assessment. Staff within the current PPRS team and Commercial Directorates would be natural candidates to staff the unit, as they are used to price negotiations with manufacturers and also have an informed sensibility to the wider policy setup of the NHS. We have assumed an additional £500,000 per year to meet additional resource requirements for the unit. This would bring the estimate of total costs required to a maximum of £11 million and of additional resources required to a maximum of £6.5 million per year. Needless to say, these are broad brush estimates and would need to be worked up in full were our recommendations to be implemented.

6.36 It is also worth noting that, although not formally included in our estimates, there are many other bodies and resources in the NHS in addition to those mentioned above involved in evaluating the clinical benefits and costs of medicines. These include the National Prescribing Centre (NPC), which disseminates knowledge about health technologies around PCTs in England through training programmes, workshops and published guidance. It also liaises with leading manufacturers about the products in their pipelines that are nearing launch, issuing reports to the NHS about their likely impact on clinical practice, service delivery and budgets. The NPC has a core staff of about 30, not including trainers working in PCTs.

6.37 Primary Care Organisation across the UK also include many experts, such as prescribing advisers, whose role is to appraise the cost effectiveness of drugs as they are used in local populations.
Comparison with other countries

6.38 As a guide to whether our resource estimates are reasonable, we have reviewed the resources employed in value-based pricing schemes in a number of other countries. It should be noted that differences between countries’ systems in terms of remits, budgeting structures and the depth of assessments mean that comparisons are not straightforward. For example, it is widely recognised by international peers that NICE undertakes probably the most detailed economic modelling of any evaluation body in the world. Bureaus abroad sometimes base appraisals on economic models submitted by manufacturers, allowing them to evaluate more drugs with fewer resources. But even adjusting for this, the resource estimates we have assumed look generous in comparison with those employed in other countries.

Box 6.4: Resources of other countries

More detail on all of the healthcare systems referred to below appears in Annexe K of this report, which accounts for case studies of health care systems abroad undertaken by the OFT in ten leading countries.

Canada (CADTH, CDR and PMPRB)

The Canadian Agency for Drugs and Technologies in Health produces HTA on medical devices and drugs for the federal, provincial and territorial governments to assist them with their reimbursement decisions. Within CADTH, the Common Drug Review (CDR) is a recently introduced process to synchronise drugs reviews for all publicly funded drug programmes.\(^{102}\)

The CDR carries out ex ante reviews. These are based on requests from the publicly funded drug programmes and from manufacturers’ submissions, which tend to cover most new drugs launched in Canada.

Ex post price reviews are carried out by the pricing body, the Patented Medicine Prices Review Board (PMPRB). The PMPRB is charged with reviewing the maximum allowable price of patented drugs. This involves a range of activities including international reference pricing to seven countries. The PMPRB will review prices of all drugs on a six month basis. The CDR decision on reimbursement is a separate process from the PMPRB pricing decision but these two bodies engage in close information sharing.

The CDR has a budget of around $4 million (£2 million, prorating for corporate administration as with NICE) and internal staff of 3.5 FTE clinical reviewers and 2 FTE health economists (though some of its work is contracted externally). The PMPRB has a budget of around $5 million (£2.5 million) and has a staff of 42 FTE.

Sweden (LFN)

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\(^{102}\) This process applies to the federal, provincial and territorial publicly funded drug programmes except for the province of Quebec.
The public pharmaceuticals benefits board for Sweden, LFN, decides on the reimbursement status and sets the price of outpatient medicines.\textsuperscript{103} The LFN carries out ex ante drugs reviews and applies cost effectiveness analysis to inform its decisions, but does not negotiate on price with the manufacturer. As of 2002, the LFN has begun a process to review all existing publicly funded licensed medicines. The LFN intends to complete this review by the end of 2009.

LFN has 30 employees and a government grant of approximately 60 million SEK per year (about £4.5 million). To be able to appraise all prescription medicines funded by the Swedish public healthcare system with this relatively modest budget, LFN draws on outputs produced by other bodies (such as NICE).

**Australia (PBAC & PBPA)**

The Pharmaceutical Benefits Scheme (PBS) applies both ex ante and ex post cost effectiveness evaluation to all drugs listed for public reimbursement in Australia. (Re) evaluations take place every year, and can cover the entire 700 or so products (3,000 or so presentations) listed on the PBS. Cost effectiveness appraisal is carried out by the Pharmaceutical Benefits Advisory Committee (PBAC) whilst price negotiations are the responsibility of the Pharmaceutical Benefits Pricing Authority (PBPA).

The PBS employs 168 staff\textsuperscript{104} and has a budget of AUS$46 million (about £18 million) for 'departmental outputs', which include the work of the PBAC and PBPA as well as policy advice, programme management and the delivery of specific agents (for example drugs with special storage requirements). In practice, a small proportion of the £18 million in PBS 'departmental outputs' will be spent on work comparable to HTA undertaken by NICE costing £6 million, but we have not had access to disaggregated budgetary information for the purposes of this exercise.

**Private Sector Resources**

6.39 As well as considering the resource implications of a value-based pricing system on the public sector bodies responsible for its implementation, costs to pharmaceutical companies should also be considered. Costs to pharmaceutical companies of submitting information to cost effectiveness evaluation bodies may increase as more reviews would be required per year under a value-based pricing system.

6.40 However, some of these costs would be offset as under the proposed system companies would only be required to submit ex ante reviews to a single cost effectiveness body. This contrast with the current system, in which they are required to submit to two different bodies (SMC and NICE through the STA process), which have differing processes of evaluation, thus requiring potentially differing submissions.

\textsuperscript{103} The LFN sets both the wholesale and retail price.

\textsuperscript{104} Source: Budget Statement, Department of Health and Ageing 2005/2006.
6.41 More importantly, more efficient price structures should result in better incentives for efficient marketing and thus lower marketing costs. In fact we believe any increases in required informational expenditure caused by a move to value-based pricing could entirely be offset by reduced marketing costs. That is, resources could be reallocated from marketing to submission of cost effectiveness information on drugs. It would only require a small reallocation of marketing spend to achieve this: 2004, £850 million was spent by AFR companies on marketing drugs in the UK.

6.42 We recognise, however, that, in a more value-conscious NHS, it is important to support companies in developing robust cases for the cost effectiveness of their products. Several recommendations to help companies do so are discussed in the recent Cooksey Review of UK health research funding (December 2006). We welcome the recommendations of the Cooksey Review and see them as a natural complement to a value-based approach to pricing. The review and its relationship to value-based pricing is discussed further in Box 6.5.

**Box 6.5: Value-based pricing and the Cooksey Review**

The Cooksey Review has explored ways of increasing the rate at which basic research translates into healthcare interventions yielding clinical and economic benefits. On the subject of drug development the Review identifies a number of challenges in bringing new products to market.

The Review explains how developing a new drug has become an increasingly costly undertaking in recent years, in part due to the informational demands placed on manufacturers:

- The licensing process has become lengthier and more complex, increasing costs of compliance and reducing the effective patent life of a typical new medicine at launch;
- Health Technology Assessment (HTA) by NICE, SMC and AWMSG adds further costs of compliance at the end of the development process.

Other trends have also contributed to diminishing the profitability of innovation, such as a move towards developing more ‘personalised’ medicines that treat subgroups of patients with a condition (such as specific genetic types). Development costs per patient treated can be higher for products with small markets than for the last generation of ‘blockbuster’ drugs for widespread chronic conditions such as cholesterol, hypertension or dyspepsia – where ‘easy wins’ in terms of medical breakthroughs have mostly been had.

To reduce the average cost of developing a new chemical entity, major challenges will be to reduce the failure rate of candidate molecules – at least those reaching relatively late stages of development – and to increase the uptake and profitability of truly useful new drugs. To meet these challenges of easing ‘the critical path’ of drug discovery, both licensing authorities and the NHS, on the one hand, and the pharmaceutical industry, on the other, will need to show flexibility and address their appetites for risk.

The Cooksey Review calls for several new arrangements to ease the critical path,
including:

• A systematic programme of pilot studies of conditional licensing for new drugs at relatively early stages, allowing for initial use by specialists but not GPs;

• A more thoroughgoing approach to HTA, expanding it to cover a greater proportion of NHS activities and introducing assessment earlier in the development process;

• The creation of disease registries within the NHS HTA programme, to enable more effective tracking of the safety and efficacy of drugs in practice, where issues such as patient compliance and off-label prescribing can inform relatively low-cost research to augment the clinical value of drugs;

• Use of the forthcoming NHS National Programme for IT (NPfIT) to automate and expand on the measures described above.

Value-based pricing would be supported by the measures outlined above, all of which would generate more information, and earlier, about drugs than is available at present.

Conclusion

6.43 We believe there is a compelling case for adopting a value-based approach to pricing within the PPRS, as the best available means of delivering the high-level objectives of the scheme of securing value for money for the NHS whilst providing appropriate incentives for manufacturers to invest in beneficial drugs in the future.

6.44 In this respect, we believe either Options two or three would represent an improvement on current arrangements. But although the two options apply the same underlying principles they each raise different practical challenges. Taking up the system of ex post reviews proposed in Option two would involve fewer changes compared to today and allow companies commercial freedom in pricing newly launched drugs, but the trade-off would be a delay in achieving value-reflective prices and, possibly, delays in the uptake of cost effective treatments.

6.45 The ex ante value-based approach in Option three addresses these concerns and is therefore our preferred option. Fast track ex ante assessments would provide a rapid, pragmatic approach for most drugs. The option to pursue a risk-sharing contract offers the promise of being able to assess the therapeutic benefits of individual drugs in the most open-minded and case-specific way possible but would call for more administration and negotiation.

6.46 However, in the discussion above we argue that the NHS and other UK public bodies – including NICE, SMC and AWMSG – possess ample specialist clinicians and expertise in Health Technology Assessment (HTA) compared to numerous other countries that appraise every new drug at launch and review public reimbursement listings annually. The additional funding we estimate would be required to implement ex ante value based pricing would result in an overall resource base that would be far more generous than that currently employed in these other countries. The greater
robustness and rigour of HTA in the UK would therefore be maintained under our proposed reforms.

6.47 In the next chapter we consider how the institutional framework to implement our proposals could be structured in the short and long term. To allow reasonable time for a new system to be implemented, we propose that the reforms proposed in option three commence from 2010, when the current PPRS is due to expire.
7 RECOMMENDATIONS AND INSTITUTIONAL FRAMEWORK

Summary of recommendations

7.1 We recommend that Government work towards reforming the PPRS, replacing the existing profit cap and price cuts with a value-based approach to pricing. We believe that both of the value-based pricing options we have identified would be a major improvement on current pricing arrangements, helping to secure value for money for the NHS and avoiding the increasingly arbitrary nature of PPRS controls.

7.2 However, in our opinion the best long-term arrangement for the UK would be Option three: to replace PPRS profit controls and price cuts with an ex ante value-based approach to pricing.

7.3 For standard branded generics for which there is a bioequivalent generic supply subject to category M pricing, pharmacies should be reimbursed at the category M generic price.

7.4 For originator brands for which there is a category M equivalent, pharmacies should be reimbursed at the category M generic price (plus a maximum of 25 per cent).

Institutional and legal framework

7.5 The rest of this chapter sets out a proposed legal and institutional framework to administer our recommended option for reform of the PPRS. We focus on the framework for the operation of a fully reformed value-based PPRS over the medium and long term, starting from when a new scheme would be renegotiated, in 2010.

7.6 Most companies have told us that it would be a mistake to introduce wholesale reform overnight. We agree. We recognise that new institutions and procedures cannot be introduced precipitously, without a risk of undermining the quality of analysis and robustness of process on which a successful value-based approach to pricing depends.

7.7 We recognise that there are provisions for conducting a Mid-Term Review of the scheme as set out in Section 6 of the agreement:

‘6.1: In the event of major changes affecting the supply of medicines to the NHS, either party may request an interim review after two and a half years. Following such a review the terms of the scheme may be varied with the agreement of the ABPI and the Secretary of State.

6.2: If the terms of this scheme are altered with the agreement of the ABPI and Secretary of State, companies will be invited to accept the new terms. They will have the option of leaving the scheme as set out in Chapter 9.’

7.8 Whether to implement such an option is a matter for Government and ABPI to consider. If this option was adopted, it might be possible to phase in arrangements
on a transitional basis. Any such approach would have to be discussed between industry and Government, however.

7.9 Rather, the focus of this chapter is on medium and long term arrangements, during which, under our preferred approach, profit controls and price cuts would be phased out and replaced by:

- ex ante reviews to be conducted for all New Active Substances coming onto the market, and
- ex post reviews to be conducted of all drug categories over a five year period.\textsuperscript{105}

The medium term

7.10 We propose that under a fully reformed PPRS starting from 2010, maximum prices for branded drugs would be set on value-based principles. The cost effectiveness analysis required to form a view on value-reflective prices would be undertaken by NICE, SMC and AWMSG. The work between the bodies would be coordinated by agreement between the UK health departments.

7.11 In the medium term, these bodies would not be able to set prices or make reimbursement decisions on their own account. Any revised NHS list prices or rebate regime would have to be formally negotiated with companies by the Secretary of State for Health. In practice, we propose that a pricing unit within DH carry out this task, on the basis of analysis carried out by NICE, SMC and AWMSG.

7.12 Part of the appeal of this framework is its practicality since it would be unlikely to require new legislation. It reflects the fact that pricing decisions are not devolved, but are made at a UK level.\textsuperscript{106} At the same time, most aspects of devolved arrangements would be untouched because devolved bodies would continue to exist in their present form.

7.13 We believe that there are important benefits to this since NICE, SMC and AWMSG have built up institutional expertise and credibility within the UK – indeed we heard repeatedly on case study trips undertaken for this study (see Annexe K) that NICE is increasingly perceived as a world-class HTA body. Thus we propose that the pharmaceutical appraisal activities undertaken by NICE, SMC and AWMSG would be coordinated through a UK-wide programme of drug appraisals, to ensure efficient use of these resources. The other activities of NICE and the work of SIGN in Scotland would be unaffected.

7.14 Clinical guidelines (as produced by NICE and SIGN, for example) would have the same purpose and status as at present. Pricing negotiations for branded drugs should

\textsuperscript{105} As noted, some of these reviews, covering paragraphs that are uncontroversial or account for low levels of expenditure, would be very light touch.

\textsuperscript{106} We believe that there are good reasons for this – multiple prices within the UK would lead to problems of parallel trade, creating supply side instability.
inform, but be conceptually separate from, broader views of appropriate care across entire clinical pathways. There will be a case for close coordination between SMC and SIGN, to ensure that clinical guidelines reflect not just clinical but cost effectiveness considerations. All non-medicines guidance would continue to be produced on a devolved level.107

7.15 We envisage that the DH pricing unit would be staffed primarily by staff from the current PPRS team and the Commercial Directorate, given the experience of both in company negotiations and medicines policy.

Overview of the medium-term scheme in practice

7.16 The proposed operation of the scheme in practice is set out in Figure 7.1 below.

7.17 NICE, SMC and AWMSG would undertake the cost effectiveness analysis needed for ex ante pricing and associated ex post reviews as well as risk-sharing schemes. For each drug appraised, one of the bodies would take a view on a cost effective price but pass its conclusions to a pricing unit in DH to negotiate the final terms with manufacturers, on behalf of the devolved health departments.

7.18 The key challenges to be addressed in such a system, which would make use of existing cost effectiveness bodies to inform pricing decisions, is how to ensure coordination of effort and consistency of approach.

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107 NICE, for example, would continue to produce guidance on interventional procedures, public health promotion activities and devices.
Given the volumes of work generated by assessing all drugs on value-based principles, the devolved health departments would agree on a work programme to divide up assessments between the three bodies. This coordination mechanism would avoid duplication of effort and ensure that best use is made of existing resources in conducting HTA assessments.

A further advantage to any system under which all drugs would be assessed by NICE, SMC and AWMSG would come from removing the need for the current referrals process by which NICE is passed drugs to assess by DH. The process of deciding which drugs are to be assessed by NICE, described in Annexe B of this report, is itself time-consuming.

The need to achieve consistency of approach is central if key stakeholders are to have confidence in a value-based pricing system. We recognise, however, that significant differences in approaches currently exist between the three bodies. Under current arrangements, there are differences in terms of which types of drugs are reviewed and how the HTA process is carried out by the bodies. As discussed in Annexe B, the approach of NICE is generally regarded to provide the most in-depth and robust analysis.
In the short run, a pragmatic solution would be to make best use of the respective strengths of the bodies in the allocation of assessments through the work programme. As noted, assessments will vary significantly in terms of complexity of analysis required and resource input needed. For instance, a review of an uncontroversial class of established drugs or the assessment of a new strength of an existing medicine may be relatively straightforward and could be conducted using a lighter touch approach. Alternatively, a new class of innovative drugs or a complicated treatment class may require a more robust, in-depth assessment. The division of work between the bodies should take account of these resource differences. This does not imply inconsistency but rather a proportionate use of resources.

A UK-wide programme of drug appraisals, however, implies the need for greater coordination and consistency in the approach adopted by the bodies. We think a useful measure could be the establishment of an ‘HTA Pharmaceutical Forum’ as part of the medium term approach to value based pricing. NICE could initially host this forum, which would give the bodies an opportunity to discuss HTA issues arising from their input into the pricing process. The bodies could benefit from information exchange (e.g. methodologies) to better inform their work, which could lead to improved and more harmonised approaches where needed.

The work programme would set out in principle how ex ante and ex post appraisals would be divided between NICE, SMC and AWMSG although officials in the UK Departments of Health may need to show flexibility when assigning individual appraisals, according to short-term capacity constraints. We would not wish to preempt decisions on the division of economic modelling, but certain ways of working suggest themselves.

NICE and SMC currently review drugs at launch, and so between them already have well developed skills and processes to conduct the analysis to inform ex ante price setting required under our preferred option for reform. NICE and AWMSG, and the academic centres, which today undertake in-depth evaluations of drugs that have been on the market for some time, have the skills needed to manage ex post reviews and risk-sharing schemes. Further, the in-depth assessment of NICE might be more be more appropriate for evaluation of some of the more challenging NAS, while the more rapid, less resource-intensive approach of SMC and AWMSG would be suited for swift reviews of less controversial areas.

In practice, the scheme would work as follows for new drugs. A manufacturer would submit a proposed price to NICE, SMC or AWMSG, along with relevant cost effectiveness evidence. This would require the early stage engagement between manufacturers and NICE, SMC and AWMSG that the Cooksey review has recommended, as discussed above.

If the appraising body considered that, at the given price, the evidence indicated the drug would fall below the relevant cost effectiveness threshold in all indications, the drug would be recommended to the NHS. Recommendations would take the form of
guidance similar to that issued today by the SMC (and NICE through the STA process) in the assessment of new drugs at launch.

7.28 If the drug fell above the relevant threshold in some or all indications, the appraising body would publish an assessment indicating its view of the maximum acceptable price (in each indication if the prices varied). This information would inform the subsequent price negotiation that would be carried out by DH.

7.29 If the appraising body determined that there was sufficient uncertainty about outcomes, there would be an opportunity to consider risk-sharing or 'only in research' recommendations. The appraising body would publish its view to inform DH's pricing negotiations. The published assessment might include estimated volumes for each indication and, in the case of a risk sharing contract, the clinical data that would be required to inform future assessment.

7.30 Once DH received the appraising body's view, the DH pricing unit would then attempt to negotiate an agreement on the basis of the evidence provided by NICE, SMC or AWMSG. It would negotiate with manufacturers on both price level and structure, which may include, for example, rebates, or brand premiums.

7.31 Once a pricing decision was reached between DH and the manufacturer, the drug would be included in the NHS for reimbursement. At this stage, the appraising body that conducted the initial cost effectiveness appraisal would issue guidance on the use of the drug to the NHS to aid prescribers and to inform future clinical guidelines. An agreement would be required whereby the guidance of each of the bodies would apply across the UK.\(^{108}\)

7.32 We believe this transparency should give prescribers and health authorities greater confidence that any future prescribing would be cost effective, which should in turn improve uptake. The ability to negotiate an appropriate price structure should mean that restricted recommendations would be less frequent under a value-based PPRS. However, the facility to issue restricted recommendations would still exist.

7.33 Where an agreement between the manufacturer and the pricing unit could not be reached, NICE, SMC and AWMSG would issue negative guidance. For new drugs in this situation, reimbursement would be refused by the Secretary of State.

7.34 In all cases, but especially those where refusal of reimbursement would be a realistic prospect, it would be important to have in place an appropriate appeals process for cost effectiveness decisions issued by NICE, SMC and AWMSG. As under current arrangements, the appeals process would be internal to existing bodies.

\(^{108}\) There are precedents for such agreements. Since the establishment of a formal link with NICE in July 2006, guidance from NICE is to be implemented in Northern Ireland and NICE interventional procedures cover the whole of the UK.
Similarly, an appeals system would need to be in place for price negotiations between DH and the manufacturer. This accountability mechanism would promote stability and transparency in the new pricing and reimbursement process.

In addition, any pricing scheme in an EU member state must be compliant with EC legislation, including the EC Directive relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems (Directive 89/105/EEC the 'Transparency Directive') and provisions in relation to State Aid, competition law and the free movement of goods. Certain decisions taken under a UK pricing scheme would, potentially, also be open to the scrutiny of judicial review.

In practice, as elaborated upon in Annexe G, the Transparency Directive is not prescriptive as to the particular form of a pricing scheme, but rather sets the high level principles to which it should adhere – in particular that pricing and reimbursement decisions should be made on the basis of 'objective and verifiable criteria'. It also imposes certain procedural requirements. Almost all cases successfully brought under the Transparency Directive have related to a failure to keep within the prescribed time limits or to provide reasons for decisions.

This objective could therefore be met by a wide variety of forms of pricing scheme, providing the institutions that implement them had robust and fair processes.

We would expect that, at least in the short run, the period for drug review would not be significantly different from the current time lines in place. There may be economies of scale as the bodies expand their scope and role in the drug review process. The pricing decisions would need to be well coordinated with the appraising bodies to ensure that HTA assessments, pricing and reimbursement decisions were carried out in a timely manner. Some assessments could in principle be produced within a few weeks of a marketing authorisation being issued. To achieve this would require the early stage engagement between manufacturers and NICE, SMC and AWMSG that the Cooksey review has recommended.

Of particular relevance in interpreting this requirement is UK (R (on the application of Pfizer Ltd.)) v. Secretary of State for Health [2003] 1CMLR 19 in which Court of Appeal was asked to consider the decision of the Secretary of State that Viagra was not to be reimbursed on the NHS. It was alleged that the decision to restrict the use of Viagra, on the basis not of clinical or cost effectiveness but rather on the Secretary of State’s assessing the need it addressed as having a lower priority than other calls on NHS funds, failed to contain a statement of reasons “based on objective and verifiable criteria” as required by Article 7. Lord Justice Brown held on the contrary that, “For the criteria to be ‘verifiable’, all that is necessary is that they should be published and available, in particular to would-be importers, to satisfy themselves that they do not contain disguised restrictions on intra-Community trade. And the measures are ‘objective’, in the sense used by the Court in Duphar, if they are based on a legitimate aim, that of improving the economics of the state health system.”

Annexe G provides further details.
7.40 Once an agreement on prices had been reached between a company and the DH pricing unit, we would envisage that the company would not be able to increase prices unless or until a further review had been carried out.

7.41 As regards products on the market at the time our proposed reforms would begin to operate, we would envisage that their reimbursement prices would remain at then prevailing levels until reviewed by NICE, SMC or AWMSG. This would mean that such products would not be subject to further price cuts, but also that their prices could not be increased until such a change had been demonstrated to be cost effective. There would be no price modulation under this system.

Legal status of the medium term

7.42 The Health Act 1999 currently, but from 1 March 2007 the National Health Service Act 2006 (‘NHS Act 2006’), enables the Secretary of State to make a statutory scheme replacing the PPRS or to negotiate any other voluntary agreement with the pharmaceutical industry, for the purpose of limiting prices or profits of manufacturers or suppliers of NHS medicines across the UK.¹¹¹

7.43 It would be desirable for arrangements for the medium term to be negotiated through a voluntary agreement between ABPI and the UK Health Departments. We consider the likely status and content of any such scheme at the end of this chapter. If this were not possible, the Secretary of State could use the NHS Act 2006 powers to establish a statutory scheme.

7.44 The institutional framework set out here would therefore rely on existing legislation. Pricing would rely only on powers already held by the Secretary of State under the NHS Act 2006.

7.45 In relation to the mechanism for ensuring coordination between the three cost effectiveness bodies, the legal situation is relatively clear for NICE and SMC but somewhat less so for AWMSG.

7.46 In respect of NICE, section 28 of the NHS Act 2006 (replacing section 11 of the NHS Act 1977 from 1 March 2007), permits the Secretary of State to "...make such further provision relating to a body established under subsection (1) as he considers appropriate." These powers apply to NICE and would seem to be sufficiently broadly worded so as to permit provision to be made as to NICE co-operating with SMC and AWMSG.

¹¹¹ Health Act 1999 section 35, read with section 38. To be replaced from 1 March 2007 by NHS Act 2006 section 263, read with section 266. See Annexe G for details.
With regard to SMC, acting essentially as a consortium of Scotland’s Health Boards, section 2(5) of the NHS (Scotland) Act 1978 provides the means by which its relationship with other bodies can be legislated for.  

The legal situation of AWMSG is less clear because it is not covered explicitly by legislation in the way that NICE and SMC are. As with the other bodies, AWMSG would need to agree to participate in the reforms to the PPRS proposed here. Further steps to formalise the relationship would include securing agreement from the Welsh Assembly Government Health Department.

### Longer-term options

Into the longer term it may be considered desirable to extend the joint working arrangements proposed above. This section briefly considers the issues. We stress, however, that these ideas represent only one option for a long-term direction of travel and would not be desirable before the arrangements proposed above had bedded down. Any transition would be necessarily gradual.

One longer term option would be to formalise the coordination between NICE, SMC and AWMSG through the creation of a Commission on the Value of Medicines (CVM) that would direct the HTA activities of NICE, SMC and AWMSG. Pricing would continue to be carried out by DH using the Secretary of State’s powers under the NHS Act 2006. Ultimately the Commission could take over the responsibility for negotiating prices with manufacturers, becoming an independent Medicines Pricing Commission (MPC). While establishing the CVM may require only secondary legislation, the MPC would need to be underpinned by primary legislation. We discuss these institutional proposals in turn.

### Commission on the value of medicines

The CVM would comprise members drawn from NICE, SMC, AWMSG, the MHRA and other institutions, ensuring that all four countries of the UK were represented. Further members relevant to specific decisions, such as clinical and academic specialists in specific disease areas, would be drawn in on a case-by-case basis from a list of accredited individuals. Preferably, at least one clinician, one pharmacist and one pharmacologist would contribute to the price recommendation for every drug considered. All members of the commission would be required to be free of conflicts of interest.

Detailed economic evaluation would continue to be carried out by NICE, SMC, AWMSG and the academic centres as an input into the decision making of the CVM.

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112 ‘In carrying out the purposes mentioned in subsection (1) and in exercising any function otherwise conferred on them by or under this Act each Health Board shall act subject to, and in accordance with, such regulations as may be made, and such directions as may be given, by the Secretary of State; and such regulations and directions may be made or given generally or to meet the circumstances of a particular area or matter.’
Common standards governing their processes would be developed through the CVM. Clinical evaluation would be carried out by specialists from the NHS as at present. To ensure consistency in viewpoints, existing and new clinical networks would appoint liaison members to inform CVM decisions.\(^{113}\)

7.53 The CVM would retain many of the advantages of our proposals for reform outlined above. For example it would help ensure efficient use of HTA assessment resources across the UK, while reflecting the legitimate desire to have many important functions – notably the provision of clinical guidelines to prescribers – produced at a devolved level. Bodies from the separate countries of the UK, such as NICE, SMC and AWMSG, would directly influence prices across the UK but continue to exist in their present form.

7.54 The figure below illustrates how the CVM might work in practice. The model of an independent body providing cost effectiveness evaluations as an input into the pricing decision of a separate authority is one that has been employed to good effect elsewhere, notably Australia (see Annexe K).

**Figure 7.2: Commission on the value of medicines**

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\(^{113}\) Many clinical networks exist in the NHS, from local initiatives to those for major conditions such as heart disease and cancer, led (in England) by National Directors.
Medicines pricing commission

7.55 A longer term option would be for the MPC to replace the CVM as a body with legal authority for making pricing and reimbursement decisions. In principle, a number of measures could be used to underpin the independence of the MPC. Principles for appointing and dismissing members and their length of tenure could be set out in legislation for example. There may be a case, with a genuinely independent MPC, for a separate appeals panel to consider contested decisions.

7.56 The revised process is shown in the diagram below, which illustrates how the MPC would work in practice.

Figure 7.3: Medicines pricing commission

The case for an independent pricing body

7.57 There are arguments for and against a fully independent MPC. In principle, it seems reasonable to strive to remove political influence from essentially technocratic decisions on the consistent pricing of the clinical value of medicines – which can only properly be determined by specialists.

7.58 Furthermore an independent pricing body could help create stability and improve investment incentives by providing a mechanism by which Government could credibly commit to paying reasonable prices to companies in the future. In a variety
of policy fields, Governments have successfully created independent bodies with clear objectives set down in statute in attempts to improve dynamic incentives. The Bank of England and independent utility regulators provide examples. Creating an independent pharmaceutical pricing body would be consistent with this broader trend towards the use of constrained discretion in policy making. It would also be consonant with the thrust of recent policy proposals in relation to the health service: these have suggested that the NHS should be run more independently of ministerial intervention, through the establishment of an NHS board.

7.59 However, we regard this framework as a long-term possibility for a number of reasons. First, it would require legislation to implement – both to give the body, on a UK wide basis, pricing and reimbursement powers currently accorded to the Secretary of State and to bolster its independent status, as set out above.

7.60 Second, while some companies have seen merit in the creation of an independent body in principle, it would take time for the policies and processes of a new PPRS, and the working practices of the CVM, to establish a track-record of credibility and fairness with companies. Once pricing decisions had been shown to be robust and fair and, ideally, to improve uptake of cost effective medicines in the NHS, moving to an independent structure would be more tenable.

7.61 Third, the current expertise of the main constituent bodies of the Commission is in the field of technical analysis and assessment rather than commercial decision making. It would therefore take the body time to build up the capacity for commercial negotiations.

7.62 Ultimately, we think that either model set out here – either the medium term or long term approach – could work. There are examples of effective systems in other countries based on either of these approaches (see Annexe K).

Policy input and the role of PPRS

7.63 In both the medium term and long term structures, we think there could be an important role for a PPRS-style agreement between industry and Government, to provide high-level input into pharmaceutical pricing and reimbursement arrangements.

Voluntary or statutory scheme

7.64 A feature of the current scheme to which key stakeholders attach some importance is the fact that it is a ‘voluntary’ as opposed to a ‘statutory’ scheme, as defined under the NHS Act 2006. It is therefore worth considering to what extent a voluntary scheme could be preserved in the future.

Commitment problems are discussed in greater length in Chapter 3.
It should first be noted that, under the NHS Act, a voluntary scheme is simply a scheme that is agreed with the relevant industry body, as opposed to a statutory scheme, which is established by the Secretary of State in consultation with the industry body. It is the agreement of the industry body, as opposed to individual companies, that defines a voluntary scheme. Almost all schemes in the world are voluntary in the broader sense of requiring agreement between companies and payers over the acceptable price of an individual drug.\textsuperscript{115}

A question that has been put to us is whether a voluntary scheme could be agreed under a value-based approach to pricing. By definition, such an approach distinguishes between products that are particularly valuable and those that are not and hence creates winners and losers between individual companies. It might therefore be argued that it will be more difficult for an industry body to secure the agreement of all its members – particularly the less successful innovators - to such a scheme.

However, we would argue that the current scheme also creates winners and losers between individual companies precisely by failing to distinguish between them on the basis of the value of their products. Under current arrangements, those companies that are producing particularly cost effective products, for example, lose out by accepting an price cut that is applied equally to all companies irrespective of the value of their products (as opposed to one that is targeted on areas of inefficient expenditure).

Therefore, to the extent to which securing a voluntary agreement is problematic in the future we believe this will apply to the current structure of the scheme just as much to a value-based PPRS. It is perhaps to be expected that companies with divergent interests will find it difficult to agree on the details of a scheme the mechanics of which will have very different financial implications for them.

Nevertheless, international experience shows that the broad parameters of value-based schemes can be agreed between governments and all relevant companies. For example, every four years the French Government negotiates a Framework Agreement with manufacturers in order to control pharmaceutical pricing and reimbursement. The agreement outlines the general lines of decision-making and the methodologies by which the government evaluates the therapeutic benefits of medicines.

We believe that a future value-based PPRS - if it can be agreed on a voluntary basis - is likely to focus more on high level principles, to which all companies can subscribe, than on detailed mechanisms. We set out some thoughts on the areas that may be covered under a future scheme below.

\textsuperscript{115} As discussed in Chapter 3, such agreements are the result of bargaining between companies and payers and either party can decide not to enter in to an agreement (purchasers by refusing to reimburse the product in question and companies by refusing to supply).
A value-based PPRS

7.71 A future value-based PPRS would clearly be a different sort of document to the present agreement, containing high level principles for the conduct of reviews and setting out certain key parameters. Perhaps the most important among these would be the cost/QALY threshold that should apply to assessments. Chapter 3 gives some considerations as to the factors that should be taken into account in setting this threshold.

7.72 We think it is appropriate that this threshold be determined in discussion between industry and Government, given the significant impact it has on NHS expenditure and companies revenues.116 This would become increasingly important under any system in which pricing and reimbursement decisions are delegated entirely to an independent authority.117

7.73 Other matters that might be set out in a PPRS agreement might be which costs and benefits to consider in the assessment of the cost effectiveness of a medicine (for example, whether to include benefits to carers and whether to include non-NHS costs) and priorities of social equity such as the appropriate treatment of orphan medicines.

7.74 The document would therefore be a higher level policy document than at present. It would not be prescriptive as to the details of the methodologies and procedures to be followed by the Commission – these would be set out in guidance that the Commission itself would issue. Moreover, it would not provide the main mechanism for enforcing decisions – in most cases the bargaining position of the payer would be underwritten by the ability to refuse reimbursement or, in the case of the risk sharing approach – through separate contractual mechanisms.

7.75 The PPRS would, rather, constitute a broad framework agreement within which more specific pieces of guidance operated and individual contracts negotiated. Negotiations would take place every five years or so, as at present. The scheme would therefore continue to provide a forum for industry / government dialogue, an aspect of current PPRS arrangements that many companies value.

Conclusion

7.76 The medium and long term arrangements proposed here would provide a practical basis for implementing a value-based pricing regime in the UK, ensuring efficient use

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116 Under current arrangements it seems to us to be exposing NICE, SMC and AWMSG to excessive pressure to expect them to develop an appropriate cost effectiveness threshold without guidance or input from central Government.

117 An alternative approach is that the body be allocated a fixed drug budget (the size of which would be determined through periodic negotiations), from which a cost / QALY would be derived. The arguments for and against this approach were discussed in Chapter 3. As noted there, we think it is an option that should be considered for the long run.
of HTA assessment resources across the country, while reflecting the legitimate
desire to have many important functions carried out at a devolved level. By building
on existing expertise within the NHS we believe they will provide a robust and
flexible framework for a new, value-based PPRS in the long term, delivering benefits
to patients and innovative companies alike.