Department of Health

# Ministerial Industry Strategy Group

*Long-Term Leadership Strategy*

The Association of the British Pharmaceutical Industry

# Contents

# Foreword by the Co-chairmen

The pharmaceutical industry is an outstanding example of a sector in which UK industry is truly world class. It provides significant health benefits through the medicines and vaccines provided to UK patients in areas such as cancer, diabetes, asthma, cardiovascular disease, and other areas of priority for the NHS.

In addition to providing health benefits, the industry contributes significantly to the UK economy through investment in research and development, in manufacturing, and through direct and indirect employment.

In 1999, the Pharmaceutical Industry Competitiveness Task Force (PICTF) was created to maintain and improve the competitiveness of the industry to allow sustained investment in research and development of new medicines. The Ministerial Industry Strategy Group (MISG) was set up to oversee implementation of the recommendations made by PICTF.

Five years on, we believed that it was time to take another look at some of the key issues facing the industry and to set the agenda for how the Government and the UK-based pharmaceutical industry can work together more effectively. Our goals were two-fold: to sustain and grow the important contribution the industry can make to the healthcare received by patients in the NHS; and to facilitate the industry contributing to the Government's target of increasing private sector investment in research and development to 2.5 per cent of GDP by 2014.

We decided to develop a *Long-Term Leadership Strategy*. We identified three particular issues where progress needed to be made:

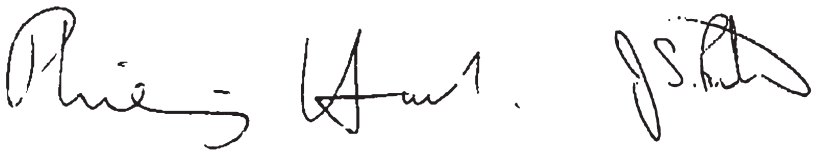
1. The NHS and industry working more effectively together to provide increased access for patients to cost-effective new medicines;
2. The UK Government working with the European Commission and Member States to improve the European environment for the pharmaceutical industry, through the Commission's High Level Pharmaceutical Forum;
3. Improving the regulatory environment for medicines.

In deciding to look at these three areas we were very much aware of the important initiatives already underway to improve how clinical research is undertaken in the NHS. We did not want to duplicate this work, but considered that the work of the Long-Term Leadership Strategy and that on research should be viewed as a package to improve the

overall environment for pharmaceuticals, hence the summary of our progress on clinical research in Chapter 5.

Sir David Cooksey recently published his Review of UK Health Research Funding. It sits alongside this Strategy, and in particular the vision of the UK environment in ten years that we have developed.

This work has been taken forward collaboratively, and we thank everyone involved in developing such a comprehensive and forward-looking Strategy. One of the important challenges for us now is to translate this joint working into practice. The provision of services is changing and innovative local partnerships can bring benefits to the NHS and the industry, but more importantly to patients. There is an important opportunity to embrace the use of cost-effective medical innovation offered by modern pharmaceuticals, both in the UK and across Europe.



**Lord Hunt**
Minister of Health
for Quality

**John Patterson**
Executive Director,
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# Executive Summary

## Introduction

1. The Ministerial Industry Strategy Group (MISG) was established in 2001 to facilitate growth of the UK pharmaceutical industry by addressing some of the key strategic issues affecting it. MISG also monitored the implementation of the Pharmaceutical Industry Competitiveness Task Force (PICTF) report, that made a number of recommendations about how the environment for the pharmaceutical industry could be improved. PICTF was co-chaired by Lord Hunt and Sir Tom McKillop.

2. The UK is home to a world-class pharmaceutical industry, with almost a fifth of the world's top-selling 100 medicines being discovered and developed in the UK. The industry contributes significantly to the UK economy by employing over 70,000 people in the UK in highly skilled jobs and generating another 250,000 jobs in related industries.

3. Pharmaceutical companies invest around £3.2 billion in research and development each year in the UK, approaching 25 per cent of total private sector investment in UK research. The industry also has a significant manufacturing base in the UK, with annual exports of around £12 billion.

4. In the face of an increasingly challenging global environment for the industry, MISG decided in July 2005 that it needed to be more proactive in understanding and engaging in the issues faced by the industry at a European level. It also saw the need to make the domestic environment more attractive to assure patient access to new cost-effective medicines and to encourage more investment in research and development. It established the Long-Term Leadership Strategy with the aims of:

   - securing the provision of safe and effective medicines for patients, and to advance healthcare innovation;
   - strengthening the environment for the pharmaceutical industry in Europe; and
   - improving efficiency of medicines regulation in the UK and Europe.

5. To achieve this the Strategy focused on three main areas:

   - improving the relationship between the NHS and industry to support the better use of cost-effective medicines;
   - supporting the European Commission's plans to improve the competitiveness of the European Pharmaceutical Industry through the High Level Pharmaceutical Forum; and
   - considering what is needed to improve the effectiveness of medicines regulation.

6. This work was taken forward by three working groups co-chaired jointly by government and industry, and including other relevant stakeholders.

7. MISG recognised that it was important to look beyond these medium-term goals, and produced a vision of what the UK environment for medicines should look like in ten years. This vision, alongside the recommendations for biomedical research and drug development from Sir David Cooksey, provides a direction for policy development in this area in the coming decade. The MISG will seek to integrate these efforts and take responsibility for realising the vision.

8. The Long-Term Leadership Strategy should be viewed alongside the initiatives underway on clinical research – the UK Clinical Research Collaboration and the Government's national strategy for health research in the NHS set out in *Best Research for Best Health*, and other initiatives to strengthen the UK science base – to provide a comprehensive view of the work being taken forward to improve the environment as a whole.

## Partnership Working Group

9. The Partnership Working Group was asked to explore ways in which the NHS and pharmaceutical industry could work in partnership to make the best use of medicines for the benefit of patients.

10. From the work undertaken it was clear that past experience of joint working between the NHS and industry was mixed. Where such projects worked well there were benefits for patients, the NHS and industry, although the benefit might be different for each of the stakeholders. To support joint working for the future, the working group developed recommendations that would improve attitudes within the NHS and industry towards joint working through (more detail in Chapter 2):

- guidance from the Department of Health on joint working for the NHS;
- a best-practice toolkit; and
- ongoing training for both the NHS and industry to encourage mutual understanding, trust and cooperation.

11. The analysis of the use of medicines in England showed a mixed picture. It found that there has been an increase in uptake across England in all of the therapeutic areas included in the analysis. The rate of increase varies quite substantially, with the biggest proportional increases in newer therapies. In terms of overall prescribing, geographic variation in prescribing:

- is higher in secondary care than in primary care; and
- reduces the longer a drug has been on the market.

12. To help reduce this variation, and improve the use of cost-effective new medicines, the working group developed a suite of recommendations under the following themes (more detail in Chapter 2):

- optimising system capacity and clarifying roles, so that a whole system approach can be taken to adoption of innovation to secure benefit to patients;
- evolution of financial and planning systems such that they support and promote adoption of innovation;
- provision of information for the NHS on uptake of new technologies that can act as a driver for improvement in their use;
- using opportunities for personal and professional development to ensure best practice approaches to evaluation and adoption of cost-effective innovation are understood and adopted; and
- support for NICE and implementation of its guidance.

## European Working Group

13. The European Working Group concentrated its efforts on providing input to the High Level Pharmaceutical Forum (HLPF), which convened for the first time on 29 September 2006, and on developing ideas and position papers, from a UK perspective, on its agenda or those of its three working groups. The three working groups are addressing pricing, relative effectiveness and patient information.

14. The key recommendations from the group were (these are provided in more detail in Chapter 3):

- advocate to have a survey undertaken to map the presence across Europe of the main sub-sectors of the biosciences industry, as part of the HLPF process;
- the UK Government to present the results of the NERA Study into Pharmaceutical Investment Decisions to the HLPF;
- the UK Government to take the agreed principles on pricing forward to the HLPF Working Group on pricing, in the hope that they can be endorsed at EU level;
- the UK Government to take the agreed principles on relative effectiveness forward to the HLPF Working Group on relative effectiveness in the hope that they can be endorsed at EU level;
- the UK Government and industry to work together to utilise the UK experience in support of the emerging HLPF model for patient information;
- the UK Government and industry to continue to support the early establishment of the Innovative Medicines Initiative and ensure that the project is adequately funded; and
- the UK Government and industry to continue to advocate the complete implementation of the G10 recommendations in all Member States.

## Regulatory Working Group

15. The Regulatory Working Group focused on a number of areas in which progress in the short term can bring real value to the UK. It also made longer-term recommendations to be championed by the UK at EU level to improve the competitiveness of Europe as a whole. Focus was given both to improving the process for medicines registration and for post-approval monitoring of medicines.

16. The key recommendations from the group were (these are provided in more detail in Chapter 4):

- Medicines and Healthcare products Regulatory Agency (MHRA) and industry to work together to increase the level and quality of scientific debate through establishing a pilot for early scientific dialogue, and the establishment of a Forum to consider new regulatory requirements where there is no guidance;
- the UK to promote EU harmonisation of regulatory requirements for clinical trials;
- UK to achieve full electronic working, and use the UK experience to both influence and comply with a standardised technical framework for electronic submissions across the EU;
- MHRA to promote better risk management planning by developing UK guidance and establishing a network of Pharmacoepidemiology Centres of Excellence in the UK;
- MHRA and industry to work together to improve pharmacovigilance by promoting increased harmonisation and the development of a single EU regulation on safety reporting;
- MHRA and industry to work to propose an improved system of sharing information about safety concerns on medicines at a European level; and
- MHRA and industry to promote a set of core messages to improve communications and understanding about medicines, their development, safety monitoring and benefit:risk issues.

## Vision Paper

17. The Vision Paper was developed by a group comprising leading academics, patient organisations, medical research charities, government officials and industry to articulate a future desired UK environment where patient care is improved through better use of new medicines. The group focused on four key areas of opportunity:

- improving the environment for translational clinical research to create a more innovation- and research-friendly NHS that is then able to deliver better care for patients;
- developing the UK's core competence to be a world-leading centre for measuring the impact of medicines when used in clinical practice, in particular through realisation of the opportunity for research provided by systems such as Connecting for Health;

- developing greater partnership between the NHS and healthcare regulators and industry to improve patient care and facilitate access to medicines; and
- empowering patients to provide them with greater opportunities to take control of their own health and to provide input to medicine development and regulatory decision-making.

## Taking the agenda forward

18. It is critical that dynamic, strategic and well-constructed steps should be taken to drive the agreed agenda forward. Focus should be on implementation of the recommendations while identifying long-term strategic opportunities to produce concrete, innovative and enduring benefits for patients.

19. The following explain how the agenda will be driven forward in the short and long term.

20. The three Working Groups have developed an outline timeframe for taking forward their recommendations. Each has put in place arrangements to ensure the recommendations are implemented: the Partnership Working Group has established an Implementation Board, and the European and Regulatory Working Groups will continue to meet, with a focus on implementation.

21. The secretariat has been asked to convene a group to map out the ideas in the Vision Paper, and consider how much is already being taken forward through existing processes and to ask the working groups to consider any new proposals.

22. MISG will monitor implementation of the Long-Term Leadership Strategy and receive updates from all the groups at its meetings in 2007.

23. MISG took the opportunity to consider whether its membership, and terms of reference, continued to be appropriate to take forward this agenda. A revised terms of reference is at Annex 1. MISG concluded that membership should be extended to include a representative from the following organisations:

- The Department for Education and Skills
- UK Trade and Investment
- The BioIndustry Association
- The Japanese Pharmaceutical Group.

24. MISG will publish the monitoring reports on its website at www.dh.gov.uk/policy andguidance/medicinespharmacyandindustry/industrybranch/ and will also publish by the end of 2008, an update on progress of implementation of the recommendations.

# Section 1:
# Current Position

**This section contains an outline of the current situation and the rationale for embarking on the Long-Term Leadership Strategy**

# 1 Introduction

## Pharmaceutical industry in the UK

1.1 The UK is home to a world-class pharmaceutical industry, which makes a significant contribution to two of the Government's major objectives: providing patient-focused quality healthcare for the public; and increasing private sector investment in research and development.

1.2 In respect of improving health through innovative medicines, almost a fifth of the world's top-selling 100 medicines were discovered and developed in the UK, more than in any other country except the USA.

1.3 The industry contributes significantly to the UK economy by employing over 70,000 people in the UK in highly skilled jobs and generating another 250,000 jobs in related industries.

1.4 Pharmaceutical companies invest around £3.2 billion in research and development each year in the UK, approaching 25 per cent of total private sector investment in UK research. The industry also has a significant manufacturing base in the UK, with annual exports of around £12 billion.

1.5 However, the environment for the pharmaceutical industry is becoming increasingly challenging. The cost of developing medicines is rising sharply, and at the same time governments are targeting expenditure on medicines as a way of reducing overall health spending. This is happening at a time where there is increasing consolidation within the industry, resulting from companies needing to augment either their research strength or their ability to commercialise new medicines at a global level. This increasing consolidation can either be an opportunity or threat to pharmaceutical investment in the UK.

1.6 The UK has a strong science reputation and infrastructure but cannot be complacent that pharmaceutical investment will continue to flow to the UK. Competition is increasing from emerging economies such as China and India, which could provide a challenge to the UK's leadership position.

## Relations between the Government and pharmaceutical industry

1.7 The Pharmaceutical Industry Competitiveness Task Force (PICTF) was initiated by the Prime Minister in November 1999. PICTF brought together the expertise of pharmaceutical industry leaders in the UK with Government policy makers to work in partnership to ensure that the industry remains competitive within the global market. Its aims were also to ensure that the right strategies are in place to allow it to contribute fully to the economy and bring safe, effective medicines to the British market. PICTF reported to the Prime Minister in March 2001.

1.8 The process set a new direction of travel for the relationship the Government had with the pharmaceutical industry. One of the main recommendations was that this close working should continue through the Ministerial Industry Strategy Group (MISG). Its first task was to ensure that the key issues identified in the report were jointly addressed to ensure that the UK-based industry maintained its competitive edge.

1.9 In 2005, the House of Commons Health Committee published its report on the *Influence of the Pharmaceutical Industry*. This looked at the relationship the Government, NHS, regulator and patients had with the industry. The Government believed that it had a balanced and appropriate relationship with the pharmaceutical industry, and transparency of this was strengthened by the acceptance of many of the Committee's recommendations. The Committee's report was taken into account during the development of this Strategy.

## Changing environment in England and Europe

1.10 During the production of the Long-Term Leadership Strategy there were a number of key developments both in England and in Europe, which impacted on the pharmaceutical industry.

1.11 Health reform is about revitalising and modernising the NHS. It is essential in order to enable the NHS to keep pace with fast-changing technology, to tackle inequalities, and to raise standards of care within England. The aim of health reform is a NHS that strives for continuous improvement, provides the highest possible quality of care, delivers care in the most efficient and cost-effective way, and is led by the needs, wishes and preferences of patients and the public.

1.12 To facilitate this, the institutional architecture of the NHS has become more streamlined and less centrally-controlled, with a reduction to ten strategic health authorities overseeing the local NHS, and budgets and decision-making being devolved to a smaller number of merged primary care trusts.

1.13 In addition, a greater focus is being placed on caring for patients in the community with the White Paper *Our health, our care, our say: a new direction for community services*, putting the focus on disease prevention and service delivery in primary care settings. In many cases these represent opportunities to provide increased access for patients to cost-effective new medicines, which often provide earlier, more cost-effective interventions in chronic disease.

1.14 There were major steps forward in research and development with the establishment of the UK Clinical Research Collaboration (UKCRC) and implementation of the Government's national health research strategy *Best Research for Best Health* which provide a comprehensive range of initiatives designed to transform the clinical research environment in order to improve the UK's competitiveness and yield benefits for patients and the public. In December 2006, Sir David Cooksey published his report *A review of UK health research funding*, calling for a range of steps designed to make the UK more competitive in health research and more attractive as a base for industry, much of which is consistent with conclusions of the Vision Group.

1.15 The pharmaceutical industry is global, conducting research in a number of countries and providing medicines in most countries of the world. In Europe in particular, the environment for the industry has become increasingly challenging. The European Commission set up the High Level Pharmaceutical Forum (HLPF) to bring together Member States with a range of stakeholders to discuss how to contribute to increasing European competitiveness by increasing the competitiveness of the pharmaceutical industry in Europe. An improved European environment for pharmaceuticals would bring benefits to the UK, since UK-based companies export significantly to continental Europe and most global companies take investment decisions on a regional rather than purely national basis.

1.16 Improving the regulatory environment could help make the environment in the UK and Europe more competitive and could have significant benefits for patients. We want to be at the forefront of this debate as a more efficient regulatory review and post-launch monitoring of medicines would result in medicines coming to the market earlier.

1.17 These changes to the NHS taken together with the changes which the pharmaceutical industry is itself undergoing, make this an optimal time to further develop the relationship between the Government, NHS and industry.

## Long-Term Leadership Strategy

1.18 In 2005, MISG decided that, as well as reviewing the current environment, it needed to take more of a leadership position in developing the environment in the longer term, and to consider how the UK could more effectively influence the European environment for medicines.

1.19 To do this MISG established the *Long-Term Leadership Strategy* (LTLS), with the following broad aims:

*"The Long-Term Leadership Strategy will develop a long-term strategy for medicines designed to: secure the provision of safe and effective medicines for patients; maintain and strengthen the UK pharmaceutical industry within Europe; and to advance healthcare innovation in the UK."*

1.20 The LTLS has three main workstreams:

- **Partnership Working Group**, improving the relationship between the NHS and industry to support the better use of cost-effective medicines;
- **European Working Group**, supporting the European Commission's plans to improve the competitiveness of Europe through the HLPF; and
- **Regulatory Working Group**, considering what is needed to improve the effectiveness of medicines regulation.

1.21 Each of the working groups was co-chaired by a representative from Government and one from the industry. The working groups were made up of relevant stakeholders, including representatives of patients, medical profession, NHS, regulators, NICE, Department of Health (including National Clinical Directors), Department of Trade and Industry, Cabinet Office, and the pharmaceutical industry.

1.22 In addition to these three workstreams, Andrew Witty, President of Europe at GlaxoSmithKline, was asked to organise a small group of forward thinking people, including Dr Mark Walport from the Wellcome Trust, to develop a strategic vision that sets out what the UK environment for developing a new medicine might look like in ten years, carrying out the necessary clinical trials for getting it licensed, and securing access for patients.

1.23 A specific workstream on research and development was not set up due to the high level of work already ongoing between industry and Government, in particular the UKCRC.

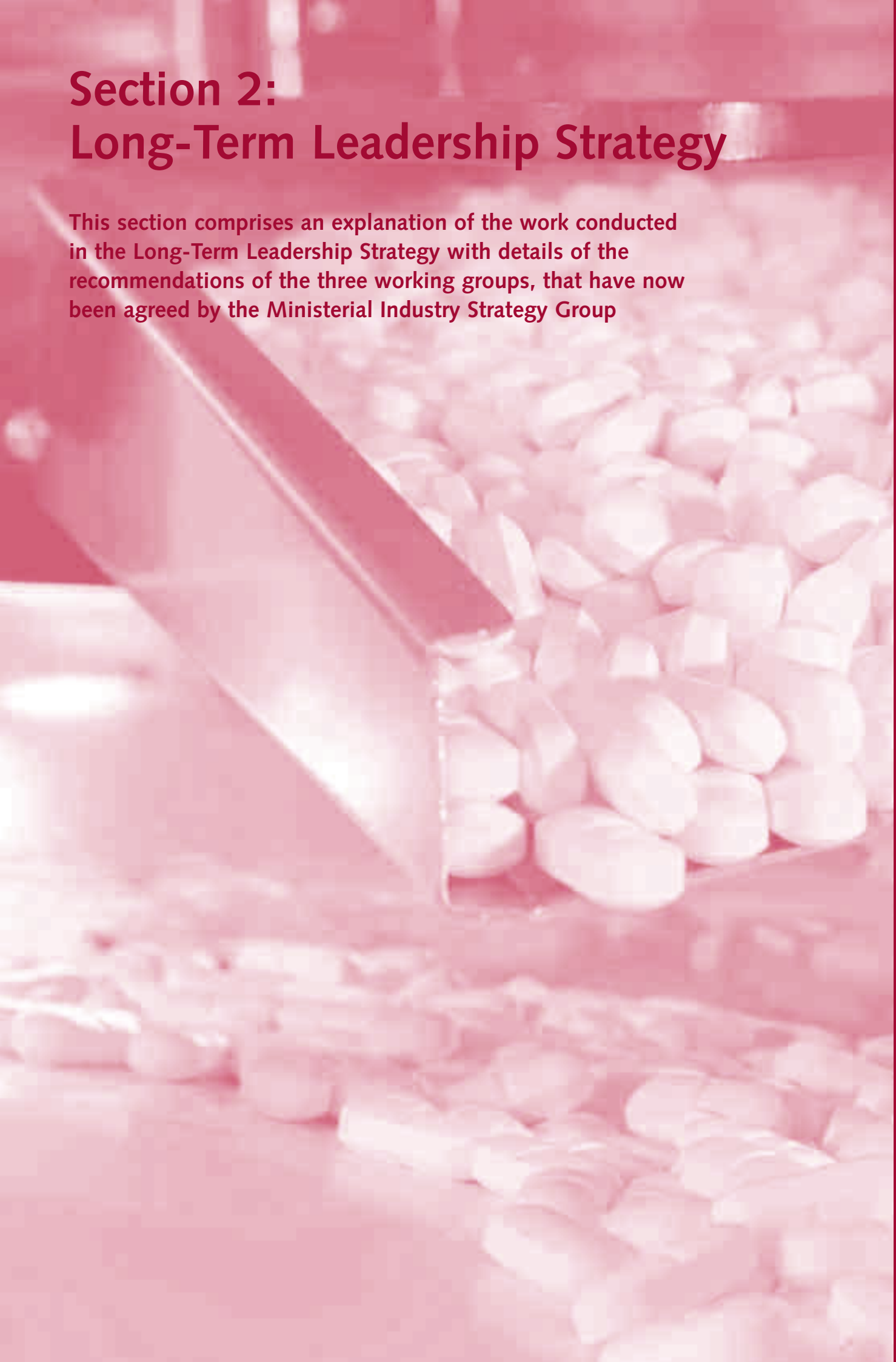
1.24 The chapters that follow outline the work that was undertaken as part of the Strategy, and how the recommendations coming from this will support the better use of innovation and benefit patients, NHS and industry. This report also includes a description of the work underway to improve the environment for research and development to provide a holistic view on how the Government and industry are working together to maintain the UK as a leader in pharmaceuticals.

1.25 The LTLS took a UK-wide remit in the work taken forward by the European and Regulatory Working Groups. The work of the Partnership Working Group is focused on the NHS in England. Scotland, Wales and Northern Ireland may wish to consider how the conclusions and recommendations relate to their health systems.

1.26 This report and all of the studies undertaken to support the LTLS can be found in full at www.dh.gov.uk/policyandguidance/medicinespharmacyandindustry/industrybranch

# Section 2:
# Long-Term Leadership Strategy

**This section comprises an explanation of the work conducted in the Long-Term Leadership Strategy with details of the recommendations of the three working groups, that have now been agreed by the Ministerial Industry Strategy Group**



# 2 Partnership Working Group

## Remit of the Group

2.1 The Partnership Working Group was asked to explore ways in which the NHS and pharmaceutical industry could work in partnership to make the best use of medicines for the benefit of patients.

## Introduction

2.2 Sir David Cooksey's Report, *A review of UK health research funding* (December 2006), looked at the development pathway for new medicines, and suggested a more systematic approach was required to support the adoption of new technologies. The Partnership Working Group had already been looking at some of the areas highlighted by Sir David, including improving attitudes towards the acceptance of innovation, and the better use of cost-effective medicines. There is therefore a synergy between certain parts of Sir David's vision of a new development pathway and the work of this Group, which can be found throughout this chapter.

2.3 There are instances where the UK is a slow adopter of modern medicines and the Group wanted to understand the reasons for this and to ensure that patients' health needs are met through the adoption of innovative solutions (both products and services) that are clinically and cost effective, and that the organisations who develop and deliver them are suitably rewarded.

2.4 The industry can bring more than just medicines to the NHS and the patients it serves in the form of skills and expertise to support a top quality and productive service. For this to happen, however, a more 'mature' relationship has to be developed between the industry and the NHS founded on mutual respect and trust and demonstrated through successful joint working on areas of mutual interest and benefit.

2.5 To fulfil its remit, the Group needed to be able to answer the following questions:

- Does, and if so, to what extent, the use of medicines vary across England and why?
- How does England compare with similar European countries in terms of adoption of new medicines?

- What are the cultural factors that underpin the current relationship between the NHS and the pharmaceutical industry?
- What could be done to open up more opportunities for productive joint working for the benefit of patients and in what kinds of areas?

2.6 In order to answer these questions a major programme of work was undertaken to explore:

- attitudes in both the NHS and industry towards each other and cultural factors that affect joint working and the uptake of medicines; and
- variations in uptake of medicines within England and in comparison with other major European markets, and the factors affecting uptake.

2.7 The work programme consisted of the following:

- market research, commissioned from Adelphi Research UK, to examine the attitudes of the NHS and pharmaceutical industry to each other, to innovation and to joint working;
- a workshop of senior NHS managers to explore potential areas of NHS/industry joint working;
- Use of Medicines Study (quantitative):
  - Variation in Use of Medicines Study: a major quantitative analysis of medicines uptake within England covering more than 50 per cent of the medicines bill
  - International Comparison of Medicines Uptake: a study of a sample of medicines comparing their rates of use per thousand population in the UK with that in France, Germany, Italy, the Netherlands, Spain and Switzerland;
- Use of Medicines Study (qualitative):
  - market research, also commissioned from Adelphi Research UK, to examine the reasons for variations in use of medicines
  - a discussion of some theories on diffusion of new technologies as applied to the health sector
  - literature reviews, commissioned from the University of York, on the factors affecting uptake of medicines in primary and secondary care.

## Understanding attitudes to joint working

2.8 The first aim was to understand what was meant by joint working. Rather than use the narrower term 'partnership', the description in figure 1 was agreed to illustrate the wide variety of arrangements for joint working between the NHS and the industry:

**Figure 1**

*Joint working between the pharmaceutical industry and the NHS refers to situations where, for the benefit of patients, organisations pool skills, experience and/or resources for the joint development and implementation of patient-centred projects, and share a commitment to successful delivery. Joint working agreements and management arrangements are conducted in an open and transparent manner.*

*Joint working differs from sponsorship, where pharmaceutical company(ies) simply provide funds for a specific event or work programme.*

2.9 The NHS and pharmaceutical industry do work together in areas separate to their traditional purchaser and provider roles. A number of innovative examples of joint working were identified at national and local level – three of these are set out in figure 2. The learning from these projects confirmed that joint working provided benefits to all stakeholders, particularly patients. It also identified the difficulties that can be faced by individual projects in starting up, and highlighted the need for generic tools to support the establishment of such projects.

**Figure 2: Examples of joint working between the NHS and pharmaceutical industry**

### Pharmaceutical Oncology Initiative Partnership

In 2004, the National Cancer Director reported that there was variation in the use of cancer chemotherapy medicines, including those approved by NICE, between the 34 Cancer Networks in England. One reason identified was constraints in service capacity for delivery of chemotherapy.

In order to address the issue of uptake and access to cancer medicines, the Pharmaceutical Oncology Initiative Partnership (POIP) was formed between the Cancer Action Team at the Department of Health, the Cancer Services Collaborative Improvement Partnership and 12 member companies of the ABPI with an interest in cancer. The POIP has developed a powerful capacity planning tool called C-PORT (Chemotherapy Planning Oncology Resource Tool) for use by Cancer Networks in the NHS. C-PORT is a simulator which enables chemotherapy units to model changes in the way resources are used to deliver chemotherapy, to maximise the patient numbers treated, improve the patient experience such as waiting time, and use resources more efficiently.

C-PORT was developed by the POIP through the engagement of healthcare management consultants and IT partners. The majority of costs have been funded by the industry and all partners contribute their particular expertise. Formal 'rules of engagement' and contracts have been drawn up and a core working group meets regularly to oversee the project and ensure appropriate governance. C-PORT is currently being rolled out in a number of Cancer Networks. The POIP is planning further projects in the future.

### Ashton, Leigh and Wigan PCT Find and Treat Strategy

Ashton, Leigh and Wigan PCT has a population with one of the lowest life expectancies in England and a high prevalence of coronary heart disease and diabetes. It saw valuable potential to work with industry to find a large cohort of people with these diseases and treat them. It also saw industry as a valuable contributor to its 'Learning Network' which aims to deliver high quality continuing professional development to the PCT's clinical and managerial staff.

The find and treat strategy involves the PCT working with pharmaceutical companies. A project manager, seconded from industry, has been appointed and is jointly funded by the PCT and ABPI to support the learning network. The pharmaceutical companies are sharing their expertise to support the PCT in the delivery of this innovative project, which aims to decrease morbidity and mortality and increase life expectancy for the people of Wigan.

A joint PCT/ABPI Project Board, which reports to both the PCT's Professional Executive Committee and ABPI's NHS Task Force, has been set up to oversee development of the Find and Treat Programme and Learning Network Curriculum and overall governance of the working relationship between the PCT and industry.

**East Lincolnshire PCT Chronic Obstructive Pulmonary Disease (COPD) Programme in collaboration with GlaxoSmithKline, Boehringer Ingelheim and Pfizer**

East Lincolnshire PCT developed a locally enhanced service, three-phase programme to target suspected COPD. Phase 1 identified patients and screened them for COPD within spirometry clinics; phase 2 involved training clinicians to manage these patients and establishing specific COPD clinics within the practices; and in phase 3 a primary care-based respiratory service was set up which integrated primary and secondary care.

Patients previously referred to secondary care for treatments such as pulmonary rehabilitation or long-term oxygen assessment are now seen in primary care and the hospital manages the most complex patients and other specialist services such as lung volume reduction surgery. Additional support was provided by an educational pathway available to all clinicians in primary care.

The programme recorded a 23 per cent fall in admission rates in COPD (neighbouring PCTs' reductions were in single figures). Over a five-month period, 78 out of 215 case-managed patients had acute episodes that were successfully managed at home. Only one resulted in hospital admission. All 37 practices in the PCT area signed up for the enhanced service.

Funding was shared between the PCT and the three companies. Industry was also able to provide essential project management support and communications and marketing expertise.

The project won the Health Service Journal's Chronic Disease Management Award and overall Secretary of State's Healthcare Management Award in 2005.

2.10 The market research study into culture and attitudes revealed some interesting insights into the dynamics of the relationship between the NHS and the pharmaceutical industry.

2.11 The research showed that the attitudes in the NHS and industry towards joint working were mixed, with some willing to work with each other, but others who, as things stand, would never consider it. From this it was clear that in developing

recommendations there was a need to increase levels of trust between the NHS and the industry, and fulfil two goals: firstly to support those who were willing to enter into joint working; secondly to change the view of those who would not consider such an approach, and highlight that such arrangements can be entered into within an appropriate governance framework.

2.12 To achieve the benefits from joint working there had to be a 'maturing' of the relationship between the NHS and industry. This had to be realised if the goal of moving more care to the community set out in *Our health, our care, our say: a new direction for community services* is to be achieved. To do this the NHS and industry had to realise that while their priorities might be different, the ultimate aim of getting cost effective medicines to patients are the same.

2.13 Through the individual projects and the market research common characteristics of successful joint working were highlighted, and are set out in figure 3. One important factor to highlight is that the benefits to each party need to be set out clearly at the beginning of a project if it is to be implemented successfully.

**Figure 3: Common characteristics of successful joint working**

- Set-up:
  - Shared vision – benefit for patients
  - Honesty about benefits for both parties
  - Measurable outcomes
  - Clear rules of engagement
  - Clear timelines and milestones
  - Stakeholder engagement
- Running/managing projects:
  - Good project management
  - Accountability for deliverables
  - Effective decision-making processes
  - Clear roles and responsibilities
- Attitudes and people issues:
  - Shared attitudes to risk and levels of urgency
  - Open-minded team players
  - Ability to compromise
  - Continuity of support and personnel
  - Dedicated resource and time
  - Commitment to the project

2.14 The market research indicated that the environment was positive to future joint working but increased trust on both sides is needed for more significant levels of joint working, in the interests of patients, to be successful.

2.15 In order to get a better feel for the potential for future joint working, a seminar of senior NHS managers was held to answer the following questions:

- What are the challenges for the NHS in the next 5–10 years in improving the quality and productivity of services?
- How can the industry usefully contribute to improving the quality and productivity of NHS services?

2.16 There was overall support and enthusiasm for the concept of joint working between the NHS and industry. It was recognised that the industry has skills that the NHS can draw on, such as marketing and communications, project and business management, and clinical expertise. Areas for future joint working were identified to best utilise these skills – whilst many are by definition conceptual, it was felt that they should be discussed further.

2.17 Recommendations have been brought forward which focus on measures to build mutual understanding, trust and confidence, and generate more appropriate behaviour by both parties.

### Recommendations for action

- The Department of Health will develop and deliver specific guidance on joint working for NHS organisations which endorses joint working.
- The Department of Health and industry will develop and pilot a best-practice toolkit for use by NHS and industry organisations to support joint working and to include information on positive examples.
- The guidance and toolkit will be presented and promoted at key conferences and other appropriate forums.
- The ideas generated at the Workshop of senior NHS managers will be further considered and a process agreed to take forward the potential areas of joint working, in particular starting with a strategic articulation of how, for the benefit of patients, the NHS and industry can work together for mutual benefit.
- The ABPI will develop with NHS managers training for industry managers who initiate and implement joint working projects.
- The industry will work in collaboration with an NHS organisation to develop ongoing training and support for NHS organisations and industry on joint working.

## Uptake of medicines within England

2.18 The quantitative analysis of the use of medicines in England showed a mixed picture. It found that there has been an increase in uptake across England in all of the therapeutic areas included in the analysis. The rate of increase varies quite substantially with use of well-established therapies tending to increase less rapidly than newer therapies.

2.19 In terms of overall prescribing:

- There is more variation between geographic areas when looking at medicines mainly used in hospitals, than those prescribed in primary care.
- Variation was higher in newer medicines and reduces the longer a medicine has been on the market.

2.20 The analysis showed that variation could not be entirely explained by measured differences in disease prevalence, nor was there generally a significant relationship with relative deprivation. Statistical analysis of the quality and outcomes framework (QOF) of the new General Medical Services contract found no statistically significant effect on overall levels of prescribing in the first year of its operation. However, recognising that the QOF had only been in place for a short period it is not necessarily the case that the QOF has no impact on prescribing.

2.21 Figures 4 and 5 show the difference in prescribing in those medicines mainly prescribed in primary care, and those mainly prescribed in secondary care.

**Figure 4: Variation in uptake of medicines in primary care**

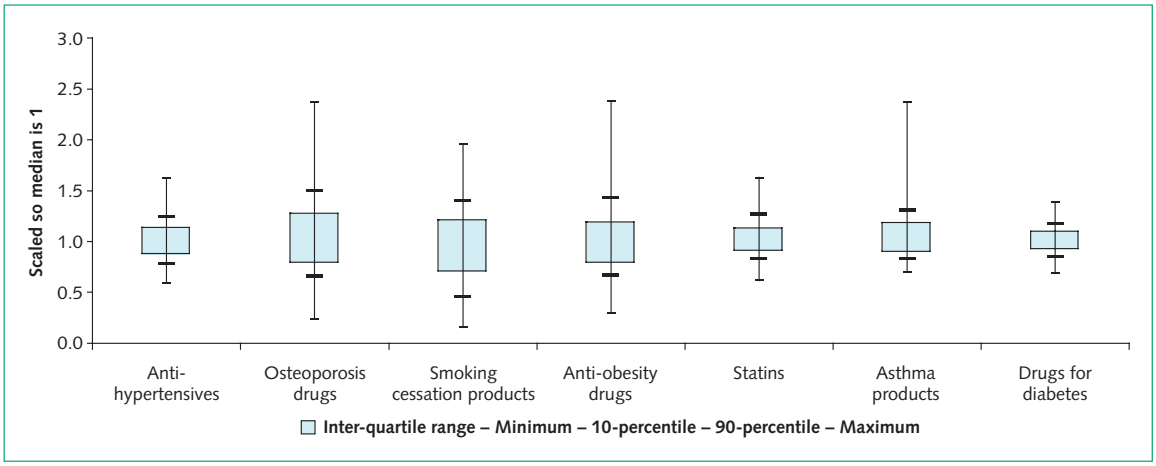
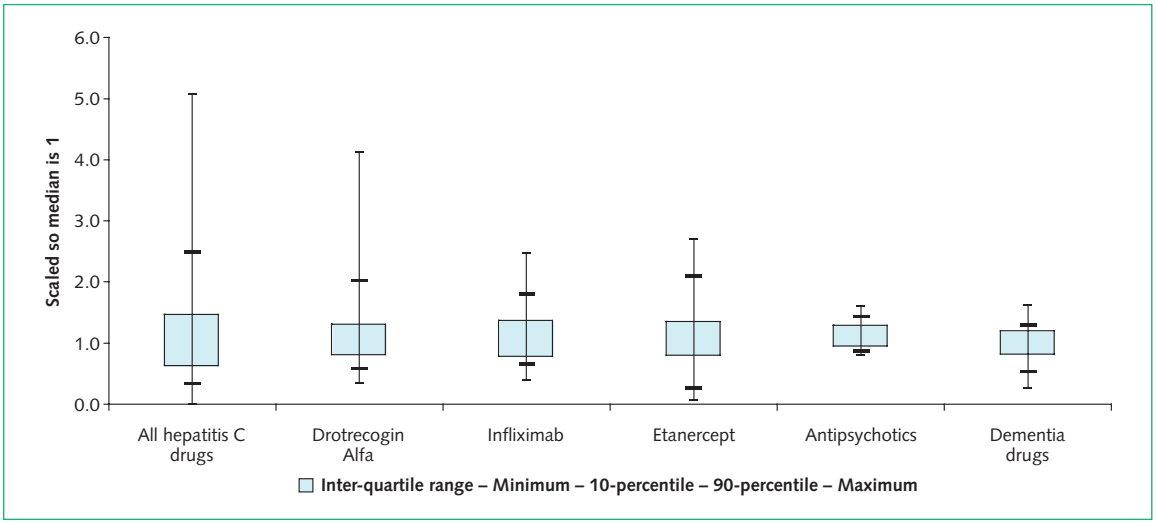


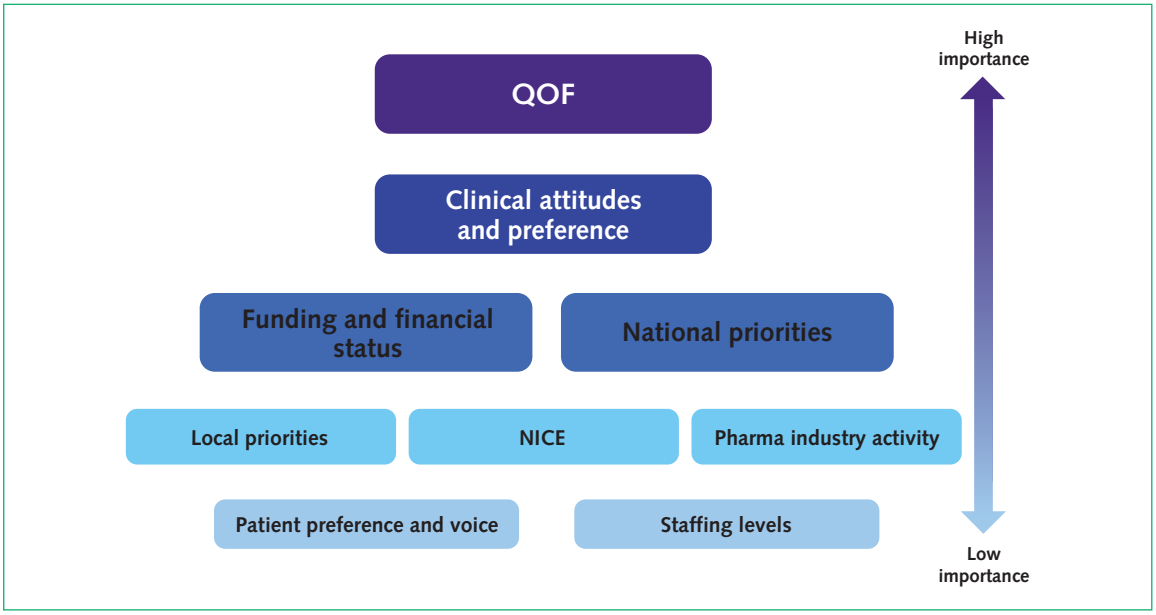
**Figure 5: Variation in uptake of medicines in secondary care**




## Factors driving uptake of new medicines

2.22 Feedback from the qualitative study market research[1] reported that the QOF, attitudes and preferences of individual clinicians, funding and financial status, and national priorities were the main factors driving uptake. The main factors reported as impacting on uptake of medicines in primary care are outlined in figure 6.

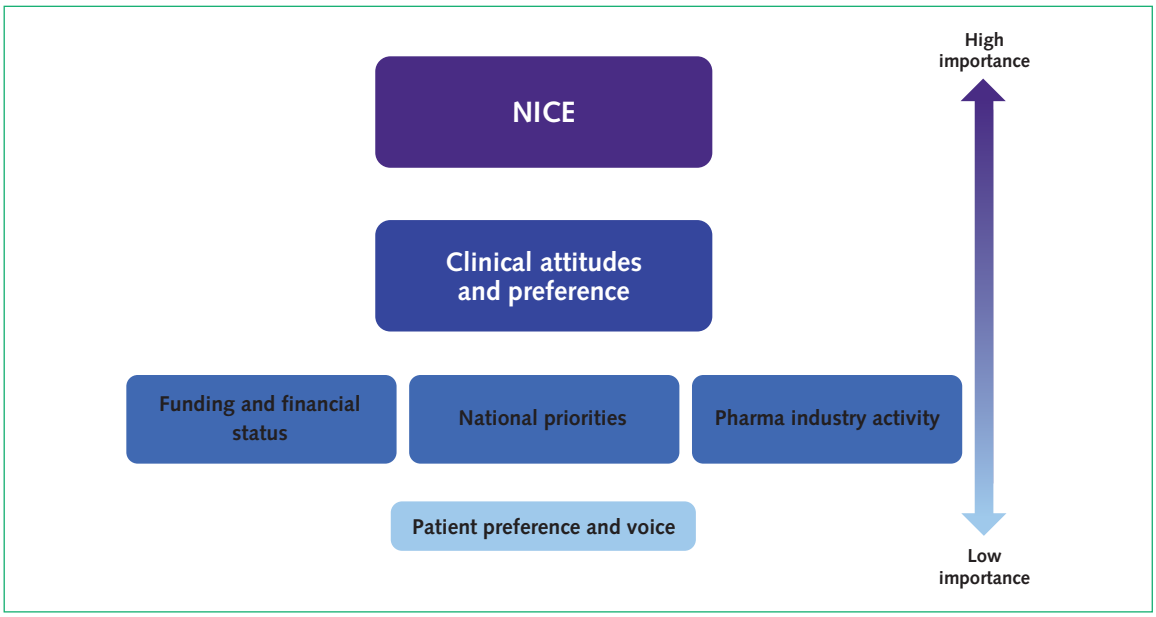
**Figure 6: Key factors reported as driving different uptake patterns in PCTs**




1 The market research study was based on a small sample of PCTs, Acute Trusts, and Mental Health Trusts.

2.23 In secondary care, the picture was slightly different with NICE guidance reported as having the most influence. The key factors reported are set out in figure 7.

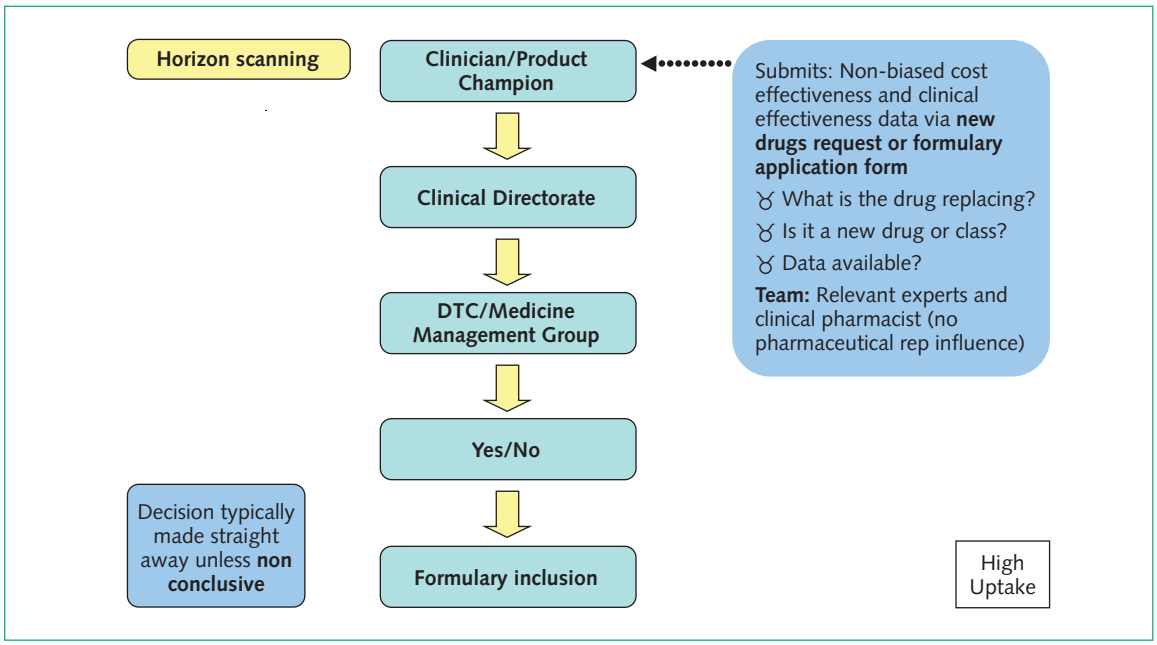
**Figure 7: The key factors reported as driving different uptake patterns in Acute Trusts**




2.24 The literature reviews generally supported these conclusions. They found that beyond the personal experience of the prescriber the factors influencing uptake of new medicines in primary care were colleagues, hospital specialists, patients, PCT prescribing advisers, and pharmaceutical company representatives, while in secondary care it was senior colleagues and peers, involvement in clinical trials, pharmaceutical company representatives, and patient groups. Central guidance and national standards had some impact but there was little empirical evidence on the impact of incentives, and no empirical study of causes of UK geographical variations in prescribing. In secondary care there was some evidence showing central guidance having an impact.

2.25 The qualitative study by Adelphi found that the processes used to manage the introduction of new medicines have an impact on different levels of prescribing. Processes tended to be more streamlined in PCTs with higher uptake levels – an example is in figure 8 – whereas processes in PCTs with lower uptake levels were more complex and lengthy. There was wide variation amongst PCTs in the length of time taken to make decisions.

**Figure 8: Synthesised process for the management of introduction of new medicines as described by PCTs with higher rates of prescribing**

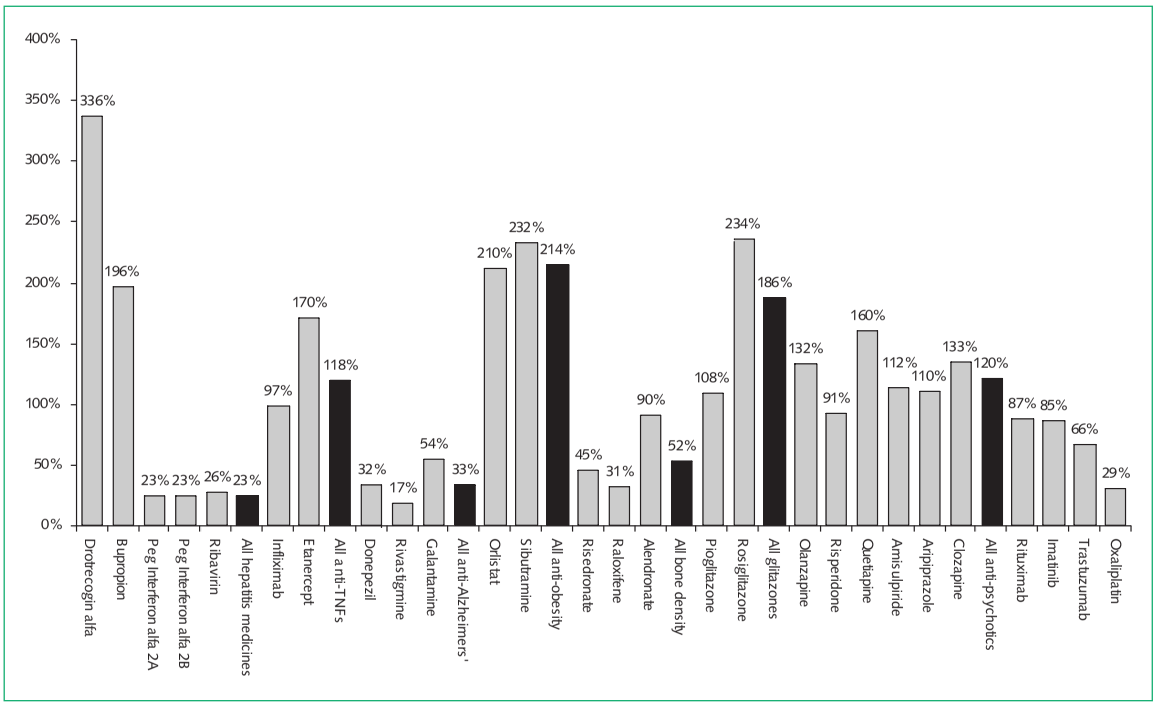



## Comparing uptake of new medicines in the UK with other countries

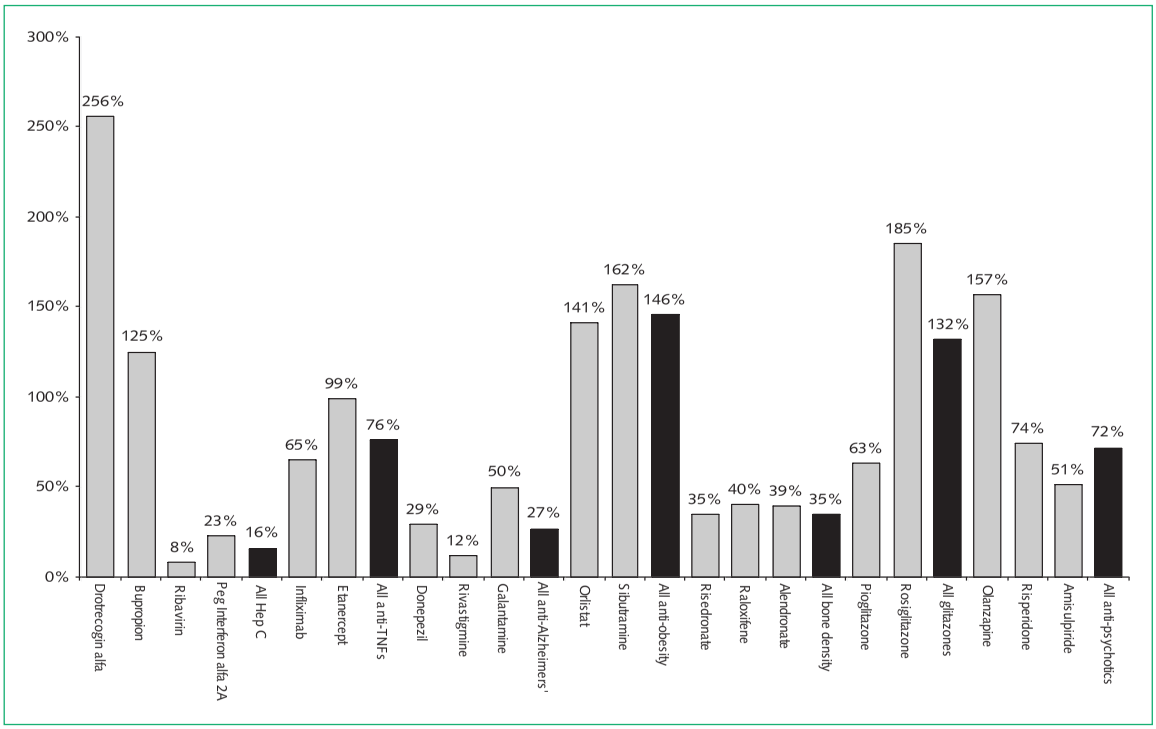
2.26 The Sub-Group studied 27 medicines in a sample of 10 therapy areas where new medicines have been launched in the UK in recent years. The treatment areas were selected from among those included in the Uptake of Medicines quantitative analysis. The analysis used IMS data and compared the rates of medicines use per thousand of total population in the UK with that in France, Germany, Italy, the Netherlands, Spain and Switzerland.

2.27 There was wide variation between individual medicines in UK uptake versus that in the other countries in the cohort. For all medicines investigated, UK use per head of population relative to the average rate of use in the comparator countries was lower three years from the medicine's launch than it was in the calendar year 2005. This reflects a pattern in the UK of early years' uptake being lower relative to eventually achieved uptake than is the case in other countries; this does not imply that any particular level of usage is appropriate. UK uptake was relatively high for anti-obesity, sepsis and smoking cessation medicines, and low in the case of drugs for hepatitis C, dementia, osteoporosis and each of the four cancer medicines. For the other three groups, anti-TNFs, glitazones and anti-psychotics, UK uptake was high overall in terms of 2005 but not always three years from launch and was not necessarily high for each drug in the group. Figure 9 shows a snapshot of the position in the calendar year 2005. Figure 10 shows relative uptake in the third year after the medicine's launch in each country as an indicator of relative use of new medicines, although it is not possible to show the comparison across all medicines.

## Figure 9: UK uptake as a percentage of population-weighted average uptake for comparators – 2005




## Figure 10: UK uptake as a percentage of population-weighted average uptake for comparators – three years from launch



2.28 Learning from these various studies a suite of recommendations has been developed to improve the use of cost-effective new medicines (including those approved by NICE).

Recommendations for action

**Optimising system capacity and clarifying roles**

In order for the value of medicines to be understood and the uptake of cost-effective innovation enhanced, clarity is required amongst the different players in the system about their roles and responsibilities in managing the impact of innovation to secure benefit for patients. The recommendations are:

- learning from the experience of the POIP process to provide a framework for discussion and action planning between the Department of Health, NHS and industry;
- ensuring that uptake of cost-effective innovation is embedded in new commissioning roles and systems as they develop;
- scoping out a broader piece of joint working to improve concordance; and
- the development of best-practice guidance for Area Prescribing Committees as they evolve in the newly-configured NHS, drawing on the learning from the research undertaken.

**Financial and planning systems**

Uptake of cost-effective innovation that supports established health priorities will be enhanced if it is promoted, and understood to be promoted, by key NHS financial and planning systems. Conversely, failing to ensure those systems are appropriately aligned and understood will hamper uptake. This will be achieved through:

- ensuring that the relationship between uptake of effective innovations and key NHS financial and planning systems is properly understood by NHS managers and Boards, and that systems do not incorporate perverse incentives or barriers to uptake and, where possible, actively promote and incentivise uptake of cost-effective innovations;
- reviewing and reissuing HSC 1999/176, which sets expectations about NHS action in managing the introduction of innovations not (yet) assessed by NICE;
- joint work between ABPI, NICE, the National Prescribing Centre and the NHS Horizon Scanning Centre to assess options for maximising the availability and use of horizon-scanning information as an aid to local planning; and
- reiterating messages from the Audit Commission study *Managing the Financial Implications of NICE Guidance.*

**Information for improvement**

Comparative information on the uptake of new technologies, and disinvestment in ineffective interventions, can in itself act as a driver for improvement. In conjunction with clarity about health priorities it helps to identify where effort should be focused both nationally and locally. To help the NHS to have robust information on medicines uptake, actions include:

- publication and active promotion to both the NHS and industry of the Uptake of Medicines Study;
- analyses conducted to support this work should be revisited in three years' time;
- active engagement by industry with NICE and the Healthcare Commission to explore ways the information and insights it has can help the Commission fulfil its role of monitoring compliance with relevant NHS quality standards; and
- seeking clarity on the future development (timing and nature) of the prescribing support module of Connecting for Health.

**Personal and professional development**

A focus on the development needs of individuals, as well as organisations, can help to ensure that best practice approaches to the evaluation and adoption of cost-effective innovation are both embedded in health systems and understood by those who have to implement them.

- In the short term, specific education/development tools will be made available to support key decision-makers involved in consideration of, and planning for, new drug technologies in the NHS, including members of Area Prescribing Committees and their equivalents.
- In the longer term, efforts will be made to incorporate awareness of Health Technology Assessment concepts more fully into training for health professionals.

**Support for NICE and implementation of its guidance**
The work of NICE can be one of the single biggest factors influencing uptake of new technologies in the NHS, and warrants a specific focus in the context of work to improve uptake.

- The industry, collectively, will offer NICE advice on effective dissemination and marketing strategies and techniques.
- The industry, collectively, will support new NICE work on reducing ineffective treatments to improve headroom for adoption of innovation.
- The industry will complement NICE's published 'How to' guide for the NHS with the development of a toolkit for pharmaceutical industry staff on implementation of NICE guidance.
- NICE and the industry will raise awareness of NICE's pilot 'ERNI' database (Evaluation of Reviews of NICE Implementation) as a source of national-level information on uptake of NICE recommendations.

## Implementation of the recommendations

2.29 The set of recommendations are aimed at:

- improving the quality and productivity of NHS care by realising the full value of medicines;
- developing recognition and acceptance within the NHS that working with industry on mutually beneficial solutions of benefit to patients is acceptable;
- better aligning industry activities with the needs and objectives of the NHS without, however, stifling truly innovative ideas in non-priority areas; and
- building mutual trust and confidence between the NHS and pharmaceutical industry.

2.30 To ensure these are delivered an 'Implementation Board' has been created to oversee implementation of the plan. The Board comprises representatives of the Department of Health, NHS, NICE, NPC, and industry, and will meet quarterly to support progress. The Board will then report progress to the Ministerial Industry Strategy Group twice a year.

# 3 European Working Group

## Remit of the Group

3.1 The European Working Group was established to provide a forum that allowed the Government and UK-based pharmaceutical industry to agree a common position on issues being debated in Europe of relevance to industry. Most of the work undertaken focused on providing input to the European Commission's (EC's) High Level Pharmaceutical Forum (HLPF).

## Introduction

3.2 The HLPF has been set up, following a long history of engagement between the pharmaceutical industry, the European Commission and Member States, to improve the European environment for the industry. This history of engagement is summarised in Annex 2. The HLPF has set up three working groups to focus on pharmaceutical pricing, relative effectiveness and patient information. To support this work the European Working Group has developed input for each of these working groups.

3.3 The UK held the Presidency of the EU in the second half of 2005 and as part of the programme for the Presidency, organised an event 'Delivering Patient-Centred Innovation in Medicines' in London on 1 December 2005. This event brought together ministers and officials from health and industry departments in many EU Member States with senior industry representatives and helped to highlight the need for practical measures to improve EU competitiveness in pharmaceuticals.

3.4 This event was pivotal in setting the stage for the HLPF that started its work early in 2006. A report outlining the key conclusions from the meeting was made available on the internet and sent to all Member States and the Commission.

**Figure 11: Quote from the High Level meeting held during the UK Presidency of the EU 'Delivering Patient-Centred Innovation in Medicines'**

*"My plea is that from the patients' perspective it is so self-evident that we must keep innovation in Europe. As the example shows, we also want to have the opportunity for our patients to take part in these early clinical trials."*

**Ms Hildrun Sundseth**
European Cancer Patient Coalition
London, 1 December 2005

3.5 In addition, the Group was also asked to oversee work by the Department of Health and the Office of Health Economics to revise the Competitiveness and Performance Indicators, used to track pharmaceutical industry performance.

## Generating a better information base about the pharmaceutical industry in Europe

3.6 While high level statistical data exist setting out the presence of the biopharmaceutical industry in each Member State (see Eurostat's November 2005 report on the EU pharmaceutical industry), there is currently no statistical breakdown available between the main industry sub-sectors (research-based, generic, biotech and Contract Research Organisations) within Member States.

3.7 It is important that the development of a new EU strategy for improving the competitiveness of the industry should be informed by a breakdown of this kind, which would indicate the sectoral strengths and weaknesses of the EU industry, both in aggregate and within Member States, and enable these to be tracked over time.

3.8 Better information about the existing presence of the main sub-sectors of the biopharmaceutical industry in each Member State would also give countries a better understanding of their stake in the further development of the industry.

Recommendation for action

- Advocate to have a survey undertaken to map the presence across Europe of the main sub-sectors of the biosciences industry, as part of the HLPF process.

## Generating a better understanding of the factors influencing biopharma company decisions on the location of their investments

3.9 The Group agreed early on that it is important that Member States understand better the reasons why companies place investments where they do. While most EU Member States are keen to attract investment from pharmaceutical and biotechnology companies, they may not possess a complete understanding of the factors that influence company decisions about where to locate different types of activity, such as manufacturing, medicine discovery and clinical research.

3.10 The ABPI and UK Trade and Investment commissioned a study from NERA Ltd to identify these factors. The goal was for an authoritative study to be presented to the HLPF, to indicate what EU countries needed to do to improve their chances of attracting such investment. The key findings of the study are outlined in figure 12.

### Figure 12: Key findings of the NERA Study into Pharmaceutical Investment Decisions

The study found that the factors that influence the general willingness of the industry to invest in a particular location are:

- **History:** Companies have substantial existing stocks of assets which it may be cost-effective to expand, to which new investments must offer a good fit.
- **Disinvestment may be as relevant as investment:** In the light of substantial merger activity in recent years, investment decisions may be as much about rationalising and consolidating as about expanding capacity.
- **Stability:** A range of factors, including low tax, low bureaucracy and a can-do attitude, a flexible labour market, and political stability signify a commitment to an effective business environment. This can positively attract investment.
- **Market conditions** (for example the pricing environment and rate of adoption of new technology) can swing investment decisions when firms have a number of alternative locations that are broadly equal with respect to other fundamentals.

**Figure 12: Key findings of the NERA Study into Pharmaceutical Investment Decisions (continued)**

Within specific functions, the following investment drivers were found important:

- **Research and development:** A location where the company can do good science, by accessing world-leading scientists and an adequate stock of well trained scientists and technologists.
- **Clinical trials:** A programme of trials will usually include major commercial markets, as they create opportunity to familiarise key opinion leaders with new products. Companies supplement key market trials in order to create a sufficient global bank of evidence. These supplementary locations will be selected by reference to cost-efficiency and the provision of timely patient recruitment.
- **Manufacturing:** There is an absolute need for manufacturing to deliver required quality. That said, a wide and increasing range of countries have this capability. In these circumstances relative costs will be important. Tax is a key driver here, although labour flexibility and other components of labour cost also matter.
- **Regional offices:** The main driver for the location of a regional office is to find an area that is attractive to internationally mobile talent and offers good transport links both within the region served and to global headquarters.

3.11 We have agreed that the results of this important study should be presented to HLPF early in 2007.

Recommendation for action

- The UK Government to present the results of the NERA Study into Pharmaceutical Investment Decisions to the HLPF.

## Agreeing principles on pharmaceutical pricing

3.12 Pharmaceutical pricing is a complex and sensitive area where competence resides at Member State level and different Member States have very different attitudes and policy ideas. In the past, European debates on pricing have tended to peter out with matters not substantially advanced.

3.13 However, sound pharmaceutical pricing policies are an important element in an EU environment that will be attractive to global pharmaceutical companies. The Group has therefore agreed some high-level principles for pharmaceutical pricing that allow

for national policy diversity, but which will still incentivise pharmaceutical innovation.

3.14 The group is also considering a selected number of practical policy ideas, bearing on pricing, which could be implemented without requiring new regulation or new institutional initiatives by the Commission.

Recommendation for action

- The UK Government to take the agreed principles on pricing forward to the HLPF Working Group on pricing, in the hope that they can be endorsed at EU level.

## Agreeing principles on the relative effectiveness of medicines

3.15 On the topic of the relative effectiveness of medicines (sometimes referred to as 'health technology assessment'), a position paper has been prepared which sets out the shared ideas of the UK Government and industry on the characteristics that make for efficient and effective assessment of the relative clinical and economic effectiveness of medicines.

3.16 As all parties share an objective of getting value-adding new medicines to patients as quickly and economically as possible, the principle aims should be to minimise any unnecessary bureaucratic or procedural delays caused by relative effectiveness processes and to avoid their use as a proxy for cost-containment.

3.17 This paper has already been provided to the HLPF working group on relative effectiveness and can be viewed at www.dh.gov.uk/policyandguidance/medicinespharmacyandindustry/industrybranch

Recommendation for action

The UK Government to take the agreed principles on relative effectiveness forward to the HLPF Working Group on relative effectiveness in the hope that they can be endorsed at EU level.

## Providing information to patients about medicines

3.18 The UK Government is leading the work being undertaken in the HLPF on the provision of non-statutory patient information. The goal is to develop a model for a package of information on medicines, non-promotional in character, that will be provided at a European level. It will be disseminated through the European Commission Health Portal, and translated into all the Community languages.

This information will be drawn from multiple sources, including input from industry and patient groups, and could possibly be delivered though a private/ public partnership.

3.19 The Group is very supportive of this concept and is providing comment and analysis, drawing on the well-established UK experience of providing information about medicines to patients.

3.20 The Group is also providing views on the other issues under discussion including improving patient access to information on diseases and medicines, and the provision of information to healthcare professionals and patients.

Recommendation for action
The UK Government and industry to work together to utilise the UK experience in support of the emerging HLPF model for patient information.

## Ensuring a competitive European environment for research and development

3.21 While the HLPF does not have a working party specifically addressing research and development, these issues are touched on frequently by the working groups that are in place.

3.22 One initiative that is important to the future success of healthcare research in Europe is the Innovative Medicines Initiative (IMI). The IMI is a proposed partnership between industry and the EC to fund and conduct pre-competitive collaborative research to address bottlenecks in the discovery and development of medicines. Industry will fund their own involvement and the EC will fund academics, smaller companies and others under its Framework 7 programme. This initiative will help attract investment into the European science base and, by pooling resources and know-how from all stakeholders, it is expected to enable faster access to better medicines for European citizens.

Recommendation for action
- The UK Government and industry to continue to support the early establishment of the Innovative Medicines Initiative and ensure that the project is adequately funded.

## G10 recommendations

3.23 The G10 process, described in Annex 2, developed a number of important recommendations, agreed by industry, the EC and Member States, to improve the EU environment for the pharmaceutical industry. A status report on implementation of the G10 recommendations show that the majority of these remain unimplemented in many Member States. This report is available at www.dh.gov.uk/PolicyAndGuidance/MedicinesPharmacyandIndustry/IndustryBranch/

Recommendation for action

- The UK Government and industry to continue to advocate the complete implementation of the G10 recommendations in all Member States.

## Implementation of the recommendations

3.24 The process of exchanging ideas and information through the European Working Group has been invaluable. It has therefore been agreed that the Group will continue to meet at least for the next year and probably for the life of the HLPF.

# 4 Regulatory Working Group

## Remit of the Group

4.1 The Regulatory Working Group was tasked to explore how to achieve and sustain a UK and European regulatory environment that will support the innovative European pharmaceutical industry and meet the needs of government, patients and prescribers.

## Introduction

4.2 Before a medicine is allowed on the market, it first has to undergo clinical trials to ensure it is acceptably safe and that it works for the condition it is intended to treat. It is then assessed to ensure it meets agreed standards of safety, quality and efficacy. The regulatory authority that does this in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA also monitors the safety of the medicine as long as it remains on the market, authorises changes to the licence, and inspects manufacturing sites to ensure that medicines are produced to the required quality standards.

4.3 The legislation that forms the basis of the medicines regulatory regime mostly comes from the EU. Although many medicines are still authorised by national regulatory agencies such as the MHRA, there is also a European Medicines Agency (EMEA) that authorises a range of medicines. However, the vast majority of medicines on the UK market are still under the direct regulatory control of the MHRA.

4.4 One of the key aims of the EU medicines legislation is to ensure that medicines on the market across the EU comply with the same rules and standards. Although the EU rules that have to be applied in each country are the same, there are often differences in the way countries implement them. This causes significant difficulties and additional costs to companies, who often have to comply with up to 27 differing versions of the requirements. One of the key aims of the work undertaken was to look for ways of sponsoring a common EU approach to key aspects of the regulations.

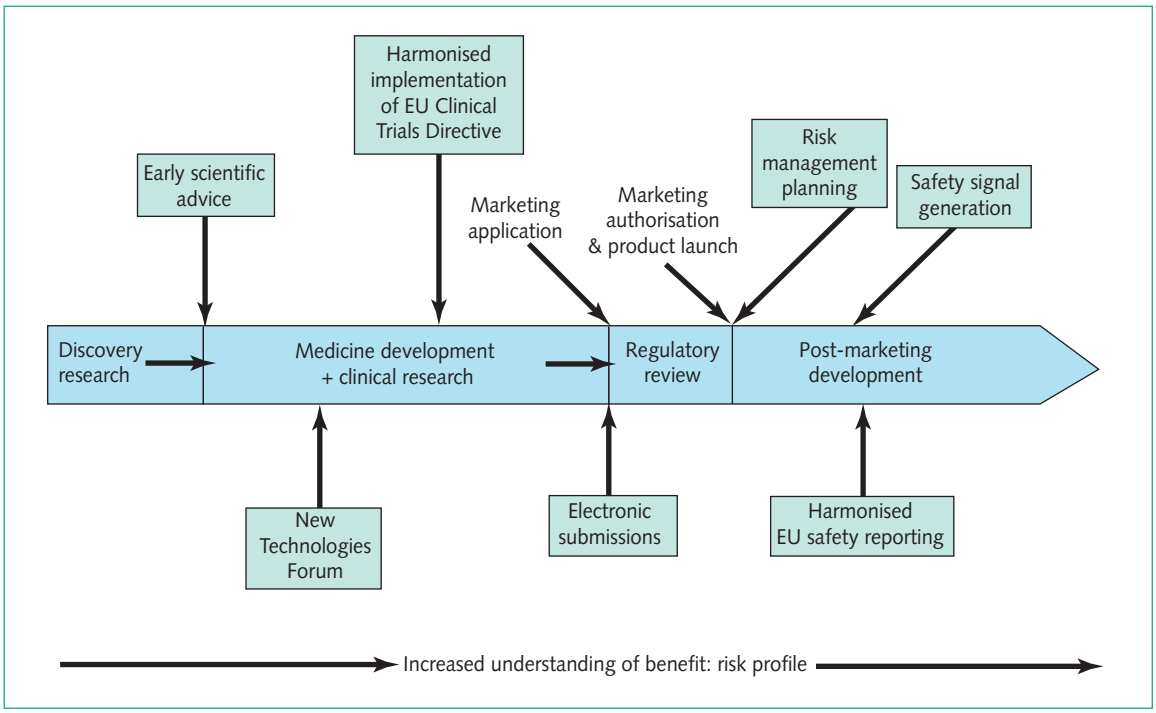
4.5 The innovative pharmaceutical industry has a strong presence in the UK and this brings significant benefits to the UK economy. The MHRA is seen as a leading regulatory agency within the EU, which means it is in a strong position to promote new ideas and to influence the way regulation develops. These two strengths have been brought together to produce some novel ideas for improving the way medicines are regulated in the EU.

4.6 The process of regulating medicines and the work of both regulators and industry in ensuring that medicines on the market work and are acceptably safe, effective and of good quality have not been explained well to patients or the wider public. No medicine is without risk, but there is little understanding of the concept of balancing benefit and risk, or that the balance of benefit and risk may change during the lifetime of a medicine, depending on safety information received, and may be different depending on the patient and on the disease the medicine is intended to treat.

4.7 At the same time, the public increasingly expects to have a say in matters affecting them and their health, and to have access to better information to enable them to make informed choices. The Group was therefore also looking for ways of increasing the public's knowledge and understanding about medicines.

4.8 Progress has been made in a number of areas and these are reflected in the report. The recommendations for action focus on medium-term opportunities that will bring real value to the UK. Many of the recommendations will make a significant contribution to the Government's Better Regulation initiative, as well as to public health protection. The Group's recommendations can be seen within the context of the current medicines development and approval process in figure 13 below.

**Figure 13: Recommendations within medicines development and approval process**



## Extending the scope of scientific debate between industry and regulator

4.9 Under the two following headings, recommendations are provided to increase the level and quality of scientific debate between the MHRA and industry.

### Early scientific advice

4.10 MHRA currently provides scientific advice to companies to assist in design of studies for a particular medicine, or to discuss plans for medicine development. This advice helps industry to understand the requirements of the regulator which will later be assessing an application for a marketing authorisation, and avoids the conduct of unnecessary research or clinical trials. To complement this, industry and MHRA have agreed to pilot the provision of meetings for companies that will allow for earlier discussion of a broader range of issues that do not have to be product specific. These might include, for example, general approaches to product development, broader complex issues of medicine-device combination products, study design and management, and risk management planning.

4.11 Such meetings will be able to draw on expertise from academia, patient groups and lay representatives as necessary. The MHRA will be the only EU regulator to provide this facility, which will mirror the early scientific advice service currently only offered by the FDA – the regulatory authority in the US. A one-year pilot is underway that will comprise around ten meetings which will be paid for by a fee and will be fully evaluated.

Recommendation for action

- If evaluation of the pilot to facilitate earlier discussion of a broader range of issues between industry and MHRA demonstrates that it works well, UK to share this best practice with EU Member States to encourage similar practices to be developed in other countries.

### New Technologies Forum

4.12 Rapid advances in science are facilitating the development of new medicines that use new techniques and methodologies. Industry and the regulator need to work together to ensure that pharmaceutical research can safely use the latest technology to deliver medicines for patients, and ensure that regulation develops to take account of novel scientific approaches.

4.13 To do this, a Forum will be established to enable industry and regulators to consider regulatory requirements in respect of techniques used in medicine development that may not yet be the subject of guidance, or for which current guidance needs updating. The Forum may focus on medicine-specific issues, or address new techniques or specific topics in the development of medicines.

4.14 This process will facilitate the development of novel, effective medicines for patients and ensure continued high levels of public health protection in areas of medicine development where new technologies and scientific advances are pushing the boundaries of the regulation of medicines.

4.15 An Advisory Panel (comprising industry, regulators, representatives of the clinical academic community and a lay representative) has been established to identify topics for the Forum with potential to challenge current regulation of pharmaceuticals. The Forum will meet twice a year and a report of the meetings will be published. The first meeting is planned for early in 2007.

Recommendation for action

- Establish a Forum to enable industry and regulators to consider regulatory requirements in respect of techniques used in medicine development that may not yet be the subject of guidance, or for which current guidance needs updating. Where appropriate, share with the EU the outcome of discussions.

## Harmonising implementation of the EU Clinical Trials Directive

4.16 The EU clinical trials legislation came into force in the UK in May 2004. The aims of the legislation are protection of clinical trial participants and harmonising requirements for approval and conduct of clinical trials in the EU. A further aim is to provide a more attractive environment for clinical research in the EU compared to elsewhere.

4.17 Implementation of the Directive across the EU, whilst generally improving harmonisation, has resulted in some variable requirements being introduced. This creates complexities for researchers and reduces the attractiveness of the EU as a location for conducting clinical trials. If companies find it difficult to conduct trials in the EU for reasons of bureaucracy, rather than protection of participants, this is likely to adversely impact on wider industry investment decisions.

4.18 The UK expert chairs the EU Clinical Trials Facilitation Group (CTFG) which is working on implementation of the legislation across the EU, and participates in the European Commission's ad hoc clinical trials group. Through these interactions, the UK will work with the EU to clarify individual Member State requirements and to sponsor work to reduce local variation/variability in requirements.

4.19 The EU working groups have already made progress by publishing a single document containing all relevant EU clinical trials documentation, and a series of related guidance.

4.20 In looking at how the UK has implemented the Directive, the MHRA has already resolved some of the concerns raised by industry, by increasing the clarity of its requirements.

Recommendation for action

- The UK will promote EU harmonisation of requirements, by clarifying differences in Member States' national requirements for approval of clinical trials, questioning the need for these, and working towards harmonisation of requirements between Member States, leading to least regulatory burden consistent with the legislation and protection of public health.

## Electronic submissions to MHRA

4.21 Applications for an authorisation to put a medicine on the market include huge volumes of data, from clinical trials to information about how a product is to be manufactured. In the past, such material was submitted to the MHRA in paper format and more recently on CDs.

4.22 The Member States of the EU have agreed that they will all have the capability to receive electronic submissions in the eCTD (electronic Common Technical Document) standard by the end of 2009. It will be important to ensure that the way in which the standard is implemented is common across all Member States.

4.23 The MHRA has developed a comprehensive IT system (known as Sentinel) to handle regulatory work electronically, which has the potential to generate significant savings in time and resources for both industry and MHRA, and to put the UK in a position in which it can lead implementation in the EU of the 2009 eCTD commitment. However, to be fully effective in operation the system needs to be used and fine tuned as a result of experience. The MHRA and industry are working together on all aspects of electronic working, including eCTD, and the MISG work programme has provided further impetus.

4.24 The safety reporting component of Sentinel went live in June 2006 and shortly after achieved electronic exchange of information with EMEA. A working group has now been established to develop exchange of safety data between MHRA and industry.

Recommendations for action

- To achieve full electronic working in UK by the end of 2007.
- To promote the use of the eCTD in order to develop combined industry and MHRA experience of using the processes and specification.
- Achieve industry compliance with initial submissions (and subsequent changes) in eCTD format for new active substances by 1 April 2008 and for all new applications by the end of 2008.
- Use the UK experience to both influence and comply with a standardised technical framework for eCTD across the EU.

## Risk management planning

4.25 Risk management planning is the process of identifying and setting out a strategy for managing identified or possible risks arising from the use of medicines on the market. Early consideration of risk management and of potential use in specific populations such as the elderly and children could reduce the possibility of delays in the approval of new medicines.

4.26 Since November 2005 the industry has been required to submit risk management plans for approval for new medicines coming to the market. In addition, plans can be asked for at any stage of the life-cycle of a medicine, particularly when a new safety issue emerges. Expertise and skills in the practice of drawing up suitable risk management plans, updating them and using them to inform the safety monitoring of medicines are in short supply, and there is no common approach to risk management planning by either industry or regulators across the EU.

4.27 Effective risk management has the potential to reduce the incidence of sudden withdrawals of medicines from the market and thus to contribute to improvement in public confidence in their safety. The MHRA has started to offer advice to companies on risk management planning within the earlier scientific advice initiative.

4.28 Industry has some concerns about the usefulness of publishing risk management plans in a raw format. These concerns focus on how the public will receive information about identified risks, and the effect they may have on litigation in a global environment. These issues need to be resolved – in part through a better understanding by patients of benefit and risk – in order to ensure that we obtain maximum benefit from provision of such information to prescribers and patients, as well as effective implementation of the plans.

4.29 The recommendations provide a focus for development of skills in risk management planning in the UK, and an opportunity to influence a common approach to their development across the EU. They also focus on improving availability of data more generally to inform medicine safety monitoring.

4.30 The Department of Health's National programme for IT offers a unique opportunity to enhance access to data to improve the safety of medicines. The MHRA is fully engaged in maximising the usefulness of this initiative through development of a package of proposals. If implemented, the proposals could significantly enhance the UK as a centre of excellence for clinical research and play a key role in the EU's proposed initiative to establish a European Centre for Drug Safety Research.

Recommendations for action

- MHRA will develop UK guidance on risk management planning and promote it as a best practice model with a view to incorporating it in EU guidance. MHRA will also work with industry to agree a model for a Risk Management Plan summary to be available to prescribers, patients and the public.
- MHRA will agree a programme of work with Connecting for Health, the Agency implementing the National Programme for IT, on the availability of data to enhance medicine safety monitoring, including provisions to address confidentiality and consent.
- Establish a network of Pharmacoepidemiology Centres of Excellence in the UK to provide a resource for industry in risk management planning.

## Harmonising EU safety reporting of medicines

4.31 Reporting adverse reactions (side effects) to medicines is key to enabling industry and regulators to take appropriate action to protect public health. EU legislation and guidelines in this area have developed over many years as science has evolved. This has resulted in a confusing array of legislation overlaying variable national regulatory systems and requirements. This means that industry has to cope with a system that requires multiple reporting of the same adverse reaction to different EU countries in different formats.

4.32 As a result, the EU system is inefficient and not currently structured to make the best use of the safety data submitted for public health purposes. In addition, there is a significant cost to industry in taking account of many variable requirements when providing safety information to individual regulators.

4.33 Public health benefits could be achieved and industry, academia and regulator costs reduced significantly if the system could be streamlined and simplified so that safety reports are made to a single EU portal from which regulators could immediately access their national safety reports for local analysis. This could save up to 30–40 per cent of current resource that could be better directed towards important risk detection and safety assessment activities.

4.34 A single European regulation is needed to replace the current disparate rules. This 'Better Regulation' initiative should create a single set of rules and support a common language for safety reporting across the EU. Such a system would enable the prompt sharing and robust analysis of safety data collected throughout the EU to improve the timeliness and consistency of decision making.

Recommendations for action

- Promote harmonised safety reporting requirements throughout the EU.
- Promote the development of a single EU regulation on safety reporting to replace the current diverse rules.

## Safety concerns – when to share information

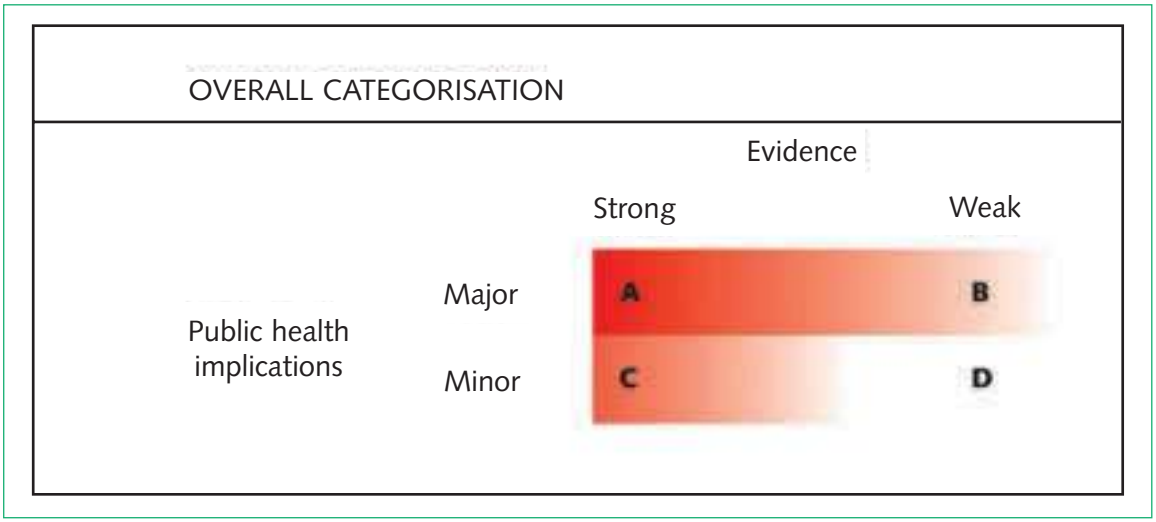
4.35 Monitoring the safety of medicines in everyday clinical use is an important public health function, for which responsibility is shared by industry and the regulator. It comprises a number of tasks:

- receipt and collation of information on suspected side effects received from a variety of sources including clinicians, patients and research sources;
- assessment of their strength and validity;
- deciding whether action is necessary and if so what action should be taken; and finally
- communication of the decision.

4.36 This process involves ongoing and close liaison between regulators and industry, although the time taken to reach a decision varies depending on the strength of the evidence for a safety concern as well as its potential public health impact. For findings that emerge over a longer timescale it can sometimes appear to those outside the safety monitoring regime that action is precipitate and unexpected.

4.37 Information that suggests a potential safety concern is referred to as a 'signal'. Signals need to be evaluated to determine whether or not they represent a true safety concern. Industry has a legal obligation to notify regulators of safety concerns that may impact on the balance of risk and benefit of their products. Figure 14 shows a table that describes a procedure for evaluating the relevance of a signal.

**Figure 14: Categorisation and consequential actions used in impact analysis**




4.38 The following consequential actions would follow logically from the categories defined above:

- (A) high priority – further evaluation required
- (B) need to gather more information (for example request new studies)
- (C) low priority
- (D) no action warranted

4.39 Early, routine sharing of potential safety concerns between industry and regulators would enhance their evaluation by both parties and provide clear public health benefits. This could also provide an earlier opportunity to engage with patients and clinicians, informing them about emerging findings which in turn could further strengthen the reporting regime and increase confidence in the regulatory process. Development and use of core messages about benefit and risk and development of transparent methods for assessing benefit and risk will be key to optimising this initiative.

4.40 We propose to develop a new procedure to support early, two way notification of potential safety concerns between industry and regulators facilitated by guidance on appropriate timelines for evaluation of an emerging issue depending on its potential public health impact. We propose to promote a rigorous EU-wide approach to this work. If a simplified, transparent reporting system (as described above) can also be introduced, there will be benefits to industry, regulators and patients and it will significantly improve monitoring of the safety of medicines in the EU.

Recommendations for action

- Pilot proposals for industry/regulator communications of potential safety concerns under investigation in the UK.
- Consult patient/public representatives on public communication of safety issues – considering the possibility of using a Citizens' Jury approach.
- The UK to work with the Commission and other EU countries to reach consensus on proposals for industry/regulator communications of safety concerns under investigation.

## Improving communications and understanding about medicines, their development, safety monitoring and benefit:risk issues

4.41 The Working Group takes the view that if the changes proposed are to be successful in meeting the needs of patients (and the wider public), it is vital to improve communication about all aspects of medicine development and about the benefits and risks of medicines in general use. The Group has, therefore, developed a set of core messages to be promoted to encourage a more consistent, comprehensible and measured debate about medicines issues. We are also initiating a programme of work, with patient and consumer input, to improve patient and public engagement in the drug development, approval and post-marketing process. This will include better provision of information, and improved dialogue between industry, the regulator, and patients/consumers or their representative groups.

Recommendations for action

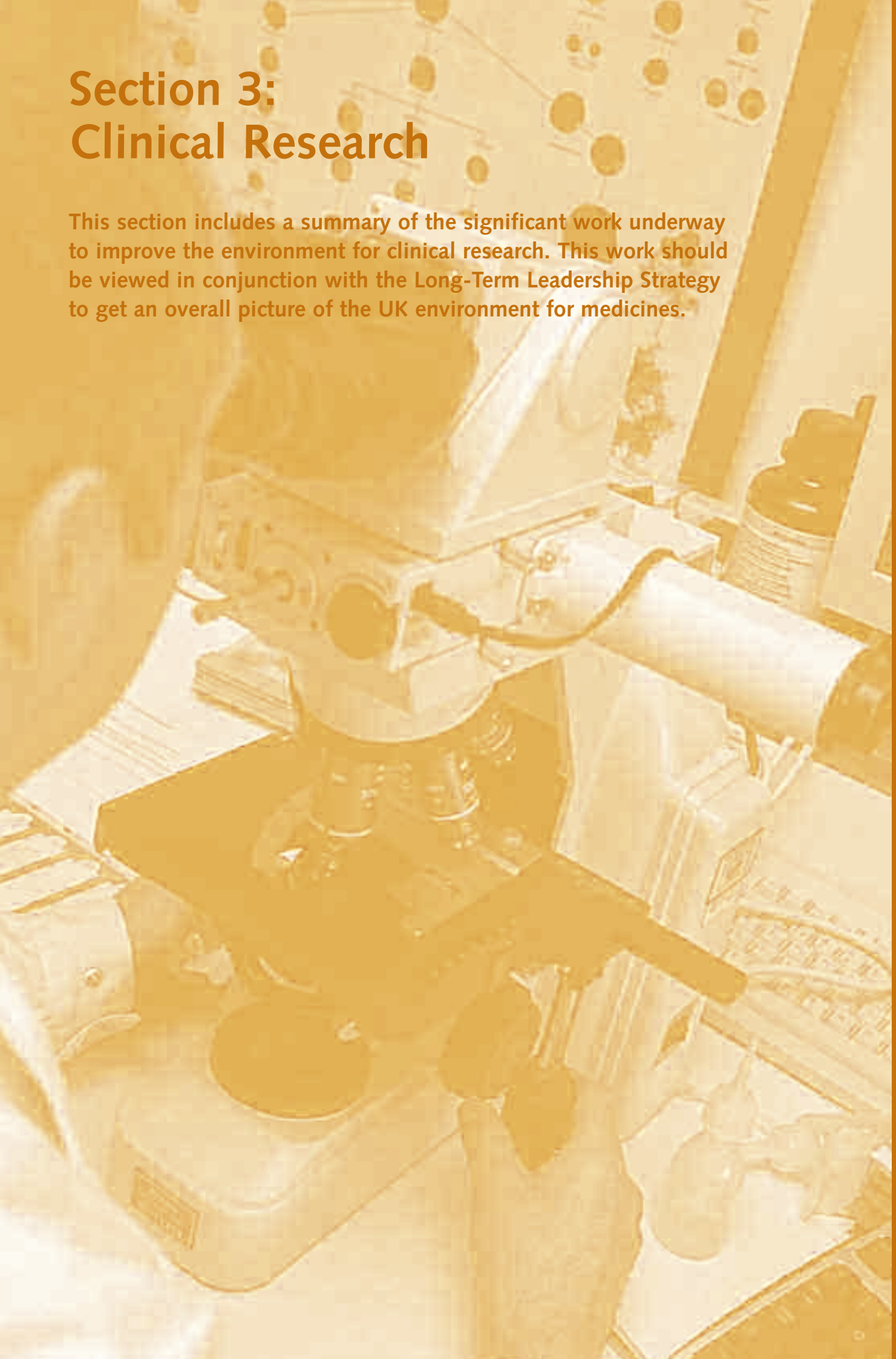
- Promote a set of core messages to improve communications and understanding about medicines, their development, safety monitoring and benefit:risk issues, suitably focused for a range of audiences.
- Improve patient and public engagement in medicines' regulatory approval processes.

## Implementation of the recommendations

4.42 The Regulatory Working Group will continue to meet to ensure the recommendations from this workstream are implemented. It will provide six-monthly reports on progress to the Ministerial Industry Strategy Group.

# Section 3: Clinical Research

**This section includes a summary of the significant work underway to improve the environment for clinical research. This work should be viewed in conjunction with the Long-Term Leadership Strategy to get an overall picture of the UK environment for medicines.**



# 5 Clinical Research

## Introduction

5.1 The quality of clinical research in the UK is one of the key reasons that attract the pharmaceutical industry to carry out its trials here. It was decided that as there were a number of major initiatives already underway that a separate workstream under the Long Term Leadership Strategy (LTLS) was not necessary, but that it was important that the work on clinical research should be viewed in conjunction with the other areas covered by the LTLS to give a complete picture of the work we are undertaking to improve the UK environment for medicine development.

## Summary

5.2 The activities of the UK Clinical Research Collaboration (UKCRC) and implementation of the Government's national health research strategy *Best Research for Best Health* provide a comprehensive range of initiatives designed to transform the clinical research environment in order to improve the UK's competitiveness and yield benefits for patients and the public. These will be further embedded by implementation of the recommendations in the Cooksey Report, which build upon *Best Research for Best Health,* and place increased emphasis on translation of research into health and economic benefit.

5.3 Major achievements over the last two years include:

- funding awarded for the creation of NIHR Biomedical Research Centres focused on translational clinical research (£450 million);
- launching a £134 million coordinated initiative to build a national framework for experimental medicine, supported by a range of funders;
- establishing a UK-wide infrastructure within the NHS to underpin clinical research, the UK Clinical Research Network (UKCRN), with initiation of the first industry-sponsored trials;
- developing, funding and implementing a new integrated and flexible training pathway for clinical academics;

- agreeing major initiatives to streamline the regulatory and governance environment and starting to implement change, including launch of a revised model Clinical Trials Agreement (mCTA), endorsed by industry, the NHS and Health Departments, for routine use without modification in contract research in patients in NHS hospitals;
- engagement with NHS Connecting for Health England to ensure that the new NHS IT system is developed to support research for the benefit of patients;
- developing a joint initiative to fund Public Health Research Centres for Excellence in the UK; and
- carrying out the first ever UK-wide analysis of health research funding.

5.4 The UK aims to provide access to a single system (the NHS) which reliably delivers distinctive quality and rapid access at reasonable cost. In order to improve the UK's reliability and performance in 2007 the UKCRN will be introducing:

- centralised and coordinated study feasibility and capability assessments based on a national perspective, knowledge of competing trials, and (eventually) proven site and network track record;
- central sign off for R&D at a national level for multi-centre trials, with routine use of the mCTA to speed up trial initiation; and
- a standard costings template and guideline tariff for trials.

## Background

5.5 Whilst the UK still attracts a larger share (23 per cent) of European pharmaceutical R&D investment than any other country, the gap with US R&D investment is widening and there is growing competition with countries such as Singapore, China and India. The Ministerial Industry Strategy Group (MISG) therefore considers it essential that the UK does all it can both to maintain its traditional strengths and to find new sources of competitive advantage. Given the establishment of the UKCRC in 2004 and continuing work of the Pharmaceutical Industry Competitiveness Task Force (PICTF) Clinical Research Working Group, MISG did not consider it necessary to establish an additional workstream to focus on clinical research as part of the LTLS, but monitors progress.

## Best Research for Best Health

5.6 The Government's national strategy for health research in the NHS was published in January 2006 following public consultation and amendment in the light of stakeholder comments, including senior level input from industry. It set out a five year R&D strategy for the NHS in England and established the National Institute for Health Research (NIHR) to:

- provide the framework through which the Department of Health can position, maintain and manage the research, research staff and research infrastructure of the NHS in England as a national research facility;
- enable the NHS to become an organisation that supports outstanding individuals (both leaders and collaborators), working in world-class facilities (both NHS and university), conducting leading-edge research focused on the needs of patients and the public; and
- developing the reputation of the NHS as a world-class environment for collaborative research in the public interest and preferred host for multi-centre clinical research in partnership and for industry, as outlined in the Government's 10-year Science and Innovation Investment Framework, in order to benefit patients, society and the NHS.

5.7 Project implementation plans, including milestones and timescales, were published with the strategy. These are updated regularly and published on the NIHR website (www.nihr.ac.uk).

5.8 Ringfencing of the Department of Health R&D budget was announced by the Chancellor of the Exchequer in April 2006.

## UK Clinical Research Collaboration

5.9 The UKCRC was created as a partnership between government, the voluntary sector, academia, patients and industry in October 2004. Its vision is to establish the UK as a world leader in clinical research by harnessing the power of the NHS for the benefit of national health and national wealth, making the UK the best place in the world to conduct research by 2014. Its priorities for achieving this are to:

- build up the infrastructure in the NHS – clinical research facilities for experimental medicine and the UKCRN;
- build up the research workforce – including addressing training and career structure;
- build incentives for research in the NHS – at the individual and institutional level;

- streamline regulatory and governance processes; and
- coordinate clinical research funding.

5.10 In addition, the UKCRC Partners are promoting cultural change through activities in the following areas: promoting patient and public involvement in research; raising public awareness of clinical research; establishing a new paradigm for working with industry.

## Progress in past two years: building up the infrastructure for research in the NHS

### NIHR Biomedical Research Centres (BRCs)

5.11 Funding for five 'comprehensive' and six 'specialist' BRCs has been awarded, to commence in April 2007, after a competition involving an international selection panel. These are sited in the most outstanding NHS/university partnerships in England and will receive considerable levels of sustained funds to drive progress on innovation and translational research. These centres form a key component of the NHS contribution to the nation's international competitiveness by making the best centres even better.

### Experimental medicine

5.12 Experimental medicine research is a traditional strength of the UK. UKCRC Partners and other funders including the Wellcome Trust, the Medical Research Council, Wolfson Foundation, UK Health Departments, Cancer Research UK, the British Heart Foundation and the Health Research Board of Ireland have taken action to boost this area and work towards establishing a National Framework of Experimental Medicine through a coordinated initiative providing up to £134 million of new investment. Key elements of this initiative include:

- further funding for 11 Clinical Research Facilities across the UK and one Facility in Ireland;
- establishment of a network of 17 Experimental Cancer Medicine Centres, with two more in development; and
- a major programme of funding for experimental medicine, 28 new awards with many in collaboration with industry.

### Clinical Research Networks

5.13 The UKCRN, developed and funded by the Health Departments of the four UK nations, provides a network of professional and dedicated research staff working in the NHS. Formally established in February 2005, all of its elements will be fully operational by 2008.

5.14 The UK-wide infrastructure is designed to underpin clinical trials and other well-designed studies in the NHS. It is made up of UKCRN England, the Northern Ireland Clinical Research Network, Research Networks in Scotland, and Clinical Research Collaboration Cymru. The total commitment to building up this infrastructure across the UK currently exceeds £60 million. UK-wide coordination is provided through the UKCRN Coordinating Centre.

5.15 In England, Topic Specific Research Networks have been established for Cancer, Diabetes, Mental Health, Dementias and Neurodegenerative Diseases, Stroke, and Medicines for Children. The latter offers a real opportunity for the UK to become the main European Centre for paediatric clinical research, now that the European Regulation on Paediatric Medicines has been approved. Industry leads have been appointed for each Topic Specific Research Network and at the UKCRN Coordinating Centre to facilitate engagement with companies. By the end of November 2006, 17 industry-sponsored trials had been adopted by UKCRN. In addition, a Primary Care Research Network with eight Local Research Networks, covering all England, was created in 2006 and a Comprehensive Research Network, to address all other areas of disease/need and play a key role in streamlining R&D management and governance, will be set up from April 2007.

### Realising the research benefits of NHS IT programmes

5.16 The creation of cradle-to-grave electronic patient records for its large (> 60 million), socially and ethnically diverse population, coupled with the fact that almost all the population receives its healthcare via the NHS, gives the potential to confer unique benefits to the UK as a site for clinical research. All four Health Departments across the UK are working to achieve this goal and the Government has committed to ensure that the capability exists within the NHS national IT system to facilitate, strictly within the bounds of patient confidentiality, the recruitment of patients to clinical trials and gathering of data to support research on the health of the population and the effectiveness of health interventions.

5.17 In a major new development, a UKCRC R&D Advisory Group to NHS Connecting for Health (CfH), whose membership includes industry, has been established to provide collaboration between the research community and CfH, in realising the potential benefits for research of the national care record infrastructure and to establish a joint work programme. Its Terms of Reference were approved by Ministers. Four simulations have been initiated to pilot the capability of the infrastructure to support recruitment of patients for clinical trials, active surveillance (focusing on pharmacovigilance), prospective tracking of an identified cohort and an epidemiological study. Industry is leading the first two pilots.

### Building up the research workforce

5.18 The UKCRC Partners, working with a wide range of stakeholders, have developed, agreed and implemented a new integrated career pathway for training clinical academics. In England and Wales, new training programmes are being established to support up to 250 Academic Clinical Fellowships and 100 Clinical Lectureship trainees per year in the NHS. In addition, the Higher Education Funding Council for England is investing £50 million in an award scheme to support 'new blood' Clinical Senior Lectureships. In Scotland, plans for additional training at pre-doctoral, clinical lecturer and senior clinical lecturer levels are being implemented. A report on training and careers for nurses in clinical research will be published shortly, with work on other elements of the research workforce starting shortly.

5.19 Plans for establishment of an NIHR Faculty, which encompasses researchers from all relevant professional backgrounds, are being developed for implementation from April 2007. Honorary membership will be offered to suitably qualified researchers in industry.

### Developing incentives for research in the NHS

5.20 Work is in progress to build incentives for R&D within the NHS. A transparent funding mechanism for research in the NHS in England has been established as part of *Best Research for Best Health* and the criteria for Clinical Excellence Awards have been changed to reward clinical academic activity.

### Streamlining the regulatory and governance environment

5.21 The UKCRC Partners have agreed a timetable for implementation of major changes aimed at delivering a new streamlined regulatory and governance environment. Key elements will include:

- Restructured NHS approvals. The Comprehensive Research Network in England will deliver a system for central sign-off for R&D at a national level for multi-centre trials to speed up trial initiation.
- Streamlined permissions and approvals systems. In England, the User Requirements for an integrated NIHR Research Information System to support bureaucracy busting has been produced.
- UK-wide Advice Network for consistent, authoritative advice (piloted from July 2006).
- A suite of model agreements.
- Full implementation of 'Research Passports' for Honorary Contracts from April 2007.

5.22 A key achievement for the PICTF Clinical Research Working Group in 2006 was the revision and updating of the mCTA for industry-sponsored trials involving patients in NHS hospitals. The revised mCTA was launched in October 2006 and has been endorsed for routine use in an unmodified format by the Health Departments, NHS Confederation, Monitor, Council of Heads of Medical Schools, ABPI and BIA, and is a good example of Government, the NHS and industry working together on initiatives to speed up the initiation of trials in the UK. A tripartite Agreement designed for use by CROs is scheduled for launch in spring 2007.

### Coordinating research funding

5.23 In the first exercise of its kind to be carried out anywhere in the world, the UKCRC Partners have published the first ever analysis of health research funding in the UK and is available at www.ukcrc.org/PDF/UKCRC_Health_Research_Analysis_Report.pdf

5.24 A consortium of funders working as part of the UKCRC Public Health Research Strategic Planning Group have agreed a joint initiative to fund Public Health Research Centres for Excellence in the UK.

### Patient and public involvement in research and raising awareness

5.25 The major stakeholders are working together to pursue a joint strategy to promote patient and public involvement in research. Patient and public involvement in clinical trials is also a central aim of the UKCRN. The UKCRC has established a Task and Delivery Group for Public Awareness. Amongst its plans include development work on educational materials to support elements of the national curriculum. In addition, the UKCRC has developed a booklet and a leaflet designed to increase patients' and the public's understanding of clinical trials.

### A new paradigm for working with industry

5.26 Industry is represented on the UKCRC Board through the Association of the British Pharmaceutical Industry, the BioIndustry Association and the Association of British Healthcare Industries, who ensure appropriate industry input across all UKCRC activities. In addition, high-level strategic advice is provided by the Industry Reference Group, chaired by Sir David Cooksey. An Industry Road Map Group was established in May 2005 as a result of discussions at the Industry Reference Group to develop proposals on how the UKCRN, on behalf of the NHS, could best deliver industry contract and collaborative research and over what timescale, taking into account sector specific needs. May 2006 saw the initiation of a scheme for industry secondees to the UKCRN to support the development of processes.

## Conclusion

5.27 Many of the areas of progress highlighted above have been taken forward further in the recent Cooksey Review. Together, these steps to improve the clinical research environment in the UK, with its benefits for patients, the NHS, researchers, government, and the industry, will continue to be an area closely monitored by MISG.

# Section 4: The Future

**This section sets out an agreed vision of the future environment for medicines and research that we should be working towards. It also includes a high level timetable for implementation of the Long-Term Leadership Strategy.**

# 6 Vision for improving patient care in the UK

This paper is the work of a group of experts brought together at the request of the Secretary of State for Health and the Minister for Delivery and Quality to define how the healthcare of patients could be enhanced through improved use of innovative medicines. The group has provided personal perspectives and the paper does not necessarily reflect the views of the Institutions the individuals represent. The paper focuses primarily on medicines, but also touches on broader public health issues.

The paper is written with a ten-year horizon in mind and lays out four key platforms of opportunity that the workgroup believes, if embraced, would go far towards creating a world-leading health and research environment in the UK. The underpinning themes are as important as the specific suggestions, and they represent a philosophy from which much flows. In large part, they are uncontroversial, but they provide a frame against which long-term evolution of a large and highly complex system can be judged. An assessment of the feasibility of the proposals in this document is underway and will be the subject of subsequent regular discussion within government and between stakeholders.

The group involved in the creation of this paper were:

Richard Barker, Director General, ABPI
Professor Sir Leszek Borysiewicz, Deputy Rector, Imperial College
Professor Sir Alasdair Breckenridge, Chairman, Medicines and Health
Mike Farrar, CE, North West Strategic Health Authority
Professor Simon Howell, Chairman, Diabetes UK
Professor Alex Markham, Chief Executive, Cancer Research UK
Professor Martin Marshall, Deputy Chief Medical Officer, Department of Health
Professor Anthony Newman Taylor, Consultant Physician, Brompton Hospital
Professor Sir Michael Rawlins, Chairman, NICE
Dr Mark Walport, Chief Executive, Wellcome Trust
Andrew Witty, President, GSK Pharmaceuticals Europe
Professor Ashley Woodcock, Consultant Physician, North-West Lung Centre

## Introduction

6.1 The UK has a proud history of public healthcare provision and claims many important firsts in the discovery and development of healthcare innovations. It is the EU leader in biomedical research and development and continues to drive the debate on healthcare issues. Integration of the research base is a key strength, particularly in the early phases of research. The UK's internationally-recognised research base feeds early clinical research, making the UK a leader in translational medicine. The UK is home to two of the world's top ten pharmaceutical companies and other research-based multinationals which collaborate widely with academia and the NHS. The UK healthcare biotechnology sector is also strong.

6.2 A unique potential competitive advantage for the UK is that patient care takes place within one linked system, creating the potential for a rich research resource. The potential of the National Programme for IT (NPfIT) as a globally unique mechanism to better understand healthcare complexities and provide an aid to modern research should not be underestimated. Ensuring the system's full exploitation for the benefit of research deserves appropriate effort. The UK should have the ambition of being a leader in research and delivery of patient care; achieving this will require new approaches and systems like NPfIT to be implemented successfully. Additionally, significant effort will be required to modernise and strengthen the academic–industry–government interface.

6.3 The UK is at an important crossroads. With a fine history of healthcare innovation and delivery, it now faces financing challenges as well as new and emergent research competitors on the global stage. Its leading position is not assured and this paper highlights a series of dimensions along which the NHS, government, academia and industry are encouraged to give serious consideration. Some of the themes in the paper are broadly under examination already, for example through the work of the UK Clinical Research Collaboration (UKCRC). The Government is also addressing some of these issues through *Best Research for Best Health*, a strategy that highlights areas for action to be taken.

6.4 The UK should be proud of its current skills and capabilities but needs to recommit to a *culture of excellence in research*; this will require specialisation in both research fields and institutions. Alignment of a variety of different players within the NHS is crucial, as well as a greater sense of *partnership* between players. The UK should lead the world in the development and delivery of long-term innovations in medicine which aim to *maximise patient well-being*, at an affordable cost to society. As the UK continues to modernise, it should embrace *greater patient involvement*. It should also ensure that reward and decision-making systems remain dynamic, flexible and able to keep pace with and exploit fully the benefits of research which constantly evolves, updates and surprises.

## Facilitate the development and use of better treatments through attracting more clinical research to the UK

The aspiration is to make the UK a world-leader in clinical research, particularly in the emerging field of translational research, through building expertise and partnership and increasing efficiency. The goal is to improve patient care through significantly increasing the amount of clinical research undertaken in the UK and creating a mindset of taking basic research through development and into routine clinical care.

6.5 Increasing clinical research offers great advantages to the UK. Widespread involvement of the NHS in research would facilitate early opportunities for new technologies and medicines to be assessed for use in the UK. Patients would benefit from early potential access to breakthrough science; physicians would benefit through greater opportunities to collaborate on a broad, global scientific front; the Government would benefit from both increased investment in R&D and the opportunity to build an institutional view of the cost-benefit of new medicines. Research operates in a global environment and other countries are successfully establishing a competitive position via a selection of levers such as research excellence, cost and simplicity. The UK must evolve to remain competitive.

6.6 There are two key areas of research where the UK could develop a global competitive advantage.

1. Early phase translational research that takes research from 'bench to bed' or proof of concept studies designed to generate initial ideas and from which all downstream research flows. This is already a UK area of strength.

2. The measurement of safety, effectiveness and health outcomes for medicines and other interventions used in clinical practice.

6.7 The UK should thus focus its activities on building capacity to undertake intelligent proof of concept, phase I and II studies as well as phase IV studies that measure the impact of medicines used in a real-life setting. Funding should be focused in areas where health need is greatest and there is a good chance of scientific success. Five such areas are suggested encompassing infection and immunity, cardiovascular disease, diabetes, neuropsychiatric disease and cancer.

6.8 If phase II and IV capacity is in place, then more phase III studies will be attracted to the UK. In addition, a continued focus on making the UK an efficient trial location where quality is high and execution is fast, will further underpin the retention of these types of trials in the face of growing competition from low cost countries. Large, multi-centre, publicly-funded clinical trials should also be accommodated within the NHS in order to investigate areas of significance to healthcare but which are unattractive to commercial sponsors. The clinical research facilities being funded through the UKCRC Partnership should facilitate the development of all these activities.

### Creating a culture of excellence

6.9 The UK is competing globally; it needs to be able to partner with the best global contributors. To do that, the UK itself needs to develop a culture of research excellence, with national centres for clinical research created, lead by clinicians who are recognised globally in their field, that rank with the best available in the US, EU and Asia. To achieve this, resources must be focused and more courage is needed to 'pick winners' in funding decisions as the UK can realistically support around only five centres of *real* global significance in clinical research.

6.10 However, a much broader group of universities and hospitals need to be engaged if the desired transformation in clinical research is to be achieved. They should support and be supported by the national centres of clinical research mentioned above, in a 'hub and spoke' mechanism. For this model to work, internal competition within the system needs to be managed significantly better as there are currently around 25 UK research-focused universities competing with each other for projects and funding; collaboration is low. If this is not addressed, funding will remain spread across an increasing number of centres, and the opportunity to create and maintain true worldwide centres of excellence will be missed. Competition can drive short-term benefits but to drive excellence and address the issue of very long lead-times for R&D, competition needs to be managed to the benefit of the UK as a whole.

### Creating partnership between industry and academia

6.11 Much greater connectivity between the academic sector, the NHS and industry is needed. There remains an 'us and them' mentality between academia and industry, so that research conducted in collaboration with industry is seen as of lower value than 'pure' academic research. Academic research should be rewarded on the basis of the meaningful, utilisable outcomes it delivers. Increasing secondments between industry and academia should be encouraged, for example by facilitating academics to spend time in pharmaceutical company laboratories. Industry should be more willing to collaborate with academia to answer questions of mutual interest. Supporting the Innovative Medicines Initiative (IMI) and the FDA Critical Path initiative may advance this agenda.

6.12 NHS trusts and clinicians are incentivised to deliver healthcare but they should also be actively encouraged to participate in research, particularly collaborative research with industry that answers questions that would improve patient care. The NHS consultants' clinical excellence awards scheme, that recognises and rewards the exceptional contribution of NHS consultants, over and above that normally expected in their job, could be used to achieve this. The work being done by NHS R&D will encourage trusts that are already engaged in research to do more but more consideration needs to be given to how to engage trusts which are not currently research-focused.

6.13 One example of best practice of industry-academic partnership today is the Medicines Evaluation Unit at the North-West Lung Centre in Manchester. This organisation is a private company (and registered charity). It has a dedicated trials unit on the hospital site, and conducts trials on behalf of industry in an efficient and effective way. It has informal agreements with other UK-based academic centres and shares the workload of trials it conducts. The centre is profitable and its profits go back into the hospital to fund non-commercial clinical research and its associated infrastructure.

### Improving efficiency of research

6.14 The UK is likely to remain a relatively high-cost location for clinical research and is unlikely to compete with lower-cost countries on the dimension of cost. While cost is important, efficiency and speed are of greater importance as reducing the time to conduct a trial results ultimately in earlier product launch, which is of value to industry and patients. This is particularly important for phase III trials but also has a big impact on earlier phase trials.

6.15 The Government should aim to provide a regulatory environment that is proportional to the activities being undertaken and that nurtures biomedical research. Trial approval times need to reduce significantly. An aspirational target is to achieve approval in ten working days, from when an application to the regulator is made. To get even close to this target, national approvals would be needed, rather than the current mix of national and local approvals. Another enabler is the creation of clinical research networks that provide a single access point to conduct trials and facilitate physician and patient recruitment. These are being developed today under the UKCRC. It is critical that networks are developed in partnership, with speed of recruitment as a top priority.

6.16 Creating good IT connectivity through electronic medical records is also a key enabler to increasing efficiency. The greatest opportunity to increase later stage clinical research is to use systems such as the NPfIT to create a step-change in the efficiency of recruitment of patients into clinical trials and monitoring patients whilst in trials. Pilots, to understand research needs, are under consideration in advance of the system being available; these should be encouraged. This is a potential area for Public Private Partnership programmes. In addition, use and development of existing systems such as the General Practice Research Database (GPRD) should be encouraged.

### Generating a skills base for clinical research

6.17 For this integrated approach to be realised, the number of physicians with a good understanding of clinical pharmacology needs to be increased. There is a real lack of clinical pharmacologists established or in training in the UK; these people are needed by the NHS, academia, regulators and industry. Encouragement should be given to clinicians to achieve either specialty, or subspecialty, recognition. More training at medical school in clinical pharmacology should also be delivered to train all doctors and it needs to be provided more effectively. The industry could contribute to this through funded positions within medical schools. Facilitating the development of clinical pharmacology skills would have benefits beyond research as it would improve the delivery of patient care through healthcare professionals using medicines more effectively. Academia would also welcome education on regulatory approval of trials.

6.18 Overall, to strengthen the biomedical research base in the UK, enhancements in science education at primary and secondary as well as tertiary level are needed; this is being addressed in the Government's 10-year Science and Innovation Framework.

### Linking research to service delivery

6.19 Provision of excellent, research-based service delivery is important; the results of research, be it for medicines or other interventions, must be introduced rapidly into clinical practice. Increasing the evidence-base of healthcare interventions would have significant benefits for patients, healthcare professionals and the system as a whole and could address some of the prescribing conservatism that is inherent in the UK. An NHS National Clinical Director has taken the lead in some areas, including cancer, with success; national leadership should be further encouraged.

## The UK to be a world leader in measuring the impact of medicines when used in clinical practice

The aspiration is to make the UK a world-leading centre for the measurement of safety, effectiveness and health outcomes of medicines once they are used in clinical practice. The vision would be to develop medicines that address unmet health needs and that are introduced rapidly into clinical practice in the knowledge that their use will be monitored proactively and routinely in real-time, for safety and other outcome parameters, such as effectiveness.

6.20 Clinical trials are conducted on narrowly-defined patient populations under strictly controlled conditions, often comparing active drug to placebo, although comparative trials are becoming increasingly common. These placebo-controlled trials deliver the data needed for regulatory approval, but tend to not provide the overall health outcome and economic data that NICE needs; nor do they give a real indication as to the experiences patients will have when taking the medicine in an uncontrolled environment, on either the safety or effectiveness of the medicine. Industry trials should be designed to demonstrate health outcomes but equally, there would be benefits to generating new ways of understanding how medicines perform in patients in a real-life setting. Improving the effectiveness of traditional pharmacovigilance would also bring considerable benefit. This subject is addressed in the work of the Regulatory Working Group included in Chapter 4 of this report.

6.21 Post-launch monitoring of medicines would provide an evidence base on which to either expand, contract or maintain the population base best suited to the medicine. Good information exists already in primary care as a result of the GMS contract and this will improve in the future. Building on this expertise through using electronic medical records for research purposes would establish the UK as the only country in the world to be able to do this in an integrated fashion on a large population. Exploration of approaches to address a more dynamic approach to the lifecycle of new treatments and interventions would be worthwhile.

## Creating better dialogue between industry, regulators and payers about medicines in development

6.22 The development of a medicine takes 10–12 years, but there is little dialogue between government and industry usually until a medicine has a licence. Increasing dialogue between NICE and industry early in the development of new medicines, for example at the end of phase II, would be of benefit to all parties if it could be achieved without adding to development times. Industry would benefit by being able to devise a development programme for a medicine with a greater likelihood that NICE approval would be received at launch. Dialogue would also be of benefit to government to allow better planning for the introduction and funding of new medicines.

6.23 This early dialogue should be in parallel with or possibly integrated into an earlier dialogue with medicines regulators such as the Medicines and Healthcare products Regulatory Agency (MHRA) – to ensure that clinical development could be designed optimally to meet the needs of all parties, without adding further to the number of trials required for registration. Currently there is little engagement between industry and NICE during development of a product and the dialogue with MHRA starts relatively late.

6.24 It is recognised that achievement of joint or parallel dialogue would be difficult, with a European medicines regulation system assessing safety and efficacy and national systems assessing value. It is *not* suggested that a European system for health technology assessment should be created, as this should clearly remain a national competency. The MHRA and NICE should, however, take a leadership role in initiating dialogue with the European Medicines Agency (EMEA) and other stakeholders as the UK could create a leadership position if a pragmatic solution is developed.

### Developing a capacity to measure the impact of medicines and other interventions in clinical practice

6.25 A key enabler to improving the quality and quantity of data collected about the use of medicines in clinical practice is to develop systems that collate the primary and secondary medical records of patients electronically. Systems such as NPfIT provide a unique opportunity to achieve this but leadership is required to agree how the system should be designed to facilitate these 'secondary' uses of the data in anonymised form.

6.26 Going further than this, increased linkage, access and the effective use of anonymised data resources across government, including the eventual linkage to personal care records through NPfIT, would enable public health research to be undertaken on a scale never before seen and be invaluable to public policy development. It is important that the NHS can understand and address health inequalities, and develop disease registers to improve delivery of care. Achieving this would require linking data on, for example, health, housing and employment. These benefits will only materialise if these data can be shared and used in an anonymised way for research.

6.27 In the shorter-term, consideration should be given to using existing databases to gather safety, effectiveness and outcomes data today. Such databases could include population databases such as the GPRD or networking other existing GP systems. The creation of specific registries could also be encouraged for different issues or diseases. Some disease registries are already in place; there are 14 for cancer and an example of a database linking primary and secondary care data is the Diabetes/ Obesity Research Network (DORN) in Salford. Consideration should be given to making it easier to set up registries as currently each requires its own infrastructure. Clear guidelines are also needed on who can access the data.

6.28 In a similar way that networks are being created for clinical trials, collaborating networks of academic centres encompassing the UK's leading health economics centres would be of benefit. There is shortage of key personnel in the areas of statistics, health economics and epidemiology. People with these skills are needed by both regulators and industry.

## Develop partnership between all stakeholders with a goal of increasing access to medicines for patients

The aspiration is to generate partnership between the NHS, industry and other relevant stakeholders that focuses on how the partners can work together to improve health outcomes for patients being treated in the NHS. In short, the goal is to increase the likelihood that the NHS delivers the right treatment for each patient.

The number of new technologies that will become available in medicine over the next ten years will rise significantly. Pharmacogenetics may revolutionise prescribing and increasingly, genetic tests may be provided alongside new medicines. Advances in engineering will continue to produce new devices that possibly today are not even considered and new medicine-device combinations will become available. These advances will provide challenges for healthcare professionals in keeping up to date with the latest information, in order to be able to give the right treatment to each patient. They will also challenge payers with limited funds available to spend on healthcare and regulators that traditionally consider medicines and devices separately.

Encouraging appropriate use of medicines has considerable benefits for government, patients, healthcare professionals and industry. The goal should be to have healthcare professionals equipped to give the most appropriate treatment, based on current evidence, for each patient. To achieve this, change is needed by all stakeholders.

### Focusing resources to achieve greatest health gain

6.29 In socially-funded healthcare systems, such as the UK, resources invested need to deliver the greatest health gain. Interventions such as medicines, surgery and devices should be examined routinely to ensure that investment follows the technologies or procedures where the greatest chance of health gain is delivered.

6.30 As well as making decisions about which technologies and procedures should be used within the NHS, decisions should also be taken about which procedures and technologies should *not* be used. Today the system is better at deciding which technologies and procedures to start using than making decisions about decommissioning technologies and procedures that are not cost-effective. Consideration should be given to providing funding to do work to consider the areas of most need for 'disinvestment focus' and to suggest 'stopping strategies' that would result in targeted disinvestment. Primary Care Trusts and their practice-based commissioning schemes should be used to enforce plans for disinvestment, and implementation will be the key success factor.

### Creating a system where cost management and incentives for R&D are balanced and the dynamic nature of R&D is recognised

6.31 Gateways in the system of medicine evaluation tend to be relatively static. High emphasis is placed on analysis at the time the medicine is first introduced – for both regulatory review and health technology assessment. Although this is beginning to change, with the European New Medicines Legislation emphasising the requirement for a five-year regulatory review post-licensing, a more flexible approach could bring benefits to all stakeholders.

6.32 The amount of data available about a medicine and other treatments, is far from static, evolving during development and then continuing to evolve once it is used in clinical practice. Further work could be done, involving relevant stakeholders, to assess the feasibility of dealing more effectively with the evolving information available about technologies and procedures. It is critical that utilisation, value delivered and maintaining sufficient incentive for R&D are all finely balanced.

6.33 Demonstration of relative- and cost-effectiveness will increasingly be required by payers to allow widespread use of new medicines in patients. If a medicine does demonstrate value at launch, the system should facilitate wide and rapid uptake to all appropriate patients, at a price that rewards the value delivered. Industry needs to put greater effort into demonstrating health outcomes in clinical trials. However, there will be some medicines where value cannot be demonstrated at launch but for which collection of additional data would provide a good chance of proving value. Without some give by both industry and government, in the future there is a possibility that these medicines will not be used in the NHS. A compromise needs to be found that allows a degree of risk-sharing to ensure that the government does not pay for medicines that do not work but that equally, patients get access to medicines that may help them. These important issues need to be discussed and a solution agreed that meets the needs of payers, patients and industry. This is an area where the UK has the potential to take a world-leading position on both the techniques and level of collaboration between government and industry.

### Challenging all stakeholders to adapt to the changing environment

6.34 Achieving a significantly greater level of partnership between stakeholders in the delivery of patient care should be explored. If the industry could work in partnership with the NHS to support appropriate use of medicines and to develop cutting edge treatment approaches to maximise patient outcomes, this would be of great benefit and could contribute to reducing overall healthcare costs to society. For this to be achieved, change is needed by both industry and the NHS. This subject is explored in further detail by the Partnership Working Group in Chapter 2.

6.35 For industry to become a true partner with the NHS, the industry needs to be transparent and demonstrate integrity. It should be a consistent champion of appropriate prescribing, not simply an advocate for its products. Companies should also consider spending a greater proportion of revenue on R&D, focused on areas of unmet need where the potential healthcare benefits are greatest. Within marketing activities, companies should consider having a greater focus on education and provision of support services, for example to encourage patients who are undiagnosed with a disease to consult their doctor. They should also consider working with other stakeholders to promote an evidence-based approach to prescribing; the industry partnership with the British Thoracic Society to promote asthma guidelines is a good example of best practice. Other single disease charities may equally provide suitable partners in this activity, adding independence and credibility to the advice proposed.

6.36 The industry must also accept that the NHS is prepared to pay for better patient outcomes and must set itself up to deliver better health outcomes data on the medicines it develops. The industry is beginning to respond to this agenda and is urged to continue to do so.

6.37 The Government and the NHS should challenge thinking and take a long-term view to improving health outcomes. Long-term procurement of innovative new diagnostics, surveillance tools, medicines and devices could be made a key part of the mission of the NHS. New models of public private partnership – analogous to the public private partnerships to combat neglected diseases in the developing world – could also play a major role in funding R&D in areas of unmet need.

## Empower patients to take charge of their health and get more involved in decision-making about the use of healthcare technologies

The aspiration is to empower patients to be more responsible for their health through understanding more about their conditions and treatments. This should lead to better patient compliance and to attention to implementing preventative strategies. Although significant efforts are being made to engage patients, the level of involvement of patients in medicine research, development and regulation is currently low. The system needs to deliver what well-informed and engaged patients want, rather than what it thinks they want. Consideration should be given to augmenting the work of the MHRA communications team that is currently ongoing and commissioning work to include all relevant stakeholders and the advice of professional communicators, to discuss how greater patient engagement could be achieved.

### Patient involvement in medicines development

6.38 Industry engages with patients to discuss the development of new medicines but this is patchy and could be increased significantly. There would be benefits to industry and research if a better way could be found to understand and quantify true unmet patient need. Other benefits could be greater patient engagement in clinical trials and greater understanding of risk and benefit.

### Patient involvement in medicines regulation and HTA review

6.39 How to achieve greater patient involvement in the regulatory process is something currently under consideration. Radical proposals are needed such as conducting research with patients to understand their areas of unmet need and the risk-benefit profile they would accept for any given medicine. This could be done by using an organisation such as MORI to create different stakeholder panels. Greater consultation may also help the public to better understand risk.

### Better provision of balanced information to patients about diseases and treatments to drive behavioural change

6.40 How to provide information about medicines and other treatments to patients in a balanced, professional and effective way needs greater consideration. Currently much of the information patients receive, outside of their interactions with their GP and other healthcare professionals, is through the media. Patients are not a uniform group: some are passive and some are engaged already; different strategies will be needed for different groups, including different ethnic groups. Information is important but what is really needed is personal communication to drive behavioural change. It is also recognised that no one solution will fit all patients. Industry could work, with charities where appropriate, to provide education programmes, for the chronic diseases in particular, as it is here that the 'aware' patient can benefit most.

### Public health

6.41 The promotion of good health and the prevention of ill-health involves numerous players and many have little or no relationship to the delivery of healthcare. Nevertheless, the NHS, industry and academia can make important contributions. Pharmaceutical products to control risk-factors for cardiovascular disease, to assist in smoking cessation, and to help in the management of obesity are obvious examples. Equally, the development of vaccines also requires effective interactions between the academic community, industry and government. Historically the UK has been a leader in this area, and there are real opportunities for the future. A particular area for consideration should be the field of behavioural sciences as the delivery of high quality public health will depend on the ability of society to change or adapt behaviours with the goal of reducing health risk. A quality health service must give as much priority to audit, research and training as it does to delivery of care. To achieve this, a shift in resourcing and change in culture will be needed.

## Conclusion

6.42 The group that developed this paper considers it to be a coherent and constructive set of suggestions that warrant further investigation and thought. These ideas will be discussed further within government, the NHS, academia and industry and agreement reached on how to move forward with this agenda, as part of the future work of the Ministerial Industry Strategy Group (MISG).

## Implementation

6.43 MISG agreed that the secretariat would organise a small joint Government and industry group that should go through the paper to map:

i. What areas are already being taken forward through programmes which are underway such as the Long-Term Leadership Strategy and the R&D Strategy.

ii. What issues we can ask these programmes to consider.

iii. Draw up a timetable when it would be optimum to consider any areas that are outstanding.

6.44 This group will report back on its conclusions to the MISG meeting in May 2007.

# 7 Taking the Agenda Forward

7.1 The Long-Term Leadership Strategy (LTLS) has developed recommendations that can improve the environment for medicines in the UK and in Europe. The next challenge is to make sure that these are taken forward.

7.2 The three Working Groups have developed a high-level timeframe for taking forward their recommendations. This is set out in Annex 3 to this report. This provides a challenge but one that we must take forward jointly if patients are to benefit from what has been achieved to date through the LTLS.

7.3 To ensure the recommendations are taken forward the Working Groups have put in place governance arrangements to ensure they are delivered: the Partnership Working Groups has established an Implementation Board, and the European and Regulatory Working Groups will continue to meet with a focus on implementation. In addition, a group will be established to map out the ideas in the Vision Paper, and consider how these might be taken forward through the three elements of the LTLS and the work underway on research.

7.4 The overall monitoring of implementation of the LTLS will be undertaken by the Ministerial Industry Strategy Group (MISG), who will receive reports on progress at its twice yearly meetings. To ensure that MISG had the proper constitution to achieve this it reviewed its membership at its meeting in November 2006. It concluded that membership should be extended to include a representative from the following organisations:

- The Department for Education and Skills
- UK Trade and Investment
- The BioIndustry Association
- The Japanese Pharmaceutical Group.

7.5 These representatives will be invited to attend the next MISG meeting in May 2007.

7.6 In addition to its membership, MISG took the opportunity to consider whether its terms of reference continued to be appropriate to take forward this agenda. It decided that it should have formal terms of reference that take account of the implications of the LTLS. The agreed terms of reference is attached in Annex 1.

7.7 MISG will publish the monitoring reports, with the other papers discussed at its meetings, on its website at www.dh.gov.uk/policyandguidance/medicinespharmacyandindustry/industrybranch
It will also publish by the end of 2008 an update on progress of implementation of the recommendations.

# Annex 1: MISG membership

## Co-chairmen

| | |
|---|---|
| Lord Hunt | (Minister of State for Quality, Department of Health) |
| John Patterson[2] | (British Pharma Group & Executive Director, Development, AstraZeneca) |
| David Brennan[3] | (British Pharma Group & CEO, AstraZeneca) |

## Members

### Government

| | |
|---|---|
| John Healey | (Financial Secretary to the Treasury) |
| Malcolm Wicks | (Minister for Science and Innovation, DTI) |

### Industry

| | |
|---|---|
| Richard Barker | (Director General, ABPI) |
| Simon Best | (Chairman, BioIndustry Association & Chairman, Ardana) |
| Nigel Brooksby | (President, ABPI, & UK Managing Director, Sanofi-Aventis) |
| William Burns | (European Medicines Group & President of Pharmaceuticals, Roche) |
| Haruo Naito | (Japanese Pharmaceutical Group & CEO, Eisai) |
| Ian C. Read | (American Pharma Group & President, Worldwide Pharmaceutical Operations, Pfizer Inc.) |
| Andrew Witty | (British Pharma Group & President, Pharmaceuticals Europe, GlaxoSmithKline) |

Officials from the Department of Health, DTI, DfES, The Treasury, Medicines & Healthcare Regulatory products Agency, and UK Trade and Investment also attend.

Ministers and officials from other government departments and other representatives from industry attend as and when necessary.

2 Co-chair of MISG 2007

3 Co-chair of MISG 2008 onwards

## Terms of Reference

The Ministerial Industry Strategy Group (MISG) will bring together government and the pharmaceutical industry:

i. To promote a strong and profitable UK-based pharmaceutical industry capable of sustained research and development that should lead to the future availability of new and improved medicines.

ii. To lead on the strategic development of the UK environment and foster a transparent relationship between the NHS and pharmaceutical industry that will facilitate joint working for the benefit of patients, the NHS and industry.

iii. To provide a forum to discuss how the UK Government can be a leader in promoting the health and economic benefits of a strong pharmaceutical industry in Europe and the rest of the world.

iv. To monitor the implementation of the Long-Term Leadership Strategy.

v. To publish the competitiveness indicators on an annual basis, and review their implications for the UK.

The MISG will be co-chaired by the relevant DH Minister and the chairman of the British Pharma Group. It will meet at least once a year. The secretariat will be provided jointly by the Department of Health and the British Pharma Group.

The membership of the MISG, and its Terms of Reference will be reviewed every two years.

# Annex 2: History of engagement between the European Commission and the pharmaceutical industry

On 1 June 2005, Gunter Verheugen, European Commissioner for Enterprise and Industry, announced a new industrial strategy for the EU-based pharmaceutical sector. This sprang from accumulating evidence of a steady decline in the EU as a base for industry investment and as a source of new medicines. The Commissioner's initiative followed a number of previous efforts over previous years to improve the EU environment for the research-based pharmaceutical industry, and its importance can only be understood against that background.

In 1993, in response to concerns about potentially declining competitiveness, Commissioner Bangemann set up a joint Task Force with industry, and in March 1994 published a Communication on industrial policy for the pharmaceutical sector. This concluded that *"the legitimate concern to limit public expenditure must not be allowed to jeopardise the future of pharmaceutical research in Europe. Public health and social security have nothing to gain from a weakening of the European pharmaceutical industry, because… pharmaceutical spending will … have to be reimbursed … even if innovative activity is pursued in the United States and Japan in the future"*. It advocated a dialogue between Commission, Member States, and the industry about measures to improve EU industrial competitiveness. The Council accepted the diagnosis.

Commencing in December 1996, Commissioner Bangemann therefore convened a series of Round Tables on 'Completing the Single Market' – coincidentally three days after the European Court of Justice, ruling in the Merck/Primecrown case, had noted that the imposition of price controls was a factor likely to distort competition among Member States and had called on Community authorities to remedy these distortions. Further Round Tables took place in 1997 and 1998 and they reviewed national intervention in the market for medicines, the free movement of goods principle, health policy and industrial policy, and the collective provision of healthcare as against individual responsibility.

In May 1998, at the initiative of the UK Presidency, the Council asked the Commission to issue a Communication on completion of the single pharmaceutical market. The Council noted that this would require Member States to take account of the EU dimension in their domestic regulations. It recognised the importance of innovation for the whole pharmaceutical sector and the continuing need to contribute to research and development costs in prices paid for in-patent products.

In November 1998 the Commission presented a Communication as requested; but at the December 1998 Bangemann Round Table, the industry expressed its disappointment that the new Communication did not provide a basis for a new industry policy to enhance innovation, competitiveness and access. This view was shared by the European Parliament, which observed that the Commission did not seem to have addressed the questions raised by the Council.

In March 2000 the European Council resolved at Lisbon to make Europe "the most competitive and dynamic knowledge-based economy in the world" by 2010; and later that year Commissioner Liikanen (who had succeeded Dr Bangemann) convened a symposium to discuss the global competitiveness of the European pharmaceutical industry. This received a report from Professor Pammolli of the University of Siena, which demonstrated that the European pharmaceutical industry was losing competitiveness compared to the USA, and that R&D investment was increasingly gravitating towards North America.

This assessment was the main driver to the setting up of the 'G10', High Level Group on Innovation and Provision of Medicines, by Commissioners Liikanen and Byrne (Public Health). The G10 brought together different stakeholders – industry, the Commission, Ministers from five member states (France, Germany, Portugal, Sweden, UK), patients and healthcare providers – to explore ways of tackling the now-familiar issues of improving industry competitiveness in the EU while encouraging high levels of health provision. Its report, presented in May 2002, contained 14 recommendations.

It was received as a constructive contribution and a year later, in July 2003, the Commission offered practical proposals for implementing the recommendations in a Communication that provided a reference point for legislative initiatives aiming at ensuring more rapid decision-making and efficient registration procedures and speeding up market access for innovative medicines. The Communication was discussed by Member States at the Competitiveness and Health Councils. The Competitiveness Council invited Member States to consider the suggested actions for competition between medicines that are neither purchased nor reimbursed by the State, and for the rapid launch of medicines after the granting of Marketing Authorisation; and it asked the Commission to organise an EU-wide reflection on different approaches to pricing and reimbursement for medicines. The Health Council was similarly supportive but focused more on the assessment of relative effectiveness for pricing and reimbursement decisions, and it called for the development and expansion of information about medicines for health professionals and patients.

Over the succeeding 18 months (which encompassed the installation of a new Commission) little progress was made. Commissioner Verheugen had taken over responsibility for Enterprise and Industry, and his June 2005 announcement of a new pharmaceutical strategy was aimed at picking up this "unfinished business". On innovation, the Commissioner proposed a doubling of the R&D budget and the creation of an Innovative Medicines Initiative in partnership with industry. On pricing, there should be examination of the possibility of more flexibility (while protecting Member States' capacity to control health budgets), of speed of access to the market, and of the lifting of price controls for medicines outside the state sector. In addition, there should be a stock-take of national relative effectiveness systems. On information for patients, the Commission proposed to establish a tool for making high quality information accessible to the public.

To take these deliberations forward, Commissioner Verheugen announced in October 2005 the setting up of a new *High Level Pharmaceutical Forum* (HLPF). This would include all Member States and other stakeholders, and its initial activities would be conducted through specialist working groups on pricing, relative effectiveness and patient information.

# Annex 3: Recommendations: Timeframe for implementation

| No. | Recommendations | Timing |
|---|---|---|
| **Partnership Working Group** | | |
| Joint working | | |
| 1 | The Department of Health will develop and deliver specific guidance on joint working for NHS organisations which endorses joint working | 2007 |
| 2 | The Department of Health and industry will develop and pilot a best-practice toolkit for use by NHS and industry organisations to support joint working and to include information on positive examples | 2007 & ongoing |
| 3 | The guidance and toolkit will be presented and promoted at key conferences and other appropriate forums | 2007/08 |
| 4 | The ideas generated at the Workshop of senior NHS managers will be further considered and a process agreed to take forward the potential areas of joint working, in particular starting with a strategic articulation of how, for the benefit of patients, the NHS and industry can work together for mutual benefit | 2007 |
| 5 | The ABPI will develop with NHS managers training for industry managers who initiate and implement joint working projects | 2007 |
| 6 | The industry will work in collaboration with an NHS organisation to develop ongoing training and support for NHS organisations and industry on joint working | 2008 & ongoing |
| **Uptake of medicines** | | |
| Optimising system capacity and clarifying roles | | |
| 7 | Learning from the experience of the Pharmaceutical Oncology Initiative Partnership process to provide a framework for discussion and action planning between the Department of Health, NHS and industry | 2007 & ongoing |
| 8 | Ensuring that uptake of cost-effective innovation is embedded in new commissioning roles and systems as they develop | Ongoing |
| 9 | Scope out a broader piece of joint working to improve concordance | 2007 |
| 10 | The development of best-practice guidance for Area Prescribing Committees as they evolve in the newly-configured NHS, drawing on the learning from the research undertaken | 2007 |

| No. | Recommendations | Timing |
|---|---|---|
| Financial and planning systems | | |
| 11 | Ensuring that the relationship between uptake of effective innovations and key NHS financial and planning systems is properly understood by NHS managers and Boards, and that systems do not incorporate perverse incentives or barriers to uptake and, where possible, actively promote and incentivise uptake of cost-effective innovations | 2007 & ongoing |
| 12 | Reviewing and reissuing HSC 1999/176, which sets expectations about NHS action in managing the introduction of innovations not (yet) assessed by NICE | 2006 |
| 13 | Joint work between ABPI, NICE, the National Prescribing Centre and the NHS Horizon Scanning Centre to assess options for maximising the availability and use of horizon-scanning information as an aid to local planning | 2007 |
| 14 | Reiterating messages from the Audit Commission study *Managing the Financial Implications of NICE Guidance* | 2007 |
| Information for improvement | | |
| 15 | Publication and active promotion to both the NHS and industry of the Uptake of Medicines Study | 2007 |
| 16 | Analyses conducted to support this work should be revisited in three years' time | 2009 |
| 17 | Active engagement by industry with NICE and the Healthcare Commission to explore ways the information and insights it has can help the Commission fulfil its role of monitoring compliance with relevant NHS quality standards | 2007 & ongoing |
| 18 | Seeking clarity on the future development (timing and nature) of the prescribing support module of Connecting for Health | 2007 |
| Personal and professional development | | |
| 19 | In the short term, specific education/development tools will be made available to support key decision-makers involved in consideration of, and planning for, new drug technologies in the NHS, including members of Area Prescribing Committees and their equivalents | 2007 |
| 20 | In the longer term, efforts will be made to incorporate awareness of Health Technology Assessment concepts more fully into training for health professionals | 2008 & ongoing |

| No. | Recommendations | Timing |
|---|---|---|
| Support for NICE and implementation of its guidance | | |
| 21 | The industry, collectively, will offer NICE advice on effective dissemination and marketing strategies and techniques | 2007 & ongoing |
| 22 | The industry, collectively, will support new NICE work on reducing ineffective treatments to improve headroom for adoption of innovation | 2007 & ongoing |
| 23 | The industry will complement NICE's published 'How to' guide for the NHS with the development of a toolkit for pharmaceutical industry staff on implementation of NICE guidance | 2008 |
| 24 | NICE and the industry will raise awareness of NICE's pilot 'ERNI' database (Evaluation of Reviews of NICE Implementation) as a source of national-level information on uptake of NICE recommendations | 2007 & ongoing |
| **European Working Group** | | |
| 25 | Advocate to have a survey undertaken to map the presence across Europe of the main sub-sectors of the biosciences industry, as part of the HLPF process | 2007 |
| 26 | The UK Government to present the results of the NERA Study into Pharmaceutical Investment Decisions to the HLPF | 2007 |
| 27 | The UK Government to take the agreed principles on pricing forward to the HLPF Working Group on pricing, in the hope that they can be endorsed at EU level | 2007 |
| 28 | The UK Government to take the agreed principles on relative effectiveness forward to the HLPF Working Group on relative effectiveness in the hope that they can be endorsed at EU level | 2006 ongoing |
| 29 | The UK Government and industry to work together to utilise the UK experience in support of the emerging HLPF model for patient information | 2007 |
| 30 | The UK Government and industry to continue to support the early establishment of the Innovative Medicines Initiative and ensure that the project is adequately funded | 2007 |
| 31 | The UK Government and industry to continue to advocate the complete implementation of the G10 recommendations in all Member States | Ongoing |

| No. | Recommendations | Timing |
|---|---|---|
| **Regulatory Working Group** | | |
| Scientific debate | | |
| 32 | If evaluation of the pilot to facilitate earlier discussion of a broader range of issues between industry and MHRA demonstrates that it works well, UK to share this best practice with EU Member States to encourage similar practices to be developed in other countries | 2008 |
| 33 | Establish a Forum to enable industry and regulators to consider regulatory requirements in respect of techniques used in medicine development that may not yet be the subject of guidance, or for which current guidance needs updating. Where appropriate, share with the EU the outcome of discussions | 2007 |
| EU Clinical Trials Directive | | |
| 34 | The UK will promote EU harmonisation of requirements, by clarifying differences in Member States' national requirements for approval of clinical trials, questioning the need for these, and working towards harmonisation of requirements between Member States, leading to least regulatory burden consistent with the legislation and protection of public health | Ongoing |
| Electronic submissions to MHRA | | |
| 35 | To achieve full electronic working in UK by the end of 2007 | 2007 |
| 36 | To promote the use of the eCTD in order to develop combined industry and MHRA experience of using the processes and specification | 2008 |
| 37 | Achieve industry compliance with initial submissions (and subsequent changes) in eCTD format for new active substances by 1 April 2008 and for all new applications by the end of 2008 | 2008 |
| 38 | Use the UK experience to both influence and comply with a standardised technical framework for eCTD across the EU | 2008 |

| No. | Recommendations | Timing |
|---|---|---|
| Risk management planning | | |
| 39 | MHRA will develop UK guidance on risk management planning and promote it as a best practice model with a view to incorporating it in EU guidance. MHRA will also work with industry to agree a model for a Risk Management Plan summary to be available to prescribers, patients and the public | 2007 |
| 40 | MHRA will agree a programme of work with Connecting for Health, the Agency implementing the National Programme for IT, on the availability of data to enhance medicine safety monitoring, including provisions to address confidentiality and consent | Ongoing |
| 41 | Establish a network of Pharmacoepidemiology Centres of Excellence in the UK to provide a resource for industry in risk management planning | 2008 |
| Harmonising EU safety reporting of medicines | | |
| 42 | Promote harmonised safety reporting requirements throughout the EU | 2007 |
| 43 | Promote the development of a single EU regulation on safety reporting to replace the current diverse rules | 2007 ongoing |
| Safety concerns – when to share information | | |
| 44 | Pilot proposals for industry/regulator communications of potential safety concerns under investigation in the UK | |
| 45 | Consult patient/public representatives on public communication of safety issues – considering the possibility of using a Citizens' Jury approach | 2007 |
| 46 | The UK to work with the Commission and other EU countries to reach consensus on proposals for industry/regulator communications of safety concerns under investigation | 2007 |
| Improving communications | | |
| 47 | Promote a set of core messages to improve communications and understanding about medicines, their development, safety monitoring and benefit:risk issues, suitably focused for a range of audiences | 2007 ongoing |
| 48 | Improve patient and public engagement in medicines' regulatory regulatory approval processes | 2007 ongoing |

# Annex 4: Useful weblinks

*Analysis of Health Research Funding*
www.ukcrc.org/pdf/UKCRC%20PR%202004-2006.pdf

Association of the British Pharmaceutical Industry (ABPI)
www.abpi.org.uk

*Best Research for Best Health*
www.dh.gov.uk/assetRoot/04/12/71/52/04127152.pdf

British Heart Foundation
www.bhf.org.uk

Cancer Research UK
www.cancerresearchuk.org

*Clinical Trials Agreement*
www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4007010&chk=vpv1EB

Competitiveness and Performance Indicators
www.abpi.org.uk/Details.asp?ProductID=25

Connecting for Health
www.connectingforhealth.nhs.uk

*Delivering Patient-Centred Innovation in Medicines*
www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4135368&chk=YYEnto

Department of Health's National Programme for IT
www.dh.gov.uk/PolicyAndGuidance/InformationPolicy/NationalITProgramme/fs/en

*EU Clinical Trial Directive*
www.eortc.be/Services/Doc/clinical-EU-directive-04-April-01.pdf

European Commission Health Portal
http://ec.europa.eu/health-eu/index_en.htm

European Medicines Agency (EMEA)
www.emea.eu.int

*Eurostat's November 2005 report on the EU pharmaceutical industry*
http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-NP-05-044/EN/KS-NP-05-044-EN.PDF

General Practice Research Database (GPRD)
www.gprd.com

Healthcare Commission
www.healthcarecommission.org.uk

Health Research Board of Ireland
www.hrb.ie

High Level Pharmaceutical Forum (HLPF)
http://ec.europa.eu/enterprise/phabiocom/comp_pf_en.htm

*Influence of the Pharmaceutical Industry*
www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf

Innovative Medicines Initiative (IMI)
http://ec.europa.eu/research/fp6/index_en.cfm?p=1_innomed

Managing the Financial Implications of NICE Guidance
www.nice.nhs.uk/page.aspx?o=292077

Medical Research Council
www.mrc.ac.uk

Medicines Evaluation Unit
www.meu.org.uk

Medicines and Healthcare products Regulatory Agency (MHRA)
www.mhra.gov.uk

Ministerial Industry Strategy Group (MISG)
www.dh.gov.uk/PolicyAndGuidance/MedicinesPharmacyAndIndustry/IndustryBranch/IndustryBranchArticle/fs/en?CONTENT_ID=4113974&chk=7zOQmh

National Framework of Experimental Medicine
www.ukcrc.org/activities/infrastructureinthenhs/experimentalmedicine/nationalframeworkforexperim.aspx

National Institute for Health & Clinical Excellence (NICE)
www.nice.org.uk

NICE-published 'How to' guide for the NHS
www.nice.org.uk/page.aspx?o=howtoimplement

NICE's pilot 'ERNIE'
www.nice.org.uk/page.aspx?o=ernie

National Institute for Health Research (NIHR)
www.nihr.ac.uk

National Prescribing Centre (NPC)
www.npc.co.uk

NERA Economic Consulting
www.nera.com

NHS Connecting for Health
www.connectingforhealth.nhs.uk

NHS Horizon Scanning Centre
www.pcpoh.bham.ac.uk/publichealth/horizon/

*Our health, our care, our say: a new direction for community services*
www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4127453&chk=NXIecj

Pharmaceutical Industry Competitiveness Task Force (PICTF)
www.advisorybodies.doh.gov.uk/picft/index.htm

PICTF Clinical Research Working Group
www.connectingforhealth.nhs.uk/

*PICTF Report*
www.advisorybodies.doh.gov.uk/pictf/pictf.pdf

Quality & Outcomes Framework (QOF)
www.ic.nhs.uk/services/qof

*Review of UK Health Research* by Sir David Cooksey
www.hm-treasury.gov.uk/media/56F/62/pbr06_cooksey_final_report_636.pdf

Ten-Year Science and Innovation Framework
www.hm-treasury.gov.uk/spending_review/spend_sr04/associated_documents/spending_sr04_science.cfm

UK Clinical Research Collaboration
www.ukcrc.org

UK Clinical Research Network
www.ukcrc.org/activities/infrastructureinthenhs/clinicalresearchnetworks.aspx

UK Trade and Investment
www.uktradeinvest.gov.uk

US Food and Drug Association (FDA)
www.fda.gov

US Food and Drug Association (FDA) Critical Path Initiative
www.fda.gov/oc/initiatives/criticalpath/

Wellcome Trust
www.wellcome.ac.uk

Wolfson Foundation
www.wolfson.org.uk

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www.dh.gov.uk/policyandguidance/medicinespharmacyandindustry/industrybranch