

A review of UK health research funding

Sir David Cooksey

December 2006

A review of UK health research funding

Sir David Cooksey

December 2006

£25.00

© Crown copyright 2006

Published with the permission of HM Treasury on behalf of the Controller of Her Majesty's Stationery Office.

The text in this document (excluding the Royal Coat of Arms and departmental logos) may be reproduced free of charge in any format or medium providing that it is reproduced accurately and not used in a misleading context. The material must be acknowledged as Crown copyright and the title of the document specified.

Any enquiries relating to the copyright in this document should be sent to:

HMSO
Licensing Division
St Clements House
2-16 Colegate
Norwich
NR3 1BQ

Fax: 01603 723000

E-mail: hmsolicensing@cabinet-office.x.gsi.gov.uk

HM Treasury contacts

This document can be found on the Treasury website at:

hm-treasury.gov.uk

For general enquiries about HM Treasury and its work, contact:

Correspondence and Enquiry Unit
HM Treasury
1 Horse Guards Road
London
SW1A 2HQ

Tel: 020 7270 4558

Fax: 020 7270 4861

E-mail: public.enquiries@hm-treasury.gov.uk

ISBN-10: 0-11-840488-1

ISBN-13: 978-0-11-840488-4

Printed by The Stationery Office 12/06 349456

Printed on at least 75% recycled paper.

When you have finished with it please recycle it again.

PU079

Contents

	Page
Foreword	1
Executive summary	3
Chapter 1 Introduction	9
Chapter 2 The current state of play	13
Chapter 3 International comparisons and trends	29
Chapter 4 Analysis of the UK health research system	35
Chapter 5 New institutional arrangements	43
Chapter 6 Creating a research-friendly culture in the NHS	65
Chapter 7 More effective translation of research into health and economic benefits	85
Chapter 8 A new drug development pathway	105
Annex A List of abbreviations	115
Annex B Acknowledgements	119

Foreword

When I was asked to carry out this Review of publicly funded Healthcare Research by the Chancellor of the Exchequer in March, I knew that I would encounter widely differing opinions about current healthcare research performance and what needs to be done to optimise its potential to benefit patients, the National Health Service (NHS) and the wider healthcare economy. There was widespread acclaim for the strength of our basic research capability, usually funded by the Medical Research Council (MRC) or the Medical Research charities. Much credit was also given to the NHS R&D directorate for their more recent but unstinting efforts to better engage with basic researchers and with the healthcare industries to collaborate in clinical research and the development of innovative therapies and systems. The research and development continuum that should exist between all of these parties has not reached its full potential because of perverse incentives that value basic science more highly than applied research and by a lack of commitment to R&D in the NHS when massive pressure to achieve front line service targets risked diverting funds away from R&D and the innovation that flows from it — innovation which is so vital to improve the treatment of patients as well as contain the costs of healthcare delivery.

Following the Chancellor's decision to ring fence the Government's healthcare R&D commitment into a single fund, there has been an immediate benefit in terms of being able to plan the application of R&D funds in a more coherent way. This Review sets out to propose a structure for the funding arrangements for the whole spectrum of health research, with the objective of obtaining the maximum benefit from research success and, where possible, eliminating duplication of effort. This can only be achieved if all of those involved are dedicated to ensuring that they work together cohesively in the research continuum.

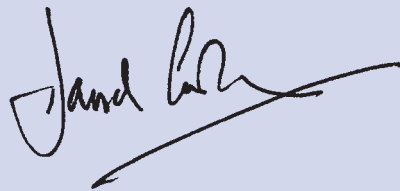
We were overwhelmed by nearly 300 written responses to our consultation and a very broad range of views expressed during many face to face meetings. All of this consultation was characterised by the real desire of all respondents to improve on the status quo. We were impressed by the willingness to embrace change which was expressed by a large majority of those consulted. Commitment to improving healthcare innovation was evident throughout. I am most grateful to all of them for their thought provoking contributions.

It is clear that our pharmaceutical, devices, diagnostics and biotech companies often find it easier to develop products outside the UK because of cost, access to patients for clinical trials, etc. Good progress has been made in tackling animal rights activists, but it is crucial that Government efforts here are maintained. Notwithstanding these deterrents, industry is attracted by our rich basic science heritage and opportunities that are now developing rapidly in the UK. First and foremost is the potential offered by the new 'Connecting for Health' IT database which will contain the medical records of the 48 + million inhabitants of England and should be accessible (with strong patient confidentiality safeguards) for important research, including clinical trials and subsequent pharmaco-vigilance studies of newly released drugs. In addition, there are the opportunities offered by the development of biomarkers and the emerging research into stem cell therapies.

Combined with the reorganisation of the NHS R&D function to make it more accessible and transparent for industry, this opens the door for the UK to excel again in healthcare innovation and service delivery. The Review sets out to describe how this can be delivered. It is a once in a generation opportunity to do so and for Britain to take a leading position in a major sector of the knowledge based economy.

In delivering this Review, I have been supported by an outstanding team comprising Paul Devenish from HM Treasury, Alison Austin from OSI and John Connolly from DH. They have all contributed hugely to the effort and I am most grateful to them. The team would like to thank Ilona Blue, Caroline Barr and Dan Micklethwaite from HM Treasury for their help towards the end of the review process with finalising the report.

The recommendations of the Review are a coherent attempt to make the very best of the resources that we devote to health research. If organised as we suggest, we believe that they will improve on the value for money achieved today and will substantially deliver improved patient benefit as well as a sustainable reason why this will be an outstanding location for healthcare companies to develop their businesses.

A handwritten signature in black ink, appearing to read 'David Cooksey', with a long horizontal stroke extending to the right.

David Cooksey

Executive summary

1 In March 2006, the Chancellor of the Exchequer and the Secretaries of State for Health and Trade and Industry invited Sir David Cooksey to undertake an independent review to advise on the best design and institutional arrangements for the public funding of health research in the UK.

2 The Review found that the UK Health Research system has many strengths. It has a long tradition of producing excellent basic science, with the Medical Research Council (MRC) funding 27 Nobel prize winners since its establishment in 1913. The quality of the health research base, combined with a national health service, creates a major selling point that attracts R&D investment from the pharmaceutical and biotechnology industries, which form a major part of the UK knowledge economy.

3 Whilst medical advances create opportunities for health benefits, they also create considerable challenges to these industries. A number of emerging factors in medical science are coinciding to create the potential for a step-change in our approaches to diagnosing and treating illness and disease. There is an increasing complexity of types of treatments available, ranging from conventional chemical compounds to biopharmaceuticals, molecular medicines, exploitation of gene therapy and cell replacement therapy using stem cells. These discoveries are a driver for increasing drug specificity, leading to smaller and more select target patient groups, with implications for drug development business models and costs.

4 In recent years, the UK Government has taken a number of actions to ensure the UK remains at the forefront of health research and a location of choice for the pharmaceuticals industry to locate its R&D. These actions include the creation of the UK Clinical Research Collaboration (UKCRC) to improve the infrastructure for clinical and medical research; the creation of the Joint MRC/NHS Health Research Delivery Group in the 2004 Spending Review to enable a more joined-up approach between Government funders of medical and clinical research; the creation of a new strategy for research in the NHS in England, *Best Research for Best Health* (BRfBH); and the establishment of MRC Technology, to manage and commercially develop intellectual property arising from the basic research carried out by the MRC's directly-supported scientists.

5 The role of rigorous independent peer review in allocating project funding in the UK has resulted in a globally competitive research environment. In order to continue to compete in the challenging context of globalisation, the Review believes the UK should aim to sustain and continue to build on its excellent research base. This is of crucial importance to the UK maintaining its well-deserved global reputation as an excellent location to conduct health research.

6 The Review found, however, that the UK is at risk of failing to reap the full economic, health and social benefits that the UK's public investment in health research should generate. There is no overarching UK health research strategy to ensure UK health priorities are considered through all types of research and there are two key gaps in the translation of health research:

- translating ideas from basic and clinical research into the development of new products and approaches to treatment of disease and illness; and
- implementing those new products and approaches into clinical practice.

7 The Review also found that the wider funding arrangements for supporting translation of ideas from conception to practice could be more coherent or comprehensive and, where arrangements exist, they do not function well.

8 The Review identified cultural, institutional and financial barriers to translating research into practice in the publicly funded research arena. But it also found that, in the private sector, the pharmaceuticals industry is facing increasing challenges in translating research into health and economic benefit. The Review has sought to make recommendations that will increase the translation of R&D into health and economic benefit for the UK, both in the public and private sectors.

KEY RECOMMENDATIONS

9 The Review recommends that the Government should seek to achieve better coordination of health research and more coherent funding arrangements to support translation by establishing an Office for Strategic Coordination of Health Research (OSCHR). The office will report jointly to the Secretaries of State for DH and DTI, and will allow for strategic input from the Health Departments from the Devolved Administrations. The Review recommends that the effectiveness of the joint reporting arrangements in practice should be reviewed in 2011.

10 Bringing together the health research budgets of the MRC and DH, whilst retaining two separate organisations, OSCHR will carry out the following functions:

- setting the government's health research strategy, taking into account the advice, priorities and needs set out by the National Institute of Health research (NIHR) and its counterparts in the Devolved Countries, MRC and the NHS;
- setting the budget required to deliver the health research strategy and the objectives for DH and MRC, including the distribution of the research budget between NIHR and MRC;
- submitting to the Treasury a joint funding bid for the agreed strategy in each Spending Review;
- monitoring the delivery of the health research strategy against objectives (objectives will feed through into Performance Management Frameworks for MRC and NIHR), to report to Ministers and Parliament on its progress, and to advise Ministers on the effectiveness of maintaining two separate public bodies; and
- encouraging a stronger partnership with the health industries and charities.

11 The Review also found that other institutional changes are necessary to maximise the economic and health benefits arising from its single health research budget:

- whilst the MRC should retain its current institutional structure and remain part of Research Councils UK, it is essential that the MRC Boards become more representative of the broad spectrum of health research and more streamlined, and that MRC builds upon its current links with other Research Councils, to ensure that research at the boundaries of health research and other disciplines receives adequate funding and attention;

- the NIHR should become a real, rather than a virtual institute, established as an Executive Agency of the Department of Health by April 2009, when the reforms set out in *Best Research for Best Health* will have been fully implemented;
- both the NIHR and MRC should have a duty to cooperate closely with OSCHR and to work to deliver the joint strategy for health research. Both should report to the OSCHR Board on a quarterly basis against objectives;
- there should be a much clearer allocation of responsibilities between MRC and NIHR, to ensure greater efficiency and effectiveness, and that each organisation focuses on its research strengths; and
- translational research should be a joint MRC-NIHR responsibility, with strategy overseen by a new Translational Medicine Funding Board and joint working facilitated by the OSCHR, with MRC Technology continuing to play a key role.

12 The Review believes that increasing demands on health spending means greater priority should be given to supporting medicines and therapies that tackle unmet health needs in the UK. OSCHR will combine ‘top-down’ and ‘bottom-up’ inputs, from the customers of research as well as those who carry it out, to set the strategic direction for research into particular disease areas, setting the vision and long-term objectives for the UK in each disease area, and it will plan how that vision is to be realised. The Review recommends that DH, together with the Health Departments in the Devolved Countries, should undertake a review urgently to understand the impact of diseases and illnesses in the UK and on the UK population and economy to determine the UK health priorities, which will underpin the UK health research priorities to be set by OSCHR. This review should report to the acting head of OSCHR, ideally in time for the findings to inform the CSR process.

13 However, the government currently has no way of signalling its health priorities to the healthcare industries. The Review therefore recommends that OSCHR be responsible for communicating the UK’s health priorities to improve market signalling to the pharmaceuticals and biosciences sectors. OSCHR will brand research projects, whether in the public or private sector, that it believes could address an unmet health need in the UK as ‘UK Priority Health Research Projects’. This brand will reflect:

- the contribution of the project to an identified health research priority in the UK;
- the quality of the research being undertaken; and
- the likelihood of the research resulting in a finding that could have a significant impact, including a value for money / affordability assessment at later stages.

14 In addition, the Review recommends that the status of ‘UK Priority Health Research Project’ should confer institutional and procedural advantages for health research that adds real value in tackling the UK’s identified health needs. This might, ideally, include faster approval for clinical trials in the NHS, and an expedited route through NICE approval.

15 The Review has found that the impact of health research in the international development context is constrained by a lack of coordination between funders. The Government’s Chief Scientific Adviser has recommended that a forum is set up to facilitate collaboration on development research in the UK, bringing together DfID, DH, Research Councils, and other funders of research, including charities and international funders. The Review supports the establishment of this forum,

but it believes that in the case of health research that there should also be an initiative to accelerate translation and enable delivery in the field. This could be provided as an additional responsibility of this forum but it would only be effective if it includes representatives of NIHR as experts in clinical, applied and health services research as well as MRC, in order to engage the NHS in enabling delivery.

16 The Review also found that NHS needs a stronger culture to support research. The Review welcomes the announcement in Budget 2006 that the DH R&D budget will be ring-fenced, and believes this is an important first step in achieving this cultural change. However, the Review found that there are other related funding streams that remain outside of this ring-fence, and the Review makes recommendations on further areas of expenditure that should be brought within the R&D ring-fence. Further, it believes consideration should be given in the Comprehensive Spending Review (in allocations across the UK) to additional funding in a number of areas, and most importantly for Health Technology Assessment, in order to support a more positive and pro-active approach to the uptake of cost-effective new ideas and technologies, along the lines of the agenda set out in the Wanless Reports.

17 The Review found that there is a need for a more systematic approach to the adoption of new technologies and interventions in the NHS, which can make assessment of their efficacy and cost-effectiveness problematic and in turn result in low rates of adoption and diffusion. The Review recommends that a more systematic approach should be adopted based on clearly mapped out processes.

18 The Review believes that, if the UK is to succeed in achieving its health and economic objectives, the government must consider ways of bringing drugs that address UK health priorities to market faster, but without compromising patient safety. It is increasingly clear that the current way of developing drugs in the private sector is unsustainable in the long-term. The Review found that regulations around the healthcare product development process have become ever more complex, and that Health Technology Assessment arguably happens too late in the drug development process. The Review proposes that the government, regulators and industry create a new partnership to pilot a new drug development 'pathway' to create wins for all stakeholders: industry, government, the wider economy and, most importantly, patients. This pathway should enable:

- more rapid discrimination between potential new therapies at earlier stages of drug development;
- earlier 'conditional licensing' of new drugs;
- involving NICE earlier in the process of development to accelerate assessment of clinical and cost-effectiveness;
- faster uptake of cost-effective drugs;
- clearer processes for ensuring NICE initial assessments and recommendations for further research are followed-up more systematically;
- the use of the NHS National Programme for IT (NPFIT) to ensure more rapid assessment of any emerging side-effects and efficacy over longer periods;
- streamlining of processes involved in setting up and costing clinical trials; and
- the use of NPFIT to identify appropriate patients for clinical trials.

19 The Review therefore recommends that OSCHR and the Translational Medicines Funding Board work with the healthcare industries and other stakeholders to develop proposals for joint public and private investment in new technologies for medicines discovery. The Health Technology Assessment (HTA) programme and NICE should seek to work with the Association of the British Pharmaceutical Industry (ABPI) and individual pharmaceutical companies to identify new medicines under development that might be suited to piloting earlier HTA and NICE involvement. OSCHR should work with DH, the Medicines and Healthcare products Regulatory Agency (MHRA) and the ABPI to develop a strategy and timeframe for developing the idea of earlier conditional licensing, working with the European Medicines Agency (EMA) and other European partners as necessary. A coordination mechanism should be set up to oversee these activities.

20 The Review has found that the impact of health research in the international context is constrained by a lack of coordination between funders. The Review supports the recommendation by the Government's Chief Scientific Adviser that a forum should be set up to facilitate collaboration on development research in the UK.

21 Taken together the proposals set out in this report will have a major impact on the way that new healthcare products are developed. The impact will be seen from an early stage when clinicians and scientists work together, where results from basic laboratory or clinical research are identified through the development pathway and clinical trials to product approval and evaluation. It will send signals to the healthcare industries that the UK is a world leader in R&D and that the Government is serious about increasing the amount of industry R&D undertaken in the UK. As the R&D process becomes more efficient, so the cost of that R&D will decrease reducing the cost of new treatments not just in the UK but worldwide. Changing the development system, reducing the uncertainty and cost will also result in more treatments for less common diseases.

22 Finally, Sir David Cooksey and the Review Team are extremely grateful for the invaluable contributions received from the wide range of stakeholders who responded to the consultation and made time to meet us to discuss the key issues, and we would like to thank them for their positive engagement during the review process.

1

Introduction

1.1 Health Research and Development (R&D) is an area of UK strength, promoting both health and economic gains. Currently, public funding for health R&D is split between the Medical Research Council (MRC) and the Departments of Health; but the Government's vision is of a holistic health R&D system that will maximise the value of the UK's health research base, ensuring the UK's health research is more closely aligned with wider health objectives, builds on scientific progress to date, and translates the results of research into economic benefit.

Importance of health industries to the UK economy

1.2 The quality of the health research base, combined with a national health service, creates a unique selling point that attracts R&D investment from the pharmaceutical, devices and biotechnology industries. These industries form a major part of our knowledge economy. They are prime investors in R&D. The pharmaceutical industry alone accounts for 25 per cent of UK business investment in R&D and it is a significant employer of highly-skilled staff. Given the sector's contribution to the UK economy, the healthcare industries are a key driver of wider productivity and make a significant contribution to the UK Government's vision, as set out in the Science & Innovation Investment Framework 2004–2014, of increasing aggregate investment in R&D to 2.5 per cent of GDP by 2014. But the UK-based industry faces competition not only from other Western countries, but also from emerging economies, such as China and India, which can increasingly provide access to the skills and other infrastructure support which the pharmaceutical industry needs, in addition to their cost advantages. Asian countries, notably India, China, Singapore, Japan and South Korea, are becoming substantial contributors to global research output. This global interaction represents a positive driver for the development of medicines to meet unmet medical needs, but also represents an economic challenge to the UK and other countries for whom the pharmaceutical industry is a key investor.

1.3 However, emerging economies also provide new markets and opportunities which the UK is well placed to exploit, given its innate strengths: a world class health sciences base, a unified health system in the form of the NHS, a pharmaceutical industry and finance sector that are well placed to exploit increased translation of basic science into marketable products, and an NHS system reform programme that offers huge opportunities for health research.

Changing nature of drug discovery

1.4 In parallel with these economic changes, a number of emerging factors in medical science are coinciding to create the potential for a step-change in our approaches to diagnosing and treating illness and disease. In particular, there is an increasing complexity of types of treatments available, ranging from conventional chemical compounds to biopharmaceuticals, molecular medicines, exploitation of gene therapy and cell replacement therapy using stem cells. These discoveries are a driver for increasing drug specificity, leading to smaller and more select target patient groups, with implications for drug development business models and costs.

1.5 As a result of these trends, the UK and other countries face a series of challenges, including how to manage the introduction of new technologies rapidly, safely and cost-effectively, and how to manage the potential financial impact on health systems.

1.6 Patient and wider consumer pressure for rapid access to new technologies has seen the health care sector's share of the US economy grow from 13.6 per cent in 1997 to 16 per cent in 2004¹, and

¹ <http://www.washingtonpost.com/wp-dyn/content/article/2006/01/09/AR2006010901932.html>

is predicted by some to grow to above 20 per cent of US GDP by 2015². European countries face similar pressures, albeit starting from a lower base, and with tighter regulation of costs preventing as steep an increase. In the UK, NHS spending will have doubled in real terms between 1997 and 2008, with health care expected to account for around 9 per cent of GDP at the end of that period. Despite this increase in spending, there has continued to be some controversy in the media around limiting access to certain drugs on cost-effectiveness grounds, illustrating a conflict between patient demands and the reality that available resources are finite.

UK remaining at the forefront of health R&D

1.7 The seismic shift in medical science outlined above, coinciding with similarly large-scale changes in the industries which commercialise the ideas developed by medical science, therefore poses challenges for publicly-funded health research and the role of the NHS, universities and the education system in supporting the UK's continued strength in this area. In recent years, a number of actions have been taken by Government to ensure the UK remains at the forefront of health research, including:

- the creation of the UK Clinical Research Collaboration (UKCRC), a partnership between public, private and voluntary sectors which is designed to improve the infrastructure for clinical and medical research – its Two Year Progress Report has just been published, highlighting significant progress across a wide range of areas³;
- the creation of the Joint MRC/NHS Health Research Delivery Group in the 2004 Spending Review, to try to get a more joined-up approach between Government funders of medical and clinical research;
- Best Research for Best Health, a new research strategy for research in the NHS in England, was launched in January 2006. The strategy aims to create a health research system in which the NHS supports those engaged in leading-edge research to focus on the needs of the patient and the public; and
- MRC Knowledge Transfer (KT) activity and MRC Technology. MRC recognised the need to encourage technology transfer in the late 1980s, and set up the forerunner of MRC Technology (MRCT) to help its institutes and units do this. MRCT is MRC's exclusive agent for management and commercial development of intellectual property arising from the basic research carried out by MRC's directly-supported scientists.

1.8 However, more needs to be done, in particular to ensure that publicly funded health research is carried out in the most efficient and effective way, and to facilitate rapid translation of research findings into public health gains. Against this background, the Government announced in Budget 2006 its intention to create a single health research fund of at least £1 billion per annum. The purpose of creating the single health research fund was to bring together the two major elements in publicly funded health research, the Department of Health's R&D function and the Medical Research Council, in order to maximise the impact of health research, and ensure that the UK's publicly funded health research is more closely aligned with wider health and economic objectives.

1.9 The Chancellor of the Exchequer subsequently invited Sir David Cooksey to conduct an independent Review to advise on the best design and institutional arrangements for the public funding of health research in the UK. The terms of reference for the Review are set out in Box 1.1.

² See, e.g., Borger, C et al, *Health Spending Projections Through 2015: Changes On The Horizon*, Health Affairs, 25, No2 (2006)

³ <http://www.ukcrc.org/PDF/UKCRC&percent;20PR&percent;202004-2006.pdf>

Box 1.1 Terms of reference for the Review

To advise on the best design and institutional arrangements for public funding of health research in the UK, taking account of:

- health objectives — ensuring research priorities are firmly grounded in the Government’s wider health objectives, national and international, and that health research is rooted in, and a key priority for, the NHS;
- science objectives — ensuring the continued delivery of world class basic science, according to the long-standing Haldane principle, which states that day-to-day decisions on Research Council scientific funding must be taken at arms length from ministers. Funding should continue to be awarded on the basis of excellence across the full spectrum of health research, from basic to clinical and public health. This will include continued support for investigator-led research; and
- economic objectives — ensuring the delivery of high-quality translational health research to deliver real economic, as well as health, benefits from the UK’s excellent science base.

The review will particularly take into account:

- the decision announced in Budget 2006 to create a single research fund of at least £1 billion, jointly-held by the Secretaries of State for Health and Trade & Industry;
- the aim of building on recent reforms, including the creation of MRC Technology and the UK Clinical Research Collaboration (UKCRC), and the new NHS R&D Strategy set out in Best Research for Best Health;
- the need to maintain and build on the UK’s world-leading position in producing peer-reviewed, scientist-led ‘basic’ medical research and innovation in clinical research;
- the priorities and needs of the NHS, ensuring health R&D generates improvements in health outcomes, and building on successful applied research programmes, such as the Health Technology Assessment (HTA) programme and MRC Technology;
- the views of, and linkages with key stakeholders, including the NHS and universities, the health industries, research charities and the Devolved Administrations;
- economic evidence on any market failures that impinge on the development of innovative and clinically and cost effective medicines and new technologies; and
- evidence on what has worked well and what less well in other countries, particularly with regard to effective strategies for translating world-class basic research into demonstrable economic and health benefits.

Consultation process 1.10 The Review consulted widely, both in the UK and abroad, meeting a wide range of stakeholders. We met with officials from DH, OSI, MRC and other Government Departments and Agencies with an interest in the issues, including the Devolved Administrations. We also visited a number of facilities both in the UK and abroad.

1.11 The public consultation announced on 4 May 2006⁴ formed an important part of the review — just under 300 responses were received as part of the consultation from a wide range of stakeholders, including universities, NHS trusts, companies from the health industries, charities, learned societies, professional bodies, trade associations, government departments and independent groups, as well as personal responses from individuals. The comments and views were wide-ranging, from individual researchers who had an interest in one particular area of research, to organisations and groups who had detailed views on what the organisational arrangements should be. There were comments relating to the way that both MRC and DH funded research and suggestions for how the current position could be improved. Others expressed views on how to improve translation and commercialisation.

1.12 The Academy of Medical Sciences and the Royal Society jointly hosted a one day stakeholder meeting, entitled *Lost in Translation*, in July 2006. Over 70 leading representatives from science, medicine, medical research charities, the NHS, universities, Government Departments and the health industries attended the meeting.

1.13 In undertaking the Review and the associated consultation, we have looked at the process of enabling translation of health research in relation to the whole process from bench to bedside, and our analysis and recommendations, set out in the rest of this report, reflect this breadth of overview.

The report 1.14 This report is divided into the following sections:

- Chapter 2 provides background information, setting out the nature of health research and the current landscape in the UK;
- Chapter 3 reviews health research funding systems in several other countries from which the UK can learn; and
- Chapter 4 considers evidence on the balance of funding across different types of research and our analysis of the weaknesses in the current public funding arrangements for health research in the UK.

1.15 The subsequent chapters set out the Review's recommendations as to how these benefits can be delivered:

- Chapter 5 sets out the Review's objectives for and recommendations on the institutional arrangements for the new Single Fund for health research;
- Chapter 6 sets out recommendations on creating a research-friendly culture in the NHS;
- Chapter 7 explores wider issues affecting the translation of research into health and economic benefit, in particular improving translation not only from the laboratory to the creation of new products and ideas, but also translating those new products and ideas into clinical practice; and
- Chapter 8 makes further specific proposals to support the development of a new drug development pathway, laying out how the UK can develop a leadership position, building on US Food & Drug Administration's (FDA's) *Critical Path Initiative* and the European Innovative Medicines Initiative.

⁴ Full details of the consultation and questions asked can be found on the Treasury Website http://www.hm-treasury.gov.uk/Independent_Reviews/independent_reviews_index.cfm

2

The current state of play

Chapter overview

This chapter provides some historical context to health research in the UK. It explains what is meant by basic, applied and translational research and the “health research continuum”. The two main public funders of health R&D in the UK are the Medical Research Council and the Health Departments of England, Wales, Scotland and Northern Ireland. The MRC has traditionally focused attention on basic research, while the Health Departments have focused more on clinical and applied research. Across the piece, however, the majority of public funding for health research has been spent on basic research.

TYPES OF HEALTH RESEARCH

2.1 Classifying health research into different types is not a straightforward process. Health research spans a broad spectrum of research from very basic / fundamental research carried out in laboratories and aimed primarily at expanding knowledge, to very applied clinical research which sets out to answer a very specific clinical question, with a whole range of research in between, including public health and social care research. Whilst it may be easy to define what falls into the basic research category and what falls into the applied research category at the extremes of the spectrum, it is often difficult to do so towards the centre, and some may argue that this research should not be classified as basic or applied.

2.2 However, for the purposes of this report, the Review’s working definitions for the different types of research divide the research spectrum into three main groups: basic research, translational research, and applied research. Clearly, we recognise that this is not definitive; but on the other hand, it is also clear that there are different challenges facing different types of research, which need to be reflected in the report.

Basic research

2.3 Basic research, also referred to as ‘fundamental’ or ‘blue skies’ research, asks questions about health and disease without any primary driver for practical application. It is driven by a quest for knowledge via scientific study rather than addressing specific clinical or needs and has traditionally been the preserve of laboratory-based researchers at universities or research institutions.

2.4 Basic biomedical research is a major strength of the MRC. The UK is a world leader in this area, and we, as a country, are rightly proud that major discoveries such as the discovery of penicillin and the structure of DNA took place in UK laboratories. The results of laboratory research have been exploited in a variety of ways, including the development of therapies which are used in the clinic, for example:

- at the University of Leicester, a team led by Alec Jeffreys used molecular biology techniques to study genetics variation in human DNA, resulting in the discovery of DNA fingerprinting in 1984. This has had a major impact in healthcare as well as

society more widely. It has revolutionised genetic markers for disease and the way that organs available for transplantation are matched with patients, and it is also commonly used forensically in criminal investigations; and

- the isolation and reproduction of monoclonal antibodies in 1975 was originally developed by Dr Cesar Milstein and Dr George Kohler at the MRC Laboratory of Molecular Biology as a research tool to study the immune system. The production of therapeutic monoclonal antibodies has had a dramatic impact on biomedical research and on therapeutic products being developed to treat a variety of diseases, including cancer, asthma and arthritis. The MRC was paid over £100 million for its human monoclonal antibody Humira® last year.

2.5 Basic research is becoming increasingly inter-disciplinary in nature, equipment and methodologies more complex and expensive. It includes large-scale and systematic research programmes as exemplified by the Human Genome Project (see Box 2.1).

Applied research 2.6 Applied research covers a wide range of research, primarily involving human volunteers (either diseased or healthy volunteers). It includes research into the prevention, detection and diagnosis of disease and the development of interventions (effectively most of ‘clinical research’); the evaluation of interventions (e.g. Health Technology Assessment); the management of disease; and the provision of health and social care services. It is driven by the desire to answer a specific health-related question, need or desire to improve services or care.

2.7 As a consequence, clinical research in particular has delivered many groundbreaking medical advances, such as the development of new uses for aspirin, radiotherapy and chemotherapy, without necessarily understanding the detailed mechanisms of action of such therapies. Applied research often stems from clinical observation and need. An interesting example lies in the field of ophthalmology. Observations during World War II on RAF personnel who had sustained perforating eye injuries from Perspex plane canopies led Harold Ridley, consultant ophthalmologist at St Thomas’ Hospital and Moorfields Hospital, London, to the conclusion that Perspex was inert. This observation and his subsequent clinical research led to the development of intraocular lenses which revolutionised cataract surgery.

Box 2.1 The Human Genome Project

The UK, through the Wellcome Trust Sanger Centre, was a major contributor to the Human Genome Project. Often heralded as the beginning of ‘The Genetic Revolution’, the ambitions of the Human Genome Project spanned from laboratory-based research to drug discovery, through to individual patient diagnosis and treatment. The goal was to embed the principles established in the study of molecular biology over the previous decades within healthcare to produce global benefits in disease treatment and prevention. The Project would not only aid the initial identification of disease causing genes, but would also allow disease-causing mutations to be diagnosed in individual patients. New treatments could be developed based on an increased genetic understanding of disease. Optimal treatments could be matched with the patient’s specific type of illness. The impact would occur across all therapeutic areas. Before deciphering the Human Genome, however, new technologies needed to be developed if the Project was to be completed within the timescale of two decades. New automated sequencing technologies, heavily reliant on advances in chemistry, physics, IT hardware and software, were vital in allowing the sequencing project to become a reality. The Project could only advance by harnessing research from a great variety of disciplines into a single effort, driven by the desire to contribute to a common goal of sequencing the human genome.

Public health research 2.8 Public health research focuses on the wider community or population, looking at physical and mental well-being and ill health. It involves investigating issues such as how ill health varies within the population, disease prevention and how to improve public health through interventions. Research may be fundamental (underpinning) or applied and can often involve very long-term projects. Arguably, the most important and well-cited example has been the link made between smoking and lung cancer, funded by the MRC and published in the early 1950s. Government policies directed toward the reduction in levels of smoking have led to a substantial decrease in the number of cases of deaths from smoking in the UK over the subsequent decades, providing an important example of translation of public health research into tangible healthcare benefit.

Translational Research 2.9 Translational research refers to the process of taking the findings from basic or clinical research and using them to produce innovation in healthcare settings. Translational research can also be used to define research which involves both basic and applied research: the research at the interface between the two ends of the research spectrum which can include both laboratory and clinic-based aspects. It is often argued that the single most significant contribution to medicine has been the 1928 laboratory discovery of the antibiotic, penicillin, by Alexander Fleming at St. Mary’s Hospital, London. However, it was the translation of this discovery by Howard Florey and Ernst Chain at Oxford University, that resulted in the development and use of penicillin in patients (see Box 2.2).

2.10 It is useful to consider health research as a continuum with direct links between the different types of research described above. Observations made in the laboratory may lead to better understanding of disease and novel interventions to be used in clinical settings. Equally, clinical research, sometimes involving these novel interventions, will provide insight and information which can feed back into the laboratory and inform future laboratory studies. As products and novel approaches to disease are developed from basic and clinical research, health technology assessment and service delivery research are used to ascertain how and when best to apply them in practice.

PUBLIC FUNDERS OF HEALTH RESEARCH IN THE UK

2.11 Health research in the UK benefits from having a variety of funders and funding mechanisms, from the public sector, charities and the health industries. Whilst the terms of reference of the Cooksey Review are limited to the spending portfolios of the public funders of health research, it is important to note the key roles played by charities. The Wellcome Trust, Cancer Research UK and the British Heart Foundation, the three largest individual funders, undertake very substantial spending with annual research spends in the UK of over £400 million, £250 million and £60 million respectively.

2.12 In terms of the public sector, the key funders of health research are the Medical Research Council (with some funding coming from other Research Councils) and the Health Departments of England, Scotland, Wales and Northern Ireland.

The Medical Research Council

2.13 The MRC is one of eight Research Councils, and is a Non-Departmental Public Body funded through the Office of Science and Innovation (OSI), part of the Department for Trade and Industry (DTI). All Research Councils have UK-wide remits. The MRC is accountable to Parliament through the OSI. Its mission is defined by Royal Charter and can be summarised as follows:

- to encourage and support high-quality research, with the aim of maintaining and improving human health;
- to produce skilled researchers to meet the needs of users and beneficiaries (including health service providers, and the biotechnology, pharmaceutical, food, healthcare, instrumentation, and other biomedical-related industries);
- to advance and disseminate knowledge and technology to improve the quality of life and economic growth in the UK; and
- to promote dialogue with the public about medical research.

2.14 MRC is governed by a Council of sixteen members, including representatives of the UK Health Departments, industry and medical researchers, as well as lay members. The Chair, CEO and members are appointed by the Secretary of State for Trade and Industry.

Box 2.2 Translation of a Mould into a Medicine: *A Potted History of Penicillin.*

1928: Alexander Fleming, working in his laboratory at St. Mary's Hospital, London, observed a zone of inhibition in the growth of bacteria on plates that were contaminated with the *Penicillium* mould. He concluded that the mould must have been releasing a substance that was blocking bacterial growth.

1931: Penicillin was difficult to produce. The compound is highly unstable. After Fleming failed to halt infections in animals via oral administration of penicillin, he concluded that penicillin could not last long enough in the body to kill pathogenic bacteria. His initial zeal for the translation of penicillin into a medicine subsequently faded, and, apart from some sporadic research, his systematic efforts on penicillin waned.

1939: Howard Florey, Ernst Chain, and Norman Heatley, initiated their work on microbicides at the University of Oxford. After reading Fleming's original report, they re-examined the microbicidal potential of penicillin, managing to purify minute quantities of the active penicillin compound from their cultures. On 25 May, they infected eight mice with a lethal dose of infectious bacteria. They co-injected half of the same mice with penicillin. Within a day, the four infected mice that had not been treated with penicillin were dead. By contrast, the four with penicillin remained alive. Under the influence of the war, the team tried to scale-up penicillin production, using bedpans, milk churns, even bathtubs as culture vessels.

1941: By now, the Oxford team's production techniques allowed them to obtain sufficient quantities of penicillin to start tests in patients. Their first, Albert Alexander, a 43-year-old policeman, was gravely ill from an infection caused by a scratch whilst pruning roses. On February 12, he was given penicillin and started to recover over the course of the next three days. But when the team ran out of their penicillin extract, Albert deteriorated and quickly died from his infection. Recognising the need for outside expertise and the constraints imposed on their research by a Britain at war, Howard Florey and Norman Heatley transferred their research into the bulk production of penicillin to the US Department of Agriculture's Peoria laboratory in Illinois. By November 26, Andrew J. Moyer of the Peoria lab, with the assistance of Heatley, had increased yields of penicillin ten fold. As well as improved techniques of culture, the men identified a strain of penicillin, isolated from a mouldy cantaloupe in a Peoria fruit market, which produced substantially greater volumes of penicillin. On the 8th October, Florey began discussions with four members of the American pharmaceutical industry; eventually convincing them their involvement in the bulk manufacture of penicillin was in the national interest.

1942: By June, eleven US patients had been treated using penicillin supplied by Merck. The pharmaceutical industry continued to enhance penicillin production techniques, generating quantities of the compound that were needed for clinical research and widespread use.

1943: Florey had sufficient material to carry out clinical trials of penicillin in North Africa on injured soldiers. The results of that research confirmed the promise of penicillin as a potent treatment for bacterial infections.

1944: By June, penicillin was used to treat allied troops injured during the D-Day landings.

1945: Florey, Chain and Fleming shared the Nobel prize in physiology or medicine for their work on penicillin.

1948: Andrew J. Moyer was granted a patent for a method of mass production of penicillin.

2.15 As with all the Research Councils, the MRC works to a Delivery Plan which describes how it will contribute to the DTT's Public Service Agreement (PSA) targets of improving the relative performance of the UK research base and the UK economy. MRC's research strategy and funding priorities, set out in the Delivery Plan, are decided with a strong 'bottom up' input from its Funding Boards, working groups, and Directors of Units and Institutes, as well as 'top-down' input from its Council and high level committees and partnerships.

2.16 A Partnership Agreement between MRC and the UK Health Departments aims to ensure strategic co-ordination of research, and to ensure that the needs of Departments, the NHS, and public health are properly reflected in MRC decision-making.

2.17 MRC's gross expenditure for 2005–06 was £525.8 million, of which £459.5 million was core funding from Science Budget allocations. It supports research in almost all areas of basic and applied biomedical and health research. Chart 2.1¹ illustrates the types of research the MRC funds and the proportion of funding allocated. Examples of MRC research include: fundamental studies; research on disease origins and mechanisms; and translational research.

2.18 Funding decisions are based on rigorous peer review, and mostly devolved to specialist Boards and Committees, each responsible for defined areas of research or training.

2.19 The MRC supports research through its own Units and Institutes, through grants to universities, and through partnerships such as the National Prevention Research Initiative. The MRC supports national research infrastructure in universities, in the NHS (e.g. the General Practice Research Framework) and in its own establishments. As Table 2.1 illustrates, MRC puts a substantial proportion of its funding into its intramural units and institutes, which are outside the response-mode funding stream. There are clearly some advantages to this approach, in that researchers can develop long-term strategic plans for their research, knowing that funding is relatively secure. For example, this is reflected in the success of the Laboratory of Molecular Biology (LMB) at Cambridge.

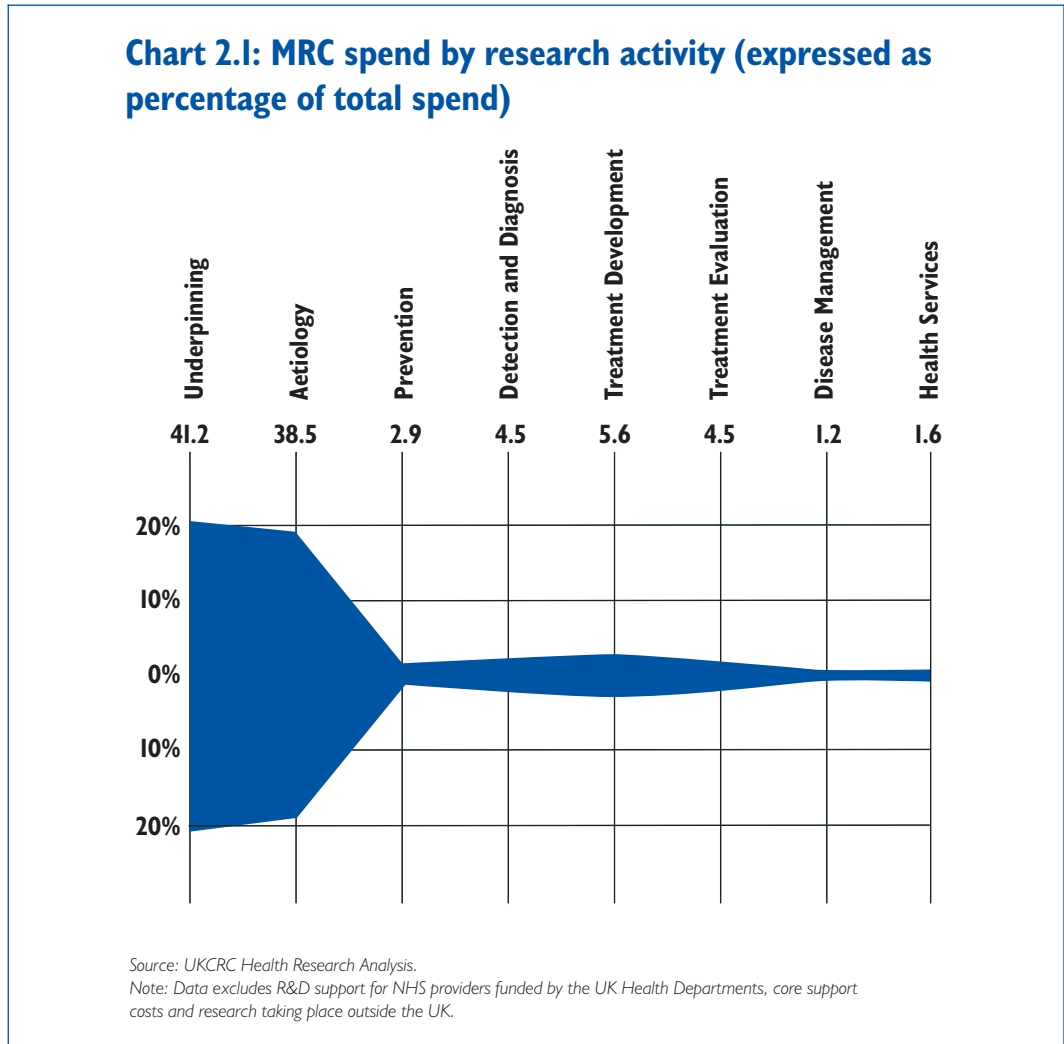
Table 2.1 MRC Spending Breakdown, 2005–06:

Intramural	£279.4m (Incl. £40m capital)
Grants to Universities and hospitals	£172.4m (851 active awards)
Studentships and Fellowships	£51.8m

2.20 As well as supporting research across the UK, the MRC supports research overseas, mainly in Africa, in areas such as HIV, malaria, TB, and growth and development. It participates in international initiatives such as the European and Developing Countries Clinical Trials Partnership, and the European Molecular Biology Laboratory. It also represents the UK in relevant EU Framework Programme discussions.

2.21 Reflecting the increasing need to conduct research across disciplines, the MRC works jointly with other Research Councils in many areas, co-ordinating work in research areas such as stem cells, genomics, informatics, and the environment and health. MRC Technology acts as MRC's exclusive agent for management and commercial development of intellectual property arising from the basic research carried out by the MRC's directly-supported scientists and is a company limited by guarantee with charitable status. Box 2.3 provides more details of its activities.

¹ In this form of kite diagram, the sum of the areas above and below the line of origin represents the proportion of each activity indicated at the top of the diagram.



Department of Health – England

2.22 The Department of Health in England (DH) funds research to ensure its policies and NHS services are based on reliable evidence, supporting the needs of the public. In 2006–07, funding for NHS R&D is £753 million (including £50 million of capital) and the DH Policy Research Programme (PRP). The PRP commissions research to support the development, implementation and evaluation of policy in public health, health services and adult social care.

2.23 Research in the NHS and the PRP is led by the DH Director General of R&D, who reports to the Secretary of State for Health through the Chief Medical Officer. The Director General is also the Department’s Chief Scientific Adviser and, additionally, has professional oversight of research undertaken by DH arm’s length bodies, including the Health Protection Agency.

Box 2.3 MRC Technology

MRC was early to recognise the importance of intellectual property and technology transfer, and provided long term investment to establish a dedicated, skilled team with sufficient financial support to appropriately protect and exploit IP, before translation became the norm. It established MRCT in 2000.

Through strong links with the MRC's research scientists, MRCT staff identify new technologies and ideas and carry out due diligence to determine their healthcare and commercial potential. MRCT will assess healthcare need, strength of IP position, need for proof of concept studies or further development, competing technologies, and market potential before determining a route for development and exploitation of the technology. Patent applications may be filed and prosecuted, whilst commercial partners are identified and approached to initiate possible collaboration or licensing of the technology. MRCT works with the commercial partner most likely to develop a treatment or medicine to improve human health and is not driven solely by financial return. Approximately 25 patent applications are filed each year and about 40 license agreements are signed. MRCT also fosters the creation of new companies arising from the MRC science base where there is a compelling business case.

Two of Europe's most successful biotech companies, Celltech and Cambridge Antibody Technology, were both MRC spin-outs supported by MRCT, and another, Ardana, has recently completed a flotation on the London Stock Exchange.

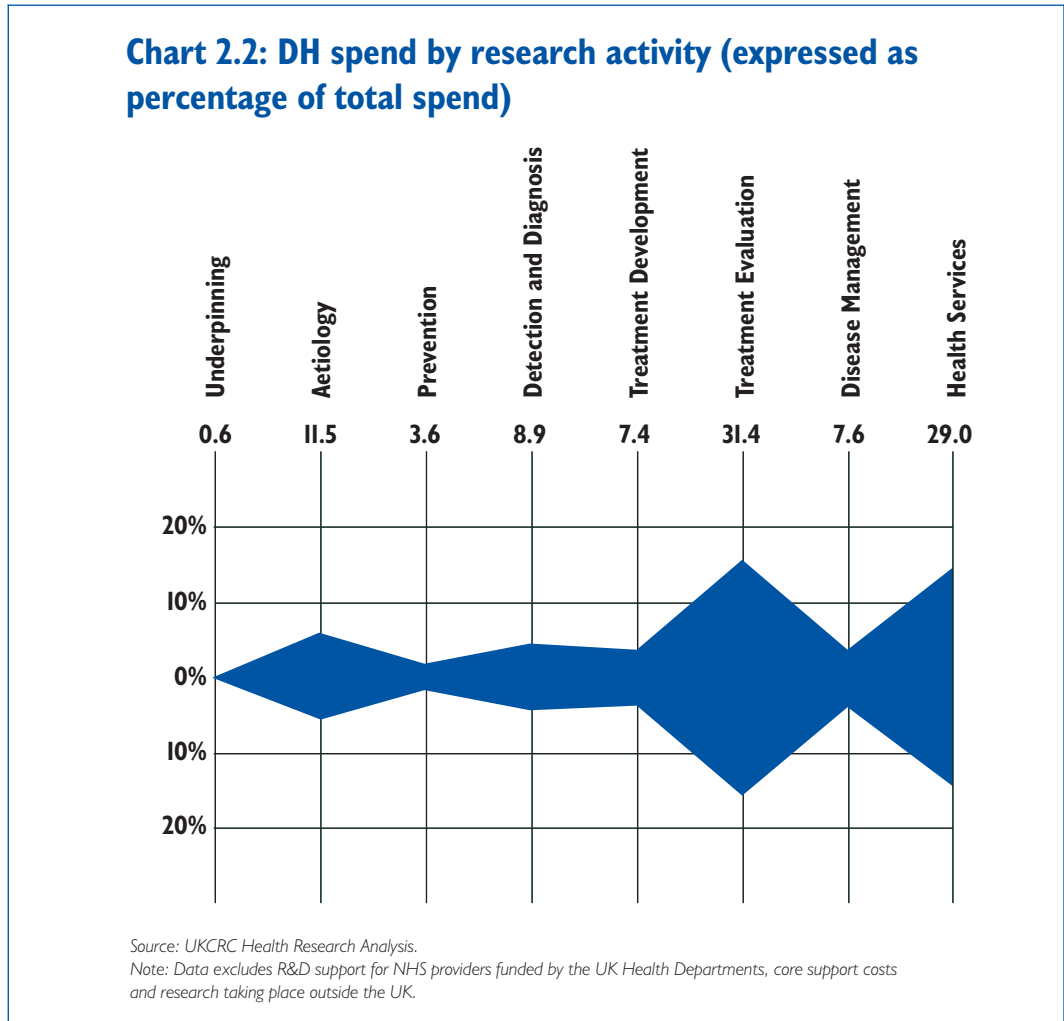
MRCT plays an important role in bridging the industry–academia divide through its extensive experience in the commercial sector. Indeed MRCT is in the process of establishing a series of Showcase events in which MRC-funded scientists will present and discuss their research with participating companies with the aim of fostering future collaborations.

MRCT may elect to add value to MRC's novel early stage technologies through its Development Gap Funding scheme, allowing development of opportunities to a stage that is attractive to companies and investors. Awards are made to support projects with commercial potential, which would not usually be funded by MRC or academic grants, and these are actively managed by MRCT to meet technical and commercial objectives.

MRCT is also able to progress early stage IP through its Drug Discovery Group, which operates to link academic research with pharma-style medicinal chemistry and works with MRC scientists to translate innovative drug targets into potent and selective lead molecules that can be partnered with industry for progression into lead optimisation and pre-clinical studies.

MRCT continues to seek out novel technologies as they arise and to ensure that these are protected and developed through the appropriate mechanism to a stage where industry will invest to develop new treatments and medicines to benefit human health in the future.

MRCT has always worked towards the MRC's mission of improving healthcare and has not been driven solely by short-term financial return. This has enabled MRCT to work with commercial partners most likely to develop a treatment or medicine to improve human health, not necessarily those generating the greatest short-term revenue for Council. Even so, MRC's income generated from the activities of MRCT from 1998–2006 is in excess of £234 million.



2.24 The NHS has carried out research of international standing since its inception in 1948. A number of separate funding streams were brought together as the NHS R&D budget in 1997, and national programmes were established explicitly to address questions faced by front-line professionals and policy makers, including:

- the Health Technology Assessment (HTA) programme — providing high-quality information on the cost, effectiveness and broader impact of health technologies. HTA is a National Institute for Health Research (NIHR) programme funded by DH, but awards funding through open competition to the best researchers wherever they are located in the UK;
- the Service Delivery and Organisation (SDO) R&D programme — providing evidence about service improvement to increase the quality of patient care, ensure better patient outcomes, and contribute to improved population health. SDO is an NIHR programme funded by DH, but awards funding through open competition to the best researchers wherever they are located in the UK;
- New and Emerging Applications of Technology (NEAT) — applying recent advances in fundamental knowledge and technology to the development of new products and interventions for improved health and social care or for disease prevention and treatment;

- research synthesis work, including the Centre for Reviews and Dissemination in York and the Cochrane Collaboration; and
- Research Capacity Development — building and supporting the skilled workforce of the NHS capable of advancing high quality research with the aim of maintaining and improving health within a knowledge based, patient centred health service.

2.25 The national programmes follow rigorous processes to ensure high quality research is commissioned where there is a gap in the evidence needed by the NHS. Final reports are also subject to peer review, and findings are widely disseminated.

Best Research for Best Health

2.26 Following public consultation, a new Government strategy for NHS R&D in England, *Best Research for Best Health: a new national health research strategy* (BRfBH), was published in January 2006. As part of this strategy, the National Institute for Health Research (NIHR) was launched on 1 April 2006 to provide the NHS in England with the support and infrastructure it needs to conduct first-class research funded by Government and its partners, alongside high-quality patient care, education and training. The strategy covers research involving patients, samples or data taken from patients, people who are not patients, populations, health technology assessment, and health services research.

2.27 The NIHR is led by the DH Director General of R&D and an Advisory Board provides advice on strategic direction, implementation and programme review. The Institute works with key partners including other funders, academia and industry, bilaterally as well as collectively through the UK Clinical Research Collaboration. The NIHR, together with the National Institute for Health and Clinical Excellence (NICE) and the National Institute for Innovation and Improvement, will play a key role in the NHS knowledge management system.

2.28 The NIHR will be fully established by April 2009 and will carry out its activities in four main blocks:

- NIHR Faculty for all NIHR-funded professionals conducting people-based health research;
- NIHR Programmes to address the broad range of health research priorities, target funding to resolve uncertainties and address areas of unmet need, and allocate NHS health research funding in a transparent manner, based on quality and relevance;
- NIHR Infrastructure to provide the support and facilities that the NHS needs to carry out first class research, including clinical research networks, experimental medicine facilities, and technology platforms; and
- NIHR Systems simplifying and streamlining the processes that can delay research, through workstreams on Governance, advice and ethics, and Research Information Systems.

NIHR making good progress

2.29 Implementation started immediately following the strategy launch in January 2006. Already established and working are the UK Clinical Research Network Central Coordinating Centre, and four new Coordinating Centres for Medicines for Children, Diabetes, Stroke, and Dementia and Neurodegenerative Diseases, to add to existing network capacity in Cancer and Mental Health. Their chief purpose is to provide a world-class health service infrastructure to support clinical research. The Clinical Research Network for England will support and conduct randomised controlled trials of interventions (including prevention, diagnosis, treatment, and care) and other

well-designed studies for commercial and non-commercial sponsors. It will also play a key role in promoting the active involvement of patients and the public in clinical research, and enable work to be conducted across the full spectrum of disease and clinical need through a managed set of research networks.

2.30 In addition, NIHR has launched a new funding stream to support ‘high technology platforms’ for clinical research, initially focussed on specialist imaging, and the Research for Patient Benefit programme, a responsive funding programme providing small grants in the regions. The HTA programme has launched a responsive funding stream for pragmatic clinical trials to assess the effectiveness of technologies within the NHS. Biomedical Research Centres and Research Centres for NHS Patient Safety and Service Quality have been shortlisted, and, following international peer review, successful applications will be announced in December 2006.

The Chief Scientist Office — Scotland

2.31 The Chief Scientist Office was established in 1973 following the Rothschild Report². Its role was to support research of particular relevance to Scotland. Originally primarily a source of grants to university researchers, it has always had the aim of supporting research relevant to the NHS and healthcare. With a budget of £17 million in 2006–07, the CSO supports a broad spectrum of research with significant spend in areas of priority. Since 1996, CSO also manages a separate budget for research infrastructure costs in the NHS; this is worth £43 million in 2006–07.

2.32 The structures and organisation of the NHS in Scotland have diverged considerably from those in England, a process that was well advanced long before devolution in 1999. The Minister for Health and Community Care is responsible for this area, but beyond that (i.e. for social care) responsibility falls to other Ministers. CSO has responsibility for a wide range of policy and operational matters relating to health and NHS research. Areas such as ethics, governance, Intellectual Property and public involvement in research parallel the responsibilities of the Department of Health in England. CSO interacts with stakeholders through its Public Involvement Group; Research Advisory Committees; Portfolio Steering Groups; NHS R&D Advisory Group and the Chief Scientist Committee that takes an overview of the breadth of CSO’s activities and delivery of its Strategy.

Northern Ireland HPSS R&D Office

2.33 The Research and Development Office (R&D Office) for Health and Personal Social Services (HPSS) in Northern Ireland aims to secure lasting improvements in health and social care by promoting, co-ordinating and supporting R&D. The Office’s remit is clinical in focus, and extends to the complete spectrum of health and social care research relevant to the needs of the Department of Health, Social Services and Public Safety (DHSSPS) and the HPSS.

2.34 The HPSS R&D Fund is the primary source of HPSS R&D support and currently stands at £12 million per annum. The fund is used for the direct support of HPSS research, including the Recognised Research Groups (approximately £7 million per annum), capacity building initiatives (approximately £2 million per annum) and infrastructure support (approximately £3 million per annum), as well as the running costs of the R&D Office. In all instances, the award of research funds by the Office is based on independent, scientific peer review. The fund also supports international

² *The organisation and management of Government R&D*, in *Cabinet Office, A framework for Government Research and Development*, London, HMSO, November 1971 (The ‘Rothschild Report’)

activities and has an All-Ireland dimension, which is reflected in a number of joint funding initiatives supported in collaboration with the Health Research Board in Dublin. The fund has proven valuable in leveraging in significant amounts of external clinical research funding from partner organisations.

Wales Office of Research and Development in Health and Social Care

2.35 The strategic aim of Wales Office of Research and Development in Health and Social Care (WORD) is to generate high quality evidence to inform policy and practice in health and social care for the benefit of patients and the public. Policy on R&D reflects the health and social care priorities of the National Assembly for Wales, which is set out in the Welsh Assembly Government's 10-year strategy, *Designed for Life*. WORD is directly accountable to the Welsh Assembly Government ministers and specifically the Minister for Health and Social Services.

2.36 The WORD Advisory Board provides a mechanism for advice and consultation on the strategic direction of research and development in health and social care. The Board involves key internal and external stakeholders to ensure a coordinated approach and an effective use of services.

2.37 WORD's budget is used to develop a supporting infrastructure for clinical research (approximately £4.4 million per annum), runs a Responsive Grants Scheme (£1 million per annum), supports a fellowship programme (approximately £2 million per annum covering fellowships and lectureships), and contributes to national research initiatives (approximately £400,000 per annum). It also supports the Wales Gene Park, Wales Cancer Bank and the service costs of research (approximately £15 million per annum).

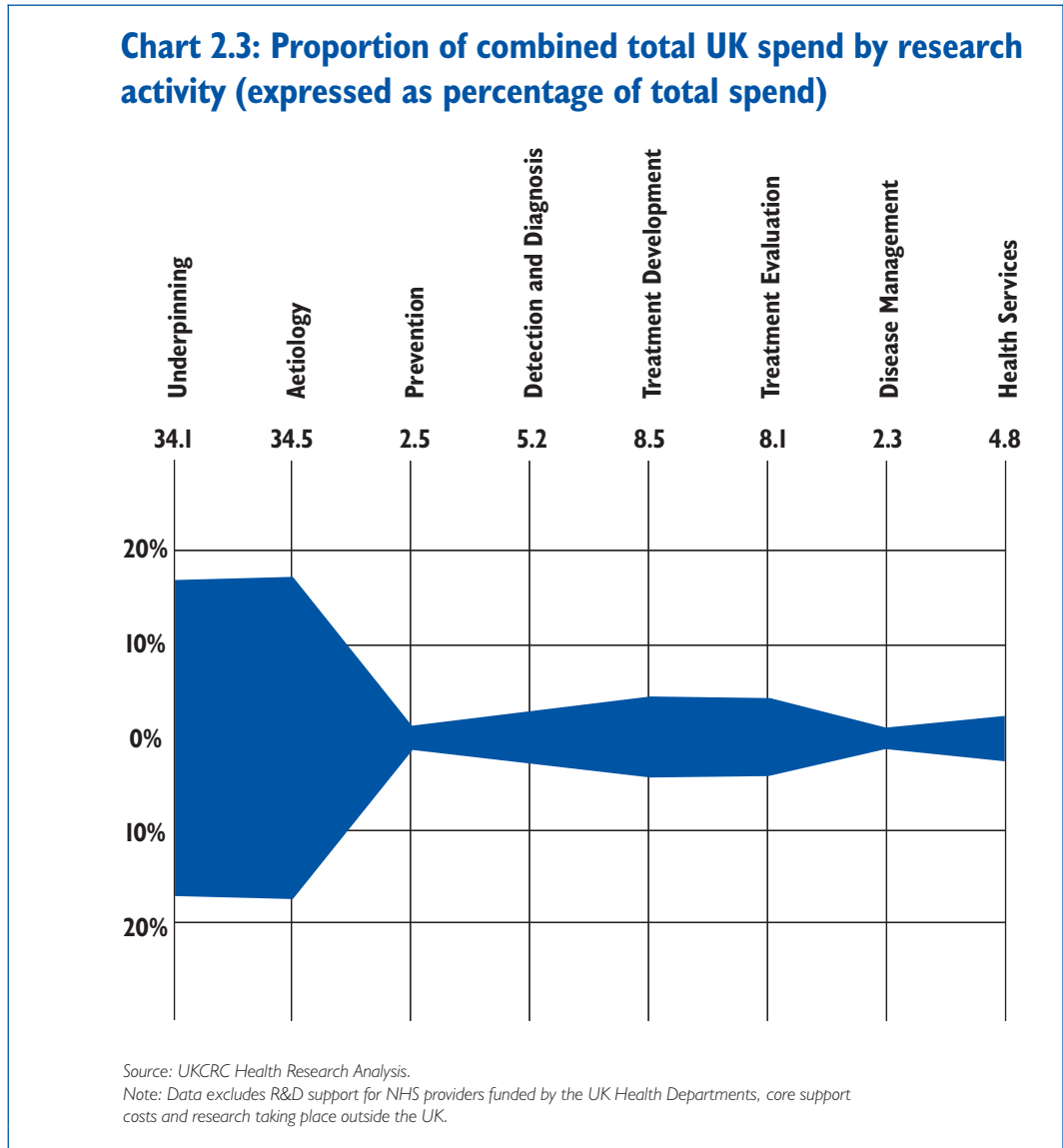
2.38 Researchers in Wales can also apply for funding through other sources including:

- the MRC;
- WORD is in dialogue with ABPI through the Welsh arm of the organisation to discuss investment from industry. The discussions to date have centred on cancer and informatics; and
- WORD is currently exploring leveraging in EU convergence funds.

THE UK HEALTH RESEARCH PORTFOLIO

2.39 The UKCRC recently analysed³ the research portfolios of the 11 largest government and charity funders of UK health related research. The analysis was based on 9,638 peer-reviewed awards, which amounted to a total spend of £950 million during the financial year 2004–05. The study revealed that, in that year, approximately two thirds of the UK expenditure on directly funded health research, or around £633 million, was allocated to understanding normal function or cause of disease, the majority of which was laboratory-based biomedical research (see Chart 2.3).

³ UKCRC UK Health Research Analysis May 2006, www.ukcrc.org



Distribution of Research across Health Disciplines

2.40 UKCRC’s analysis also looked at the relative distribution of the combined research funding of the 11 largest government and charity funders across different health specific categories. Chart 2.4 shows the distribution of the overall spend. The UKCRC analysis report concluded that the overall funding pattern was generally in line with the UK Disability Adjusted Life Year (DALY) rates⁴, with the exception of Respiratory and Gastrointestinal research, where funding is substantially lower than the comparative burden of the disease. Infection research is one area where the relative funding rate is higher than the UK DALY ranking (but worldwide, infection is a huge cause of morbidity and mortality).

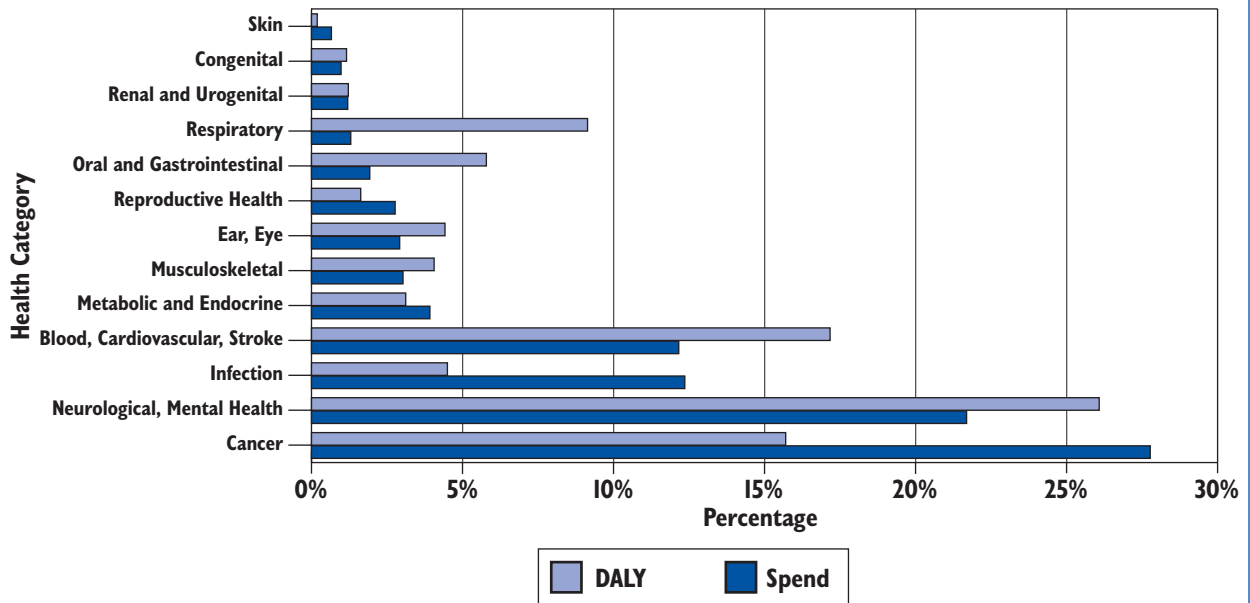
2.41 UKCRC has carried out some additional analysis for the Review, which demonstrates that while the funding pattern of the total public spend across the health specific categories (Chart 2.5) is similar to the pattern seen when looking at the overall UK spend (Chart 2.4)⁵, there are a couple of noticeable differences. The public funders spend a smaller percentage of their total budgets on

⁴ Disability Adjusted Life Years (DALYs) are a frequently used measure of the burden of disease. DALYs are a measure of the sum of life years lost due to premature mortality and years lived with a disability adjusted for severity, and thus they take into account the impact of mortality and morbidity in a single measure.

⁵ i.e relative to the combined public and charities spend

'Blood, Cardiovascular, Stroke' and 'Cancer' research but a higher percentage on 'Neurological, Mental Health' research. In the case of 'Cancer and 'Neurological, Mental Health' research, the level of funding is more in line with the DALY ranking. However the gap between DALY ranking and research spend is greater in the case of 'Blood, Cardiovascular, Stroke' research. These differences in funding patterns perhaps reflect the level of funding contributed by major charities such as the British Heart Foundation or Cancer Research UK which have a disease specific focus.

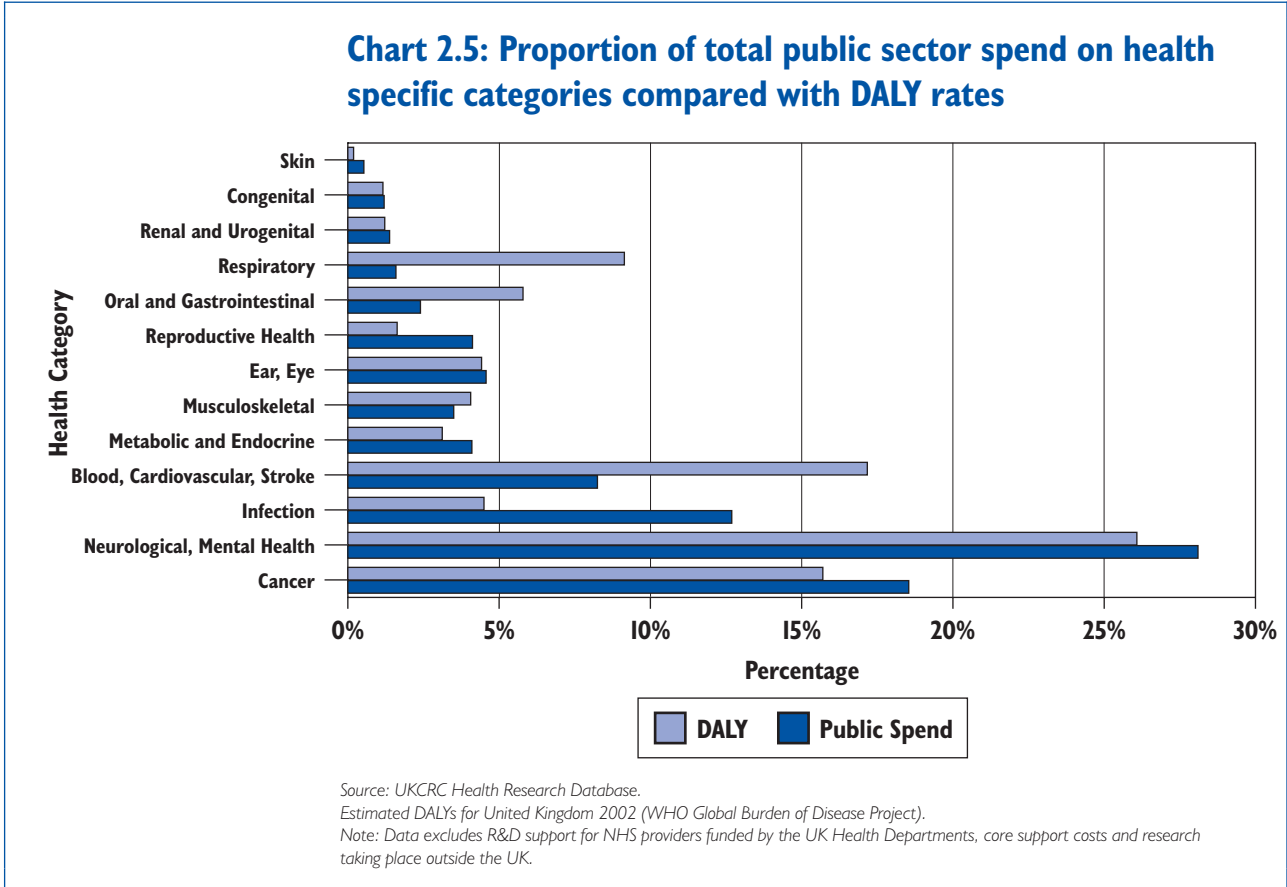
Chart 2.4: Proportion of combined spend on health specific categories compared with DALY rates



Source: UKCRC Health Research Analysis.

Estimated DALYs for United Kingdom 2002 (WHO Global Burden of Disease Project).

Note: Data excludes R&D support for NHS providers funded by the UK Health Departments, core support costs and research taking place outside the UK.



2.42 Overall the distribution of the combined research funding from government and charities will depend on a variety of factors such as the remit of research charities and possibly geographical constraints⁶. It highlights the importance of UKCRC and funders forums in bringing together different funders to allow a more holistic approach to funding research into particular disease areas.

⁶ Some funders, e.g. the Devolved Administrations, may only fund research in particular parts of the country.

3

International comparisons and trends

Chapter overview

This chapter provides background information on the health research funding arrangements in the USA, Canada and Sweden, which are recognised as leaders in this area, but which are facing, or have recently faced, similar challenges to those which the Cooksey Review has been charged with addressing. The Review concludes that there are some key areas where reflecting on international best practice could inform developments in the UK, in particular the importance of:

- leadership and strong communication between researchers and clinicians;
- keeping system complexity to a minimum;
- ensuring adequate funding across the health research continuum; and
- providing opportunities for research training for the clinical workforce.

In addition, as health research becomes more complex and expensive, there is an increased need for greater international collaboration and co-operation.

INTRODUCTION

3.1 The Review involved a series of visits, not only to the four countries of the UK, but also to the USA, Canada and Sweden, which are recognised as leaders in health research. This chapter sets out some of the main trends in health research in the USA, Canada and Sweden, and seeks to draw out the key lessons for the UK from their experiences.

THE USA

3.2 The US Department of Health and Human Services is the primary Federal agency that funds medical research in the US, primarily through the National Institutes of Health (NIH)¹. The NIH consists of 27 Institutes, the majority of which are based on a single campus in Bethesda, Maryland, which fund both intramural and extramural research. Each institute has a specific focus such as cancer; heart, lung and blood; or genome research, and develops its own strategy in consultation with its scientists and Advisory Councils. The overarching Office of the Director is responsible for setting overall policy and for planning, managing, and coordinating the programmes and activities of all the NIH components. The NIH Director is primarily responsible for advising the President on his annual budget request to Congress, and Congress in turn sets the budgets for each institute annually.

3.3 In recent years, NIH has seen a doubling of its budget to around \$29 billion per annum, although this is now levelling-off as Congress concentrates its funding increases on other areas of research. Despite this substantial increase in funding for biomedical research over the past decade,

¹ <http://www.nih.gov/>

the overall proportions of investment in basic and applied research by the National Institutes of Health (NIH) have remained static over the past decade at about 55 per cent and 45 per cent, respectively.² This has been accompanied by a significant shift in the proportion of pharmaceutical industry R&D going into clinical research, from 28 per cent of total R&D funds in 1994 to 41 per cent in 2003. It is particularly significant that NIH expenditure on clinical trials has now reached \$4.2 billion per annum.

3.4 As in the UK, there have been increasing demands in the US for a shift in the focus of its health research spending towards translational research. In attempting to address this issue, the NIH has published the 'NIH Roadmap'³, a cross-Institute initiative that aims to accelerate fundamental discovery and translation of knowledge into effective prevention strategies and new treatments. The Roadmap has three broad components:

- New Pathways to Discovery, including advancing understanding of biological systems, and developing underpinning technologies, databases and other scientific resources;
- Research Teams of the Future. This initiative is designed to increase interdisciplinary working, remove barriers to collaboration, and encourage innovative, high-risk research and public-private partnerships. Programmes include the Director's Pioneer Awards, which are intended to fund research that, although it has a high potential failure rate, may also generate truly groundbreaking discoveries; and the Interdisciplinary Research Training Initiative, aimed at broadening the knowledge base of investigators to enable them to bring new insights and approaches to health problems; and
- Re-engineering the Clinical Research Enterprise. This initiative is intended to develop networks of academic centres which are linked to health care providers with large patient groups, and which will be involved in quickly developing, testing and delivering new interventions. It will also be responsible for training clinical researchers, with approaches such as the National Clinical Research Associates scheme, designed to create a cadre of qualified healthcare practitioner-researchers who can help ensure the responsible conduct of clinical research.

CANADA

3.5 Health research in Canada is funded by both the Federal and Provincial Governments. The major Federal funding agency is the Canadian Institutes of Health Research (CIHR)⁴. The formation of CIHR in June 2000 has been accompanied by a significant increase in the Canadian budget for Health Research, with CIHR funding increasing by approximately 130 per cent between 1999–2000 and 2004–05⁵. CIHR brought together the different components of health research by combining Canada's Medical Research Council, the National Health Research and Development Programme and the Social Sciences and Humanities Research Council into a new, single body. Its aim is to support scientific excellence, and facilitate and accelerate the translation of knowledge. About 30 per cent of CIHR's budget funds strategic initiatives, with the rest being used to support investigator-led research.

² Moses, H. *et al.* (2006) *Financial Anatomy of Biomedical Research*. JAMA 294:1333–1342

³ <http://nihroadmap.nih.gov/>

⁴ <http://www.cihr-irsc.gc.ca>

⁵ See <http://www.cihr-irsc.gc.ca/e/22955.html> for a more detailed breakdown.

3.6 Central to the development of CIHR was the creation of 13 virtual Institutes, which are national, multidisciplinary networks created around specific areas such as Cancer Research, Aging and Health Service and Policy Research. Their mandate is to promote multidisciplinary research and increase translation. Each Institute has a Director and Institute Advisory Board to help develop strategies, priorities and implementation plans. These report to an overarching Governing Council.

3.7 CIHR supports multidisciplinary research in a variety of ways. It has funded strategic initiatives, such as Large Team Grants to encourage multidisciplinary research, and created an environment where collaborations and interactions can be initiated at a local level to solve specific scientific problems. Several new initiatives have been set up aimed at encouraging innovation and commercialisation, including the:

- Proof of Principle programme, which funds research at the early stages of commercialisation, in order to take ideas to a stage where they can be commercialised; and
- Science to Business programme, which aims to increase the business and financial skills in the scientific and research community.

3.8 Earlier this year, an international review of CIHR⁶ concluded that, although it was too early to arrive at conclusive judgements, CIHR was making impressive progress in unifying health research and it had already achieved a great deal. The review recognised the need to ensure accountability and transparency at all levels of an organisation and the need to ensure that funding mechanisms are not overly complex. It also pointed to the need for coordination of different federal and provincial research funding streams.

3.9 In addition to funding CIHR, the Canadian Government has, in recent years, funded a number of other initiatives aimed at building research capacity, many with a strong health research component:

- the Canada Foundation for Innovation (CFI)⁷: this was established as an independent corporation to fund research infrastructure and strengthen the capacity of Canadian universities, colleges, research hospitals, and not-for-profit research institutions;
- the Canada Research Chairs⁸: in 2000, a new programme (investing C\$300 million per year) was created to establish 2,000 research professorships in universities across Canada by 2008;
- Genome Canada⁹: launched in 2000, Genome Canada has received C\$600 million to develop and implement a national strategy in genomics and proteomics research. It invests and manages large-scale research projects in key selected areas such as agriculture, environment, fisheries, forestry, health and new technology development; and
- Canadian Health Services Research Foundation (CHSRF)¹⁰: CHSRF was established with endowed funds from the federal government and its agencies in

⁶ http://www.cihr-irsc.gc.ca/e/documents/irp__2000-2005__e.pdf

⁷ <http://www.innovation.ca>

⁸ http://www.chairs.gc.ca/web/home__e.asp

⁹ <http://www.genomecanada.ca>

¹⁰ http://www.chsrf.ca/home__e.php

1996. Its aim is to promote and fund management and policy research in health services and nursing to increase the quality, relevance and usefulness of this research for health-system policy makers and managers.

SWEDEN

3.10 Sweden has a population of 9 million, and has a landmass nearly two and a half times that of the UK. Despite the relative spread and size of its population, the standard of Swedish research is very high by comparison with other developed economies and it is top of the 2005 EU Innovation Scoreboard. It is a world leader in a number of important fields of health research, such as neuroscience. Sweden also ranks highly in terms of scientific publications, the proportion of workforce involved in R&D and patent intensity, and an astonishing 25 per cent of Swedish physicians have a PhD. Like the UK, Sweden has a national health care system serving the entire population, but it is funded locally, through its twenty-one county (regional) councils. Sweden also has a strong industrial base in pharmaceuticals.

3.11 The Swedish Government's research policy is aimed at maintaining and strengthening its leading status as a research nation. 3.98 per cent of GDP is allocated to R&D, with around 75 per cent of this investment coming from industry. Publicly funded R&D is therefore currently just below 1 per cent of GDP, the target set out in the EU's Lisbon strategy. In the 2005 budget, £247.8 million (SEK 3345million) was allocated to the Swedish Research Council for basic research. For applied research, VINNOVA (the Swedish Agency for Innovation Systems) received £81.6million (SEK1122 million) in 2005, which is to be increased by nearly 50 per cent to £118.5million (SEK1600million) as a result of the recent research policy bill. Between 2005 and 2008, research allocations specifically for medicine are planned to increase by £29 million (SEK 400 million).

3.12 Nevertheless, there are concerns over Sweden's R&D performance in health research, including over the adequacy of needs-oriented publicly-funded research. The Swedish Government has chosen to focus attention on some of the areas where Sweden is internationally outstanding and that have great importance for the public and private sectors alike. In December 2005, it published its new strategy for life sciences research¹¹, with its key aims being to:

- develop collaboration between the state, industry and other affected players;
- further develop world class life science research and development in the life science industries;
- promote the commercialisation of research results;
- ensure the supply of competent people & develop dialogues (with society, interested parties, mentor programmes for suppliers);
- improve the conditions for industry-specific production;
- ensure quality in healthcare;
- ensure competitive conditions (tax breaks, importing foreign expertise, reduced administrative load); and
- meet the challenges of internationalisation and globalisation.

¹¹ *Pharmaceuticals, biotechnology and medical technology – an Integral Part of Innovative Sweden*. Regeringskansleitet. The Ministry of Industry, Employment and Communications, Sweden. 6 December 2005

The Karolinska Institute

3.13 The strength of Sweden in the health sciences is due, in no small part, to the key role played by the Karolinska Institute in Stockholm. The Institute is a medical university which performs 43 per cent of the medical research in Sweden, with an annual budget of approximately £291million (SEK4billion). It carries out world-class research in areas such as stem cell research, neuroscience, cancer, diabetes, epidemiology and clinical research. Crucially, the Institute is also responsible for awarding annually the Nobel prize in medicine or physiology, which helps it to attract scientists and clinicians of high calibre, and also means that its researchers are strongly networked with other health researchers across the globe.

3.14 The training programmes at the Karolinska Institute have a very strong reputation. A substantial portion of the faculty's energy is dedicated to education. For PhD training, there is one year of 'pre-funding' before the student commences active research, to familiarise the students with the area of study, and develop specific ideas for their research proposal. As well as offering PhD programmes, the Institute awards licentiate degrees for students who have undertaken two years of research and a dissertation. These degrees are highly valued and not considered to be 'inferior versions' of PhDs, nor awarded as 'second prizes' for students who have failed to attain the required level of achievement for a doctoral degree – rather, they serve a role that is considered essential for Swedish health research, by allowing healthcare professionals to become 'research literate.' The licentiate degree also qualifies healthcare workers to participate actively in research while maintaining their clinical activities, but without necessarily having to lead full research programmes.

COMPARISONS AND KEY LESSONS FOR THE UK

3.15 It is clear that other countries are facing many of the same challenges as the UK with regard to how to increase the successful translation of health research into health and economic benefits. As might be expected, each country is tackling the issues in different ways, and as yet there is no overall 'right answer' which could or should be emulated by the UK. However, the Review's research into other systems has provided important examples and stimulated debate as to what that 'right answer' might be. Some critical success factors identified are set out below.

Communication and leadership

3.16 The first key to successful translation is effective communication between researchers at the various stages of health research and with those working in the clinical environment. This sounds deceptively simple in theory, but is much less so in practice. Actively encouraging clinicians, lab-based researchers and researchers from other key disciplines to discuss their work, research and needs develops a culture of mutual understanding, trust and co-operation. This often results in multidisciplinary groups being formed 'spontaneously' to address common problems and needs. Institutional changes can both help and hinder these processes. The Review was impressed by examples of how this worked within universities and university hospitals, at Karolinska and at the Duke University Medical Centre, where the leadership of Prof. Robert Califf has been crucial to establishing a cross-disciplinary culture, which, in turn, has led to the development of world-leading research.

3.17 Leadership and communication are not only vital in individual research institutions, but also in the national (or, indeed, regional) institutions that fund research. One example of the early successes following the creation of the CIHR in Canada has been the leadership role of the CIHR's virtual institutes in formalising and helping to support multidisciplinary teams. More broadly, the leadership of Dr. Alan Bernstein has been instrumental in the success of the CIHR in its first five

years, and is further evidence of the importance of strong leadership to manage change successfully on the sort of scale achieved by CIHR. Similarly, there are lessons for the UK from the NIH's 'Roadmap' vision of how to deliver increased translation of basic research into health and economic benefits, and in particular in helping the research community to respond to this challenge.

System complexity 3.18 The recent review of CIHR considered the issue of whether the number of different funding opportunities it offers and review panels made the organisation too complex, and it recommended a reduction in this complexity, with the introduction of new management systems to support this task. Likewise, our Review found some evidence in the US that the boundaries between Institutes and the complexity of navigating the NIH's systems created barriers to translation; for example there was a significant risk of disincentivising collaboration between researchers from different areas. There is, therefore, an important challenge here for the UK in terms of how the MRC and the DH R&D function can be brought more closely together to encourage effective collaboration and a coherent strategy, whilst avoiding creating complex management and reporting structures to oversee these processes and provide accountability.

Adequate funding 3.19 The additional funding provided by the Canadian Government to underpin the changes needed when the CIHR was established is widely seen in Canada as being of vital importance to the success of the initiative. This funding ensured that researchers, for the most part, bought into the vision; while the translational agenda was seen as being championed, it was not promoted to the detriment of basic or clinical research.

Research training for the clinical workforce 3.20 Sweden has placed a consistent and strong emphasis on research training across a broad spectrum of health professionals. This has allowed the development of a 'research literate' healthcare community that believes in the real value of research as an integral part of the system. While it may not be an efficient use of resources in the UK for 25 per cent of physicians to have a PhD, there may be important lessons from Karolinska in regard to its licentiate degree, which may provide an effective route to creating a more research and innovation-friendly culture in the NHS.

3.21 It will be interesting to follow the different systems and models over the next 10 years to see how they develop. In particular, Canada has undertaken a very exciting experiment with its substantial public investments in research in recent years, and, with the US having also substantially increased its investment in health research through the NIH, it will be important to see the fruits of that investment over the next decade and beyond in the form of increased health and economic benefits.

3.22 It is, however, clear that whatever systems are in place within an individual country, there will need to be greater collaboration and co-operation internationally as research becomes more complex and expensive – the Human Genome Project being one successful example of such collaboration. The FDA's Critical Path Initiative points to another obvious area for such international collaboration, and we return to this point later in the report.

4

Analysis of the UK health research system

Chapter overview

This chapter provides analyses on the strengths of the UK health research system, and identifies barriers to effective translation of research into health outcomes. It examines the cultural issues and incentive structures that shape the current health research environment.

The consultation responses, meetings with stakeholders, international and domestic visits and wider research for the Review have brought to light a number of concerns with the current arrangements for public funding of health research:

- there are two key gaps in the translation of health research into improvements in practice that generate health and economic benefits: translating ideas from basic and clinical research into the development of new products and approaches to treatment of disease and illness; and implementing those new products and approaches into clinical practice;
- the wider funding arrangements for supporting translation of ideas from conception to practice are not coherent or comprehensive. Where arrangements do exist, they do not always function very well; and
- the current drug development pathway appears to be on an unsustainable trajectory. Publicly funded research is not addressing this with the urgency it merits given its potential to undermine the economics of drug development.

GAPS IN TRANSLATING RESEARCH INTO PRACTICE

4.1 The consultation responses were clear about the value of basic research led by MRC. It is world class. It is rightly proud of the world-wide renown it has for research excellence, as demonstrated, for example, by the number of Nobel Prize winners it has funded: 27 in total.

4.2 Whilst there have been some significant successes translating this research into practice (e.g. monoclonal antibodies), the consensus from the consultation was that the UK has failed to maximise the impact of its excellent basic research on the nation's health and economy. Furthermore, respondents said that, where basic health research outcomes have been translated into wider benefits, this has tended to occur as a consequence of the leadership and vision of specific individuals, and in spite of the lack of a framework for systematic translation.

4.3 The consultation process found that applied research is often undervalued by the NHS. Until recently, the culture and structure within the NHS did little to enhance the reputation or impact of applied research. This has impacted on the UK's ability to translate research into patient benefit. The reasons for the lack of translation from both basic and applied research are complex and inter-linked. The consultation suggested that the most important factors are cultural, institutional and financial barriers, combined with a lack of robust evaluation evidence. These are reviewed in more detail later in this chapter.

4.4 While these barriers persist, the changing global economy, advances in medical science and increased public expectations mean that successful translation of research into practice is more important now than ever before.

Cultural barriers

Haldane 4.5 A repeating theme throughout the consultation was the cultural impact of the prevailing interpretation of the ‘Haldane Principle’. Throughout the twentieth century and into the twenty-first, the ‘Haldane Principle’, derived from a report of 1918 into the structure of Government¹, has largely defined how research has been supported in the UK. The prevailing interpretation is that decisions on all aspects of research, from the development and setting of strategy to day-to-day decisions on which projects to fund and support, should be taken by scientists and at ‘arms-length’ from government, which should have little role other than being a source of funding.

4.6 However, this interpretation differs from what the Haldane Report actually said²:

- first, that Government Departments *should* have their own provision for ‘enquiry, research and reflection’ ‘before policy is defined and put into operation’³. Indeed, it specifically stated that ‘many Departments must retain under their own control a distinctive organisation for the prosecution of specific forms of research’⁴; and
- second, the Government should carry out research for general purposes via ‘a [separate] Department working under the direction of the Lord President’, essentially because of the concern that a Minister with responsibility for a particular area of Government policy might refuse to implement research where he / she did not like its outcomes⁵. Importantly, however, the report argued that the body organising such research should work ‘in the closest collaboration with the administrative Departments concerned with its activities’⁶.

The Rothschild Report 4.7 The ‘Haldane Principle’ was re-evaluated in the 1971 Rothschild Report, *A framework for Government Research and Development*⁷, and there was an attempt in the 1970s to reform the system along the lines of Rothschild’s notion of a customer-contractor relationship in research funding. However, DH did not then have the expertise or resources it now has to play the demanding role of informed customer of health research that Rothschild envisaged. In this sense, Rothschild can be viewed as being ahead of his time, with his vision perhaps only now being achievable in practice.

4.8 The vast majority of publicly-funded health research has therefore continued to be ‘curiosity-driven’ by researchers. This curiosity-led approach was, and continues to be, enormously productive and has illuminated the key underpinnings of molecular biology, developmental biology and genetics. Particularly in its ‘golden age’ of the 1950s, such research led to fundamental understanding of the key processes of life and death within cells, from enzyme biochemistry to the structure of DNA. Although the elucidation of a clinical problem was not a pre-requisite for this

¹ *Report of the Machinery of Government Committee*, Ministry of Reconstruction, Cmd 9230, 1918 (The ‘Haldane Report’),

² A more detailed analysis is set out in a background paper available on: www.hm-treasury.gov.uk/independent___review

³ Haldane Report, pg 6, para 14.

⁴ Haldane Report, pg 32, para 57.

⁵ Haldane Report, pg 34, para 67.

⁶ Haldane Report, pg 6, para 14.

⁷ *The Rothschild Report: A Framework for Government Research & Development*. (Cmnd 5046) London: HMSO, 1971

type of study, the knowledge gained from such research has, over time, led to novel approaches to medical intervention, for example the use of highly specific molecular diagnoses to target therapies for subsets of cancers.

The influence of scientific publications and the RAE

4.9 But there are disincentives to basic scientists developing the findings of this ‘curiosity-driven’ basic research:

- prestigious scientific journals and academic awards, such as the Nobel Prize for Physiology or Medicine, have tended to favour scientific breakthroughs resulting from basic research over application; and
- while the UK Research Assessment Exercise (RAE) has done much to improve the quality of research in UK universities, it has provided too little recognition of research that does not result in citations in prestigious journals, even if that research has resulted in economic and / or health benefits.

4.10 While health research articles that describe an observation from basic research increasingly also set out the potential relevance of that research to disease, this tends to be more of a superficial declaration than a detailed description of the step-by-step implementation process to translate a basic research discovery into clinical application. As a consequence, a whole body of research work can still be developed, funded and carried out without much, if any, input from healthcare specialists, who are in the strongest professional position to understand patients’ needs and relate them to emerging research.

4.11 The UK Government announced in Budget 2006 that the Research Assessment Exercise was to be reformed, a key concern being the lack of incentives across all research disciplines to develop basic research findings. This development is welcomed by the Review.

The influence of peer review

4.12 The Review has found that applied and translational research proposals tend to be channelled through a process of scrutiny that has been informed by the need to assess rigorously proposals for basic research. This type of scrutiny, which relies principally on peer review, has proved to be extremely effective in identifying high quality basic research projects, but can in some instances inhibit programmes in translational and applied health research. There are a number of underlying reasons for this:

- whilst a peer review process that produces simple positive or negative decisions on funding is usually suitable for assessing basic research proposals, funding decisions for translational or clinical research tend to benefit from a more iterative approach. An idea can be developed in partnership with a funding body via its resident expertise in statistics, pharmacy or clinical trials services. However, such in-house facilities are expensive to operate and suitably qualified personnel can be difficult to recruit;
- given its highly applied nature, with little prospect for generalisable observation, translational and applied research is also often published in specialist journals, while basic science discoveries tend to be published in more prestigious journals such as *Nature*, *Science* or *Cell*. Specialist journals carry less influence than more prestigious publications in the assessment of quality by peer review processes, creating a disincentive to develop basic science discoveries into more applied science; and

- translational research is normally multidisciplinary, making the contribution of any one investigator more difficult to assess by peer review and thus difficult to reward with further funding.

4.13 The Review has concluded that the current scrutiny process for research proposals creates a risk that translational or clinical research proposals could be at a systematic disadvantage to basic research proposals in securing funding. Translational or applied research is therefore less attractive to the public science base, and this creates a barrier to effective translation of UK research into practice. If this position is to change, it will be critical for the UK to reform the peer review process for translational and applied research, establishing mechanisms to ensure that research proposals are reviewed by specialists who are themselves capable of addressing the applied nature of the intended research programmes, in a process of genuine peer review. The current Research Councils UK consultation on peer review presents an opportunity to take this forward. In addition, the successor to the Research Assessment Exercise for higher education institutions needs to ensure that translational research is recognised and rewarded appropriately, perhaps with greater value being placed on the application of research in practice.

Career choices 4.14 Medical doctors also face major barriers to pursuing a career in health research. Clinical researchers have been both simultaneously informed and constrained by their everyday requirement to practice medicine on patients. This has meant that some clinical research has had a tendency to be underpowered scientifically and uninstructed by many of the advances in modern biology. It has also meant that the career structure for clinical researchers has been problematic, with researchers often ‘falling between two stools’ where they have been appraised separately on either their clinical practice in patients or research productivity in the clinic, but rarely on both together. The net result has been that clinical research typically has been considered as an unattractive career option for the vast majority of medical doctors.⁸

Institutional and financial barriers

4.15 The barriers to translation described above are reinforced by institutional barriers, not least those that result from the separation of research supported by the MRC from that supported by DH. The Research Councils’ portfolio of health research, developed by scientists on their Boards and Councils, has been primarily focused on basic research. More recently, through the Department of Health, there has been separate consideration by the NHS research community of practice-oriented research. But the Joint MRC/NHS Health Research Delivery Group has not been as successful as hoped in co-ordinating or joining up their strategies. If the UK is to succeed in delivering effective and systematic translation of basic research aimed at generating greater health and economic benefits, the appropriate balance of spending across the spectrum of health research will need to be considered as part of a single coherent strategy. This, of course underpins the decision to create a single fund for health research.

4.16 The consultation process found a range of further institutional and financial issues that are viewed as a barrier to the successful translation of health research into new treatments, diagnostics and processes. These issues include:

⁸ *Report of the Academic Careers Subcommittee of the Modernising Medical Careers and UK Clinical Research Collaboration March 2005: Medically-and dentally-qualified academic staff: Recommendations for training the researchers and educators of the future.* see <http://ukcrc.org/PDF/Medically—and—Dentally-qualified—Academic—Staff—Report.pdf>

- weaknesses in the UK's arrangements for funding, supporting and regulating clinical trials, some of which are addressed in the reforms announced in DH's Best Research for Best Health (BRfBH) and / or are being tackled by the UK Clinical Research Collaboration (UKCRC);
- the working relationships between key stakeholders, especially the NHS, universities and industry partners;
- the instability of clinical academic funding by the NHS including through universities;
- gaps or a lack of coordination in the funding and other support mechanisms for taking ideas from the lab to a stage at which a commercial partner might take them on, or to a stage where an SME developing such ideas might be able to access commercial financing; and
- research geared towards the translation of a laboratory-based discovery into a clinical application has a substantially greater number of potential pitfalls than basic research. So, too, do certain forms of nursing or social care research that attempt to translate improvements in patient care into everyday practice. Research involving human subjects needs to undergo ethical review and conform to EU regulations. In addition, recruiting subjects can be time consuming and costly, as can pre-clinical studies (e.g. toxicology) required by regulation before a new medical product can be tested in humans. The study itself may show that the product does not have the desired effect in man or that its disadvantages outweigh its benefits and, while this is very important information, it rarely gets the recognition it needs.

EVALUATION OF CLINICAL AND LABORATORY BASED RESEARCH

4.17 Historically, research designed to evaluate the contributions of the various sub-disciplines of health research to healthcare improvement (or 'research on research') has been rare, sporadic or contradictory. Comroe and Dripps reported that some 62 per cent of research underpinning clinical advances in cardiovascular and pulmonary medicine arose from laboratory-instigated research.⁹ However, the rigor of this research was later challenged as 'unscientific.'¹⁰ Perhaps more significantly, a study of neonatal intensive care failed to replicate the findings of Comroe and Dripps, concluding that the actual contribution of laboratory-instigated research to clinical advance in this area was somewhere between 2 per cent and 21 per cent.¹¹ However, these two studies measured the impact of research on entirely different areas of medicine. It is likely that each specific disease area will have a unique range of issues that will require an individually-tailored portfolio of research activity. In attempting to address this, Contopoulos-Ioannidis et al. took a more holistic approach to evaluation. They screened scientific publications in the top six basic science journals over the period 1979–1983 and found over a hundred articles where the authors suggested that their findings would have a major clinical application.¹² Two decades later, the authors found that only five of these suggestions materialised into licensed clinical use and that only one had a major impact on current medical practice.

⁹ Comroe, JH & Dripps, RD. (1976) *Scientific basis for the support of biomedical science*. Science 192:105–111

¹⁰ Smith, R. (1987) *Comroe and Dripps revisited*. British Medical Journal 295:1404–1407.

¹¹ Grant J, Green, L & Mason B. HERG Research Report No. 30 August 2003

¹² Contopoulos-Ioannidis DG, Ntzani, EE, Ioannidis, JP. (2003) *Translation of highly promising basic science research into clinical applications*. Am J Med 114:477–484.

4.18 Efforts to evaluate systematically the relative contributions of laboratory-instigated research and clinic-instigated research (especially by clinicians working in university hospitals) are confounded by a number of issues. Perhaps most importantly, advances from biomedical research may have different development timeframes from those of clinical research. The investment requirements also tend to be different in each case. Moreover, the types of therapeutic advance may differ depending on the origins of the research. For example, laboratory-instigated research may be more likely to lead to improved drug treatments, while clinic-instigated research may produce more interventions based on devices. What this debate does highlight is that support for research instigated from both the laboratory and the clinic are important and that they should be balanced in a manner that delivers maximum benefit to patients. It is of course important to note that whether originating from experimental observations in the laboratory or in the clinic, all research does, of course, require validation via research in the clinic.

4.19 In the absence of a significant evidence base to assess the relative contributions of different sub-disciplines of health research, decisions on the balance of support across the spectrum of health research are restricted to judgements based on empirical evidence. In that regard, numerous examples exist of research largely based in the clinic leading to significant therapeutic advances. In a similar vein, many medical advances have stemmed from laboratory-led research (See Table 4.1).

Table 4.1: Examples of therapeutic advances from research largely based in the:

clinic		laboratory	
<i>Intervention</i>	<i>Indicative use</i>	<i>Intervention</i>	<i>Indicative use</i>
Cardiac pacemakers	Arrhythmia	Insulin	Diabetes
Renal dialysis	Kidney failure	Statin	Hypercholestermia
Organ transplantation	Organ failure	Immunosuppressive drugs	Rejection of organ transplants
Radiotherapy	Cancer	Human papillomavirus vaccine	Cervical cancer prevention
Joint replacement	Arthritis	Selective serotonin reuptake inhibitors (e.g. Prozac)	Depression
Cataract removal	Visual deterioration	Combined oral contraceptives	Birth control
Sleeping position	Sudden Infant Death Syndrome	Inhaled corticosteroids	Asthma

4.20 As highlighted above there has been and no doubt will continue to be debate about the relative merits of laboratory-led research versus clinic-led research, regarding which has played a greater contribution to the advances in healthcare. It is clear that both play a key role.

4.21 Several of the responses to the consultation called for new systems or methodologies to underpin the systematic review of existing research. There was also a call for a systematic review of existing evidence on the impact of healthcare research on health and healthcare. Recently, the Academy of Medical Sciences, MRC and Wellcome Trust issued a report on the evaluation of medical research, calling for improved and more consistent methods of evaluation.¹³

4.22 The Review believes that, if research evaluation is to have maximum impact, researchers and policy-makers together should determine how to use such evidence most effectively in the development of funding strategies. Ultimately, such ‘research on research’ should help to inform

¹³ *Medical Research: assessing the benefits to society*. A report by the UK Evaluation Forum, supported by the Academy of Medical Sciences, Medical Research Council and Wellcome Trust. May 2006.

policy decisions on how limited resources can deliver new knowledge where it is most likely to have substantial impact in addressing unmet medical needs. Such research will take time to come to fruition and impact on policy, but we believe, ultimately, it will play a vital part in determining the allocation of scarce resources to the most productive areas of health research. As a first step, **we recommend that the funders of health research in the UK should work with the Economic and Social Research Council to consider the practicalities of setting up a long-term project to carry out such an evaluation.**

The balance of public funding

4.23 It was also put to the Review that the balance of public funding across the different disease areas could be improved. For example, there were calls for increased funding in specific areas such as: epidemiology; public health; health promotion; disease prevention; service delivery; diseases which burden society/chronic diseases; ageing; maternal health; orthopaedics; musculoskeletal disease; lung disease; kidney research and midwifery/maternity care. There was also a body of opinion which argued that prioritisation of spend on research should be proportional to monies spent by the NHS, to the socio-economic burden of disease, or to fill the gaps identified by the UKCRC analysis.

4.24 In addition, there was some discussion during the consultation around the ‘correct’ balance between funding for basic, translational and applied research. As set out in Chapter 2, UKCRC analysis has shown that around two-thirds of public and charity funding of health research is invested in basic science projects. Despite this current weighting towards basic research, we have found no evidence that suggests that the UK should decrease the current levels of funding to the UK’s world-class basic research base. Therefore, **we believe that current funding levels for basic science should be sustained.** However, discussions during the review have strongly suggested that the balance of opportunities to create additional health and wealth benefits from health research lies firmly in translational and applied research. As a result, **we recommend that future increases in funding should be weighted towards translational and applied research until a more balanced portfolio is achieved.**¹⁴

THE SUSTAINABILITY OF THE DRUG DEVELOPMENT PATHWAY

4.25 Of course, whilst the UK public and charity sectors fund a large proportion of UK health research, the pharmaceutical industry is also a major funder of R&D in the UK, conducting 35 per cent of the R&D undertaken by the top 800 UK R&D companies¹⁵. The industry, therefore, has a crucial role, particularly in translating research into health and economic benefits. At the same time, however, it faces increasing challenges in delivering this.

4.26 The 1970s and 80s were the era of blockbuster drugs in the pharmaceutical industry. Single chemical compounds could be used to treat large sections of the general patient population, thus providing substantial health benefit to patients and billions of dollars in return on the investment of the pharmaceutical industry. But as increasing numbers of compounds were successfully applied to the treatment of a greater number of diseases, fewer and fewer diseases with large patient populations remained without treatments. Standards and expectations also became increasingly high for the efficacy of any new therapeutic compounds.

¹⁴ For more information on the mechanisms for delivering this, see Chapter 5.

¹⁵ The R&D scoreboard 2006. DTI.

4.27 By the early 1990s, fewer and fewer blockbusters were emerging from the development pipelines of the pharmaceutical industry. It is widely argued that Government regulatory standards had become increasingly stringent, reflecting greater public concern about safety issues. Any new treatments had to surpass the efficacy and safety profiles of previous ones, if there were to be a high level of payback for the investment in their development. In short, ‘the low hanging fruit’ of drug compounds had already been harvested. Remaining drug targets were much more resistant to large improvements via the traditional chemistry-based R&D approaches of the pharmaceutical industry. Companies increasingly attempted to spread the investment risk within their pipelines by developing alternative versions of pre-existing drug compounds, aimed at delivering incremental improvements on the current treatments. These are sometimes controversially referred to as ‘me toos’. The pharmaceutical industry also sought to address the emerging shortcomings in their drug pipelines by attempting to improve efficiencies via more systematic approaches to the development of medicines from chemical compounds. In-house R&D programmes focussed more on high throughput and automated methods for screening drug candidate compounds, arguably at the expense of more diverse, but less efficient, types of research programmes. In addition, an increasing portion of industrial R&D was outsourced.

4.28 As noted in Chapter 1, the challenges facing the pharmaceutical industry, together with trends in health research towards ‘personalised medicine’, are combining to present a number of challenges to healthcare systems around the world. Smaller patient populations mean that the development costs of new medicines will need to be spread over a smaller group of patients, increasing the average cost of those medicines. In turn, this should be a driver for efforts to reduce the costs of new medicines, to ensure equitable access to cost-effective new treatments. This means not only investing in R&D to reduce the cost of drug development, but also better diagnostics so that new medicines are only given to patients that will benefit from them (efficiency gains) and also looking again at the regulatory process, to see for example whether new technologies can help reduce the length of time it takes to get a new medicine to market.

4.29 Health research can help health policy-makers, the pharmaceutical industry and other stakeholders to tackle these issues, and boost translation of health research into health and economic benefits. We explore these issues further in Chapter 8.

5

New institutional arrangements

Chapter overview

The chapter presents the criteria and critical success factors considered by the Review when determining the institutional arrangements for the single fund for health research. It presents the case for reform, highlighting in particular:

- the lack of coordination between the MRC and the Department of Health's R&D function;
- the need for greater focus on UK priorities;
- the lack of incentives for applied research; and
- the need for a research-friendly culture in large parts of the NHS.

The Review's key proposal is to create a new, light-touch organisation to ensure a more strategically-coherent approach across publicly-funded health research in England and the UK, with the Devolved Administrations joining in as appropriate. This organisation should be called the Office for Strategic Coordination of Health Research (OSCHR). The key functions for OSCHR will be to:

- work with officials from DH, OSI and the Devolved Administrations to set the Government's health research strategy, taking into account the advice, priorities and needs set out by NIHR (and its equivalents in the Devolved Administrations), MRC and the NHS;
- set the budget required to deliver the strategy and objectives for DH and MRC, including the distribution of the budget between NIHR and MRC;
- submit to the Treasury a joint funding bid for the agreed strategy;
- monitor delivery of the strategy against objectives, to report to Ministers and Parliament on its progress, and to advise Ministers on the effectiveness of maintaining two separate public research bodies; and
- encourage a stronger partnership with the health industries and charities.

In addition, the Review recommends that OSCHR should brand priority research in the public, charity and private sectors as 'UK Priority Health Projects' (PHRPs), based on an assessment of the UK's unmet health needs, as a way of sending a stronger signal to the healthcare industries as to where the UK Government would like to see R&D investment focussed. This could be reflected in decisions as to which medicines are assessed through NICE's new 'fast track' process, and potentially in other procedures.

VISION

5.1 The Government's vision is of a holistic health R&D system that will maximise the value of the UK's research base. The Government wants to ensure the UK's health research is more closely aligned with wider health objectives, builds on scientific progress to date, and translates the results of research into economic benefit.

5.2 In order to exploit the strengths of the UK's health research, the Review believes the UK must maintain the quality and quantity of its excellent basic medical research. But it must also address the barriers to translation of basic research that result from the gaps identified between basic and clinical research, and between clinical research and clinical practice. The Review envisions cultural change in both the Department for Health and the MRC, to address cultural barriers to research collaboration, and to the willingness to undertake further research to support the application and translation of basic research into patient and economic benefits.

5.3 Finally, the Review believes that the UK's drug development pathway should create better incentives for the pharmaceuticals industry to engage in R&D that results in the development of truly innovative medicines, and that there should be proper rewards for translating research into innovation in health interventions.

IDENTIFYING FUTURE CHALLENGES FOR HEALTH RESEARCH

Building on past success

5.4 During the past century, medical advances have had a major impact on the way in which medicine was practiced and health outcomes achieved, seeing a series of medical breakthroughs, including the discovery of penicillin, the causal link between smoking and lung cancer, the use of open-heart surgery, and advances in the safety of anaesthetics. Life expectancy at birth increased from less than 50 years at the turn of the twentieth century to 77 years for men and 81 years for women by 2004.

New opportunities for the future

5.5 Significant advances have been made in a relatively short period of time, and rapid technological improvements of the present and future will continuously change what it is possible for health care to achieve, with new medical interventions continuing to help prolong healthy life, as well as how treatment is carried-out.

5.6 Developments in smart materials, nanotechnologies, and body and mind sciences could lead to new and improved techniques for diagnosis and therapeutics. Progress, particularly in biotechnology, is expected to lead to the development of new drugs, advancing our abilities to treat various conditions or make new medical interventions.

The need for social debate

5.7 Some new treatments will ask difficult questions of society and government. During the last decade, there has been substantial debate about the desirability of stem cell research. Over the next decade, similar issues will arise. For example, should cognitive enhancers be further developed in the future, the desirability of approving them for general use would need careful consideration, as would the costs and cost-effectiveness of the treatments involved.

5.8 The medical research community, both public, private and third sectors, have the capacity to make spectacular advances in how medical conditions are treated, and will undoubtedly strive to rise to the challenge in making the most of these technological and scientific advances to address the health priorities of the future.

Understanding long-term strategic need 5.9 It is clear that the emerging and evolving shape of health research in the UK will need to be determined not just by short-term, sensible administrative pragmatism, but by long-term strategic intent. Developing a comprehensive understanding of the likely future challenges for the health of the nation is therefore vital in taking advantage of technological and scientific advancement, and designing a health research policy framework that is both fit for now, and fit for the future.

Future health challenges

5.10 The Review believes that increasing demands on health systems, not just in the UK, but also overseas, means a greater priority should be given to supporting therapies that tackle clearly identified and understood health priorities, be they defined by unmet needs, the degree of human suffering, poor understanding of the causes and solutions of diseases or conditions, or negative trends in known disease areas.

5.11 It has been put to the Review by many influential commentators and expert opinion formers in both UK and global health research that there are some clearly identifiable health challenges facing the UK and the rest of the world today. Clearly, there is a wealth of information, statistics and epidemiological data available to begin to develop a more definitive understanding of these priorities, but a non-exhaustive list of some of the commonly cited examples is set out below:

Cancer 5.12 Cancer accounts for around one quarter of all deaths in the UK, and around one in three people will be diagnosed with cancer at some stage in their lives. There are over 200 types of cancer, with cancers of the lung, breast, bowel and prostate being the most common, representing over 50 per cent of new cases:

- lung cancer is the second most common form of cancer, and nine times out of ten is caused by smoking or passive smoking. It represents around 37,200 new cases every year;
- breast cancer is the most common form of cancer for women in the UK, with around 42,000 new cases every year, representing one in three of all new cancer cases in women;
- bowel cancer is the third most common form of cancer in men, with around 18,700 new male cases per year, and the second most common form of cancer in women, with around 16,200 new female cases per year;
- prostate cancer is the most common form of cancer for men, with around 31,900 new cases every year and a lifetime risk for men of one in fourteen; and
- finally, leukaemia is the most common form of cancer in children, representing around 50 per cent of all children-related cancer cases¹.

5.13 The UK is at the leading edge of the global effort of cancer research, and can continue to lead the way in the next generation.

Mental health 5.14 Mental health represents a great challenge to today's society, and is ranked third by the World Health Organisation in terms of morbidity around the globe. Issues such as dementia and bipolar disorder (depression) are some of the most complex and least understood areas of health and medicine, and rely on advances in the understanding of how the brain works and what treatments

¹ Source: Cancer Research UK

work and why. It is thought that advances in neuroscience in the next 10–20 years could have significant positive implications for mental health issues. For example, further improvements in imaging technologies could make both diagnosis and response to treatment easier, and substantially quicker to understand, and could substantially reduce the length of time involved in the drug development pathway for such conditions.

5.15 Taking one condition as an example, the Alzheimer’s Society estimate that over 700,000 people in the UK suffer from Alzheimer’s, the most common cause of dementia in the UK, 18,500 of which are under 65 years of age. In addition, it is also estimated that around one million further people act as carers for someone diagnosed with dementia².

5.16 Mental health issues, such as depression, seem to be particularly prevalent in the male population, as 75 per cent of suicides in the UK are amongst males, with older men having the highest suicide rate in the UK. The issue also has significant economic consequences, as can be seen from the number of incapacity benefit claimants (it has been estimated that one in seven men who become unemployed will develop depression within six months)³.

Chronic and degenerative disease

5.17 17.5 million people in the UK today live with a long-term condition, including conditions such as diabetes, asthma or arthritis. This can sometimes place serious limits on the ability of individuals to cope with day-to-day activities, with discomfort and stress being an everyday reality⁴. Furthermore, the impact on the NHS is significant – just five per cent of inpatients, many with a long-term condition, account for 42 per cent of acute bed days⁵.

Case study 1: Diabetes

An estimated 2.35 million people in the UK today have been diagnosed with diabetes⁶, and the last 30 years have seen a three-fold increase in the number of cases of childhood diabetes. It is also estimated that a further 750,000 people are unaware that they have the condition⁷. Diabetes is the leading cause of kidney failure, limb amputation, blindness and visual impairment, and multiplies by a factor of between two and four the risk of cardiovascular disease⁸.

Case study 2: Asthma

Around 5.2 million people in the UK today receive treatment for asthma, 1.1 million of which are children. In 2004, there were nearly 1,400 deaths in the UK attributable to asthma, 40 of which were children 14 years and under. To put it another way, 4 people per day, or 1 person every 6 hours, die from asthma in the UK, yet it is estimated that 75 per cent of hospital admissions are avoidable and 90 per cent of deaths preventable. One in six people with severe asthma symptoms report weekly attacks so severe that they cannot speak. This represents roughly 430,000 people, or a body of people roughly equivalent to the population of Manchester. The economic cost is also worth noting, as asthma costs the NHS around £889 million per year, and over 12.7 million working days are lost to the condition each year⁹.

² Source: National Institute for Clinical Excellence

³ Source: MIND

⁴ Supporting People with Long Term Conditions, Department of Health, January 2005

⁵ *ibid*

⁶ Department of Health

⁷ Source: Diabetes UK

⁸ Source: BD Medical

⁹ Source: Asthma UK

5.18 Furthermore, given advances in longevity in the UK, tackling degenerative diseases in older people will become increasingly important to the quality of life of an increasing proportion of the UK population in the decades to come. As well as improving quality of life, this will help to tackle the social services burden and increase the economic opportunities open to older people. Key to this will be further efforts in the field of public health and prevention, with individuals taking more responsibility for their own health and well-being, which will complement scientific and medical advances.

Nutrition, diet and lifestyle 5.19 The percentage of UK adults who are obese has increased by 50 per cent in the last decade, and the prevalence of obesity in children continues to grow at an alarming rate¹⁰. In the UK, about two thirds of adults are now overweight or obese and, of these, 22 per cent of men and 23 per cent of women are clinically obese (at least two to three stone overweight). In the last ten years, obesity has doubled in six year olds (to 8.5 per cent) and trebled amongst 15 year olds (to 15 per cent).

5.20 This is also concerning as obesity increases the risk of individuals developing other health problems, including type-2 diabetes, heart disease, stroke, osteoarthritis, high blood pressure and infertility. Obesity is responsible for more than 9,000 premature deaths per year in England¹¹. A report from the National Audit Office concluded that obesity could shave an average of nine years from our lifespan, and the Health Select Committee estimated that the costs of obesity is between £3.3 billion and £3.7 billion per year (and of obesity plus overweight at between £6.6 billion and £7.4 billion per year)¹². It was put to the Review that reducing the number of people who are clinically-obese by one million could result in significant health gains, estimated by the National Audit Office as 15,000 fewer people with coronary heart disease, 34,000 fewer people developing type-2 diabetes, and 99,000 fewer people with high blood pressure.

Cardiovascular disease 5.21 Diseases of the heart and circulatory system (cardiovascular disease or CVD) are the main cause of death in the UK and account for just over 216,000 deaths in 2004. More than one in three people (37 per cent) die from CVD. The main forms of CVD are coronary heart disease (CHD) and stroke. About half (49 per cent) of all deaths from CVD are from CHD and more than a quarter (28 per cent) are from stroke. CVD is one of the main causes of premature death in the UK (death before the age of 75). 32 per cent of premature deaths in men and 24 per cent of premature deaths in women are from CVD, which caused just under 60,000 premature deaths in the UK in 2004¹³.

5.22 Coronary heart disease (CHD) is a preventable disease that kills more than 110,000 people in the UK each year. More than 1.4 million people suffer from angina and 275,000 people have a heart attack annually. In 2002, cardiovascular disease caused 39 per cent of all deaths in the UK, and killed almost 238,000 people¹⁴. CHD by itself is the most common cause of death in the UK. Around one in five men and one in six women die from the disease, which caused just over 105,000 deaths in the UK in 2004¹⁵. The Government is committed to reducing the death rate from CHD and stroke and related diseases in people under 75 by at least 40 per cent by 2010¹⁶.

¹⁰ Source: Medical Research Council

¹¹ Department of Health

¹² *ibid*

¹³ Source: British Heart Foundation

¹⁴ Department of Health

¹⁵ Source: British Heart Foundation

¹⁶ Department of Health

International health 5.23 Just as energy and the environment represent challenges on a global scale that require concerted action at the level of individual nation states, so health across the globe presents major challenges for the coming generation. Diseases and infections such as malaria, tuberculosis (TB) and HIV / AIDS have a disproportionate impact on the developing world and affect the lives of at least a billion of the poorest people on the planet. These conditions are preventable and treatable. The scientific understanding and capacity of the developed world can be brought to bear on issues of global importance such as these, through the work of governments around the world, together with the health research community, industry and the charity sector.

Key facts 1: Malaria

Malaria is responsible for more than 1 million deaths per year, and there are an estimated 500 million clinical cases in the world today. It has been estimated that one child dies of malaria every 30 seconds, and around 2,000 African children die of malaria every single day. In any given year, nearly 10 per cent of the world's population have the disease, and most survive after between 10 and 20 days of illness, but too many still do not.

Key facts 2: Tuberculosis

Tuberculosis is estimated to kill someone every 18 seconds, and is projected to cause 35 million deaths around the world in the period between 2000 and 2020.

Key facts 3: HIV / AIDS

HIV / AIDS kills around 3 million people every year, 99 per cent of them in developing countries. 39.5 million people in the world today are living with HIV / AIDS, 2.3 million of whom are children. It is estimated that there are around 12 million children in Africa who have lost one or both parents to HIV / AIDS, and that, of the 6.8 million people in need of life-saving drugs, only 1.65 million are actually receiving them¹⁷.

5.24 There are also many other diseases and conditions that warrant the detailed profiling given above, but the intention here is not to create an exhaustive list of definitive UK priorities, but rather to use the examples above to signify the changing nature of health demands that are important to the UK, and the implications this has for the work of the health research community over the coming generation.

5.25 This has clear implications for ensuring a clear and effective interface between the public research base (and the institutions related to this) and the wider health research community – including the biomedical industry and charitable research organisations. A clear interface with appropriate incentives will ensure that the health research community can respond effectively to health challenges such as those identified above. However, as the next section of this chapter sets out, this will require further efforts to address the remaining issues around the institutional framework that drives publicly funded health research.

¹⁷ Source: AVERT

THE CASE FOR REFORM

5.26 The implementation of reforms to the arrangements for supporting R&D in the English NHS, set out in Best Research for Best Health (BRfBH), and the ring-fencing of the Single Fund represent a good start in delivering the government's overall objective of increasing the health and economic benefits generated as a result of its investment in medical and broader health research. The key now is to build on this to create a health research system that helps deliver the government's health and economic objectives.

5.27 The consultation process has been extremely helpful both in refining the Review's understanding of the challenges facing the system which had previously been identified, and in raising others which had not. Some of these issues cannot be addressed simply by changing high-level institutional arrangements for the funding of health research: they lie at either a much broader or at a much more detailed level, and are therefore addressed elsewhere in the report. But some are very specifically related to high-level problems in the system and we would pick out four issues in particular.

Weak coordination 5.28 There is a lack of coordination between the MRC and the Health Departments' R&D function. The Joint Delivery Group set up last year to improve the position has had some successes, but ultimately did not have the 'teeth' to ensure that policy was joined-up across the two funders. It did not resolve the fundamental problem that the organisations' strategies are set separately, and so, while joint-working happens where the strategies happen to coincide, it is not straightforward to ensure joint-working where they do not. This lack of coordination not only leads to overlaps, but also leads to gaps in support which can significantly impede the UK's ability to translate its success in the basic research arena into clinical research, practice and economic benefits.

Need for greater focus on UK priorities 5.29 There is an ongoing feeling amongst many outside the basic research community that the issues identified by Rothschild in 1971¹⁸ have still not been resolved. In particular, many commented that the MRC could do more to address the needs of its customers. The consultation process concluded that a greater focus on research that responds to the UK's health and economic needs and priorities, such as those outlined above, was needed, and that this would help realise more opportunities to translate the UK's world-class basic science into health and economic benefits for the UK.

Lack of incentives for applied research 5.30 The consultation also revealed a widely-held concern that the MRC's culture was largely geared (understandably) towards maintaining its strengths in basic science, and that the MRC needed to do more if it were to have greater success in incentivising applied research. There was recognition that the MRC had made significant attempts to redress this balance, particularly in the last few years. However, there was a view that a more flexible approach to peer review, reflecting the inherent differences between basic and applied research (e.g. in terms of the need for more iteration, and recognition that novelty is of less importance, by its very nature, in applied research), could facilitate this process. It could also address the MRC's finding that, in some cases, there are not enough good applied science proposals to take up the funding that they have made available for it.

Need for a research-friendly culture 5.31 The Review also found that there is a lack of a research and innovation friendly culture in large parts of the NHS. Clearly, the NHS is under pressure to deliver service targets. Some observers have argued that many of the current reforms (e.g. Payment by Results) have a potential to impact research in the NHS. However, research in the NHS has long been considered a secondary activity.

¹⁸ *The organisation and management of Government R&D, in Cabinet Office, A framework for Government Research and Development*, London, HMSO, November 1971 (The 'Rothschild Report')

Hence, the Review believes the lack of a research friendly culture should not be attributed to current NHS reforms. A key challenge for the new Single Fund will be to help tackle the cultural and other barriers to research and innovation in the NHS.

5.32 In order to resolve these issues, it will be vital to achieve the best possible design and institutional arrangements for public funding of health research in the UK, and also to ensure that the interface between public research base and industry (and the wider health research community) fully supports efforts to tackle current and future health challenges, such as those identified earlier in this chapter.

5.33 The remainder of this chapter will focus on the following key elements of the reform necessary:

- the overall **objectives** of reform;
- the **options considered** for new institutional arrangements;
- the **proposed new arrangements** and the new Office for Strategic Co-ordination of Health Research (OSCHR); and
- building a **renewed partnership with industry** and the wider research community to meet current and future health challenges.

OBJECTIVES OF REFORM

5.34 The Review has considered the consultation responses, and concluded that, in order that the new institutional funding arrangements support the Government's vision, the new institutional arrangements should achieve the following objectives:

- significantly improve the strategic coordination of public sector funding for medical and health research in England and also the devolved administrations;
- an appropriate balance of 'top-down' direction, based on the priorities and needs of the NHS, industry and science policy, and 'bottom-up' expert input from the public science base and health 'customers';
- continued delivery of world-class basic medical and health research;
- a step-change improvement in the way the UK translates its excellent basic research into health and economic benefit, specifically by ensuring translational, clinical, Health Technology Assessment (HTA), health services, public health and social care research are delivered to the same, world-class standard as basic research;
- support cultural change across both the MRC and DH NIHR through incentives and rewards for successful translation into health outcomes;
- ensure links are maintained with and between the NHS and MRC and other relevant Research Councils, particularly to ensure that innovation that occurs at the boundaries between disciplines is supported effectively;
- deliver a settled approach for a significant period of time;

- ensure that research is seen to be integral to the NHS, and that health research plays its fullest possible role in NHS reform, industrial policy and debates about the balance between cost and health benefits of NHS interventions; and
- achieve an efficient allocation of health research funding with clear accountability.

5.35 The critical success factors identified through the Review's international analysis, together with evidence provided through the consultation process, has identified specific actions that any new health research funding body should consider in order to deliver the Government's vision:

- the research funded by the MRC and DH R&D function should be regularly reviewed to identify any gaps or duplications;
- regular analysis should be conducted and joint strategic planning undertaken by the MRC and DH R&D function, to ensure that maximum benefit is gained from research funding in any given area;
- the balance between fundamental, preclinical and clinical research between different health categories should be periodically reviewed and adjusted where necessary;
- clear goals with long-term time horizons should be set for each health category, identifying the need for fundamental science and clinical research for each category;
- a long term programme to assess the relative benefits of basic, translational, and applied research, based on empirical studies led by academic health economists, should be established; and
- methodologies to evaluate research in line with the recommendation in the AMS/WT/MRC report¹⁹ should be developed and used over time to create a robust evidence base to inform policy-makers on the economic, health and scientific impacts of the various sub-disciplines within the spectrum of health research.

5.36 In addition, it is the view of the Review that more could be done to connect the public research base with the biomedical industry and the wider health research community, to better target research efforts at current and future health challenges. Discussions with key opinion formers suggest that the following objectives should be pursued:

- a programme of work to provide a robust analytical basis on which to clearly identify the priority health challenges now and in the future;
- reforms to identify projects that aim to contribute and add value to efforts to tackle these health priorities, and confer upon them a suitable 'badge' that enables them to be recognised by Government institutions as priority projects;
- ensure that these identified priority projects receive efficient and priority treatment in procedural terms, at the various stages of the drug (or device) development process; and
- consider, in the light of the forthcoming report from the Office of Fair Trading on drug prices, whether more can be done to reward new products that add value to the ongoing effort to address these identified health challenges.

¹⁹ *Medical Research: assessing the benefits to society*. A report by the UK Evaluation Forum, supported by the Academy of Medical Sciences, Medical Research Council and Wellcome Trust. May 2006

OPTIONS FOR THE NEW INSTITUTIONAL ARRANGEMENTS

Consideration of changes to Research Council boundaries 5.37 The review has considered the case for changing the current boundaries between Research Councils in order to try to bring wider aspects of health and biological research currently covered by BBSRC, EPSRC and ESRC into the new Single Fund. We have concluded that, whilst this might be feasible, it would not be sensible. The current positive efforts to encourage cross-disciplinary working between Research Councils should not be disrupted.

Potential models 5.38 In terms of potential models, seven broad options have emerged. Some involve a full merger and others would retain separate research organisations overseen by a central body that would set the UK's strategy for health research across both the MRC and the National Institute for Health Research:

Full merger

- A fully-merged organisation operating effectively as a Research Council, working under the supervision of the Office for Science and Innovation in DTI (OSI), as MRC does now.
- A fully-merged organisation, independent of government, perhaps as a special health authority (and so part of the NHS), along the lines of the National Institute for Health & Clinical Excellence (NICE).
- A fully-merged organisation operating as an Executive Agency of DH, and therefore accountable to Government via the Secretary of State for Health.
- A fully-merged organisation accountable jointly to OSI and DH.

Separate organisations with an overarching or coordinating body

- Where the overarching / coordinating body reports either to OSI or to DH
- Where the overarching / coordinating body reports jointly to OSI and to DH

5.39 Below, we consider first the cases for and against merger, followed by alternative reporting arrangements.

Should the MRC and NIHR be merged? 5.40 The arguments for and against a merger of the MRC and NIHR are finely balanced. The key test, though, is whether a single organisation would, in practice, be more effective than separate organisations with an overarching or coordinating body in meeting the key challenge of delivering more effective translation of the UK's world-class basic science base into health and economic benefits.

5.41 The two organisations do have broadly complementary remits with some gaps between them, in particular related to translational research. There are some overlaps which might allow for efficiency savings, in turn freeing resources to fill the biggest gaps. Further, a single reporting structure and a shared set of objectives could bring about cultural change in both organisations relatively quickly.

5.42 Against these persuasive arguments, however, must be weighed two important concerns. First, a merger could be disruptive, with the focus likely to be concentrated initially on internal organisational changes rather than on the major challenges facing UK health research. There is therefore a risk that the important challenges will not be adequately addressed in the short to medium term, with consequent impacts in terms of confidence of key stakeholders not just in the research community but also, importantly, among industry investors. Second, given the dominance of basic science in the MRC portfolio and the relative size (in terms of staff) of the two organisations, there is a real risk that the MRC would dominate a merged organisation. Hence, the Review is concerned that improvements in translational, clinical and other applied areas of research might not be realised.

5.43 For these reasons, on balance, **we do not recommend at this time that the MRC and the NIHR should be merged. Rather, we recommend that the two organisations should come together under an overarching body that will ensure a more joined up strategy, but remain separate.** This does not mean that there will not be significant changes in the way that the organisations currently work. If these organisations are to deliver the Government's objective of greater translation of research into health and economic benefits, radical changes are needed, both to strategy formation and to culture.

Underlying rationale

5.44 In considering the most appropriate institutional arrangements for the Single Fund, the Review has considered the following issues:

- what form should the overarching body, or central coordinating mechanism (CCM) take?
- to whom should the CCM report?
- what powers should the CCM have?
- how large should the CCM be, and what skills will it need?
- what kind of governance arrangements should be in place?
- what should be the reporting arrangements and measures of success and failure?
- what, if any, changes are needed to MRC's institutional structures?
- should the NIHR become a real, as opposed to a virtual institute?
- what other institutional changes are needed to remove cultural and other institutional barriers?
- what should be the relationship of the new arrangements to the Devolved Administrations, the NHS, other Research Councils, other Government Departments, and to key stakeholders, including the healthcare industries and charities?

Reporting arrangements and institutional structure

Should the CCM report to DH or OSI?

5.45 Clearly, the CCM should report to one or both of DH and OSI, given that OSI and DH have the expertise and understanding of science, research and health issues.

5.46 Given the criteria outlined above, the Review believes that the new organisation should retain strong reporting links to DH and the NHS. This would therefore rule out those options which involve a single accountability and reporting line to OSI.

5.47 On balance, we also do not think that it would be appropriate to remove OSI's oversight role for the research currently undertaken by MRC. OSI represents important science and industrial policy interests, and there is considerable benefit from coordinating certain DTI sponsored programmes, not only in science policy but also in areas such as funding for proof of concept and SME development, with health research funding. The Review found that, in the US and Canada, the failure to link health research with science policy probably resulted in lost synergies. In addition, given the devolution of health policy and expenditure, a single reporting line to DH creates considerable national coordination challenges.

5.48 **We therefore recommend that there should be a joint reporting line to both DH and OSI/DTI, together with structures to allow strategic input from the Health Departments from the devolved administrations.** This is not to underestimate the challenge involved in dual reporting relationships, but these have worked well elsewhere in Government, for example in relation to UK Trade & Investment, which is jointly run by the Foreign & Commonwealth Office and the Department of Trade & Industry.

5.49 Should the joint reporting system fail to work effectively, having been given sufficient time to do so, it will be necessary to revisit the recommendation to fund research through two separate bodies. **The Review recommends that a review of the effectiveness of the joint reporting arrangements in practice should be carried out after around four years of operation, in 2011.**

Institutional Structures

5.50 In operationalising the CCM, a number of existing Government structures could be used as a model:

- the most straightforward route would be to create a joint Office of DH and OSI, similar to the Office of Charity and Third Sector Finance located in the Cabinet Office;
- a second possibility would be to establish the CCM as an Executive Agency of DH or OSI, which would formally give it a greater degree of operational independence; and
- an alternative would be to establish the CCM at even greater arms-length from Government, for example as a non-Ministerial Government Department, along the lines of the Office of Fair Trading, or as an Executive Non-Departmental Government Body (NDPB), or as a Special Health Authority (along the lines of NICE).

5.51 Whilst the relative simplicity of the first model, a Joint Office of DH and OSI, is attractive, the Review has also considered:

- the level of independence needed to ensure that the CCM will work effectively; and

- the financial arrangements for the Single Fund for health research – in particular, whether the Single Fund will be managed by the CCM or whether accountability for spending remains, as now, with DH and OSI.

Strategic priorities and day-to-day decision-making

Distinction between ‘customers’ and ‘contractors’ 5.52 The Review believes the Rothschild proposed model of creating a distinction between the Government ‘customers’ of health research, who in turn represent other stakeholders, and those public and Government bodies which commission research, in this case the MRC and the NIHR, is essential to ensuring that decisions on research priorities are driven by a combination of ‘bottom-up’ advice from the scientific community and the ‘top-down’ priorities and needs of stakeholders in the NHS, industry and elsewhere.

Balanced inputs into strategic decision-making 5.53 This is, in turn, essential to tackling a key concern of the consultation: that funding decisions for health research projects do not sufficiently reflect the health needs and economic priorities of the UK. This is not to say that researchers should not have a key role in setting priorities. They should, not least because their expertise is crucial in advising on scientific possibilities and definitions of excellent science. But their views and preferences need to be considered in the wider context of the needs and priorities of the UK.

5.54 It is clear that the ‘Haldane model’ as it has evolved in practice is correct in its insistence that government (that is, ministers and civil servants) should not be involved in day-to-day decisions on specific research issues, e.g. which specific projects to fund and which to reject. This is a level of detail that is better left to specialist commissioners. The Review believes that a new model of decision-making on the strategic priorities for health research, consistent with the Haldane principle of non-interference by government in day-to-day decision-making, but based on a balance between scientific and customer input, is achievable without creating a bureaucratic burden.

5.55 Given this differentiation between strategic and day-to-day decision making, it is unnecessary for the CCM to be established as a body at complete arms-length from government. Day-to-day decision-making will continue to be left to experts through the peer review process, but strategic decision-making can be made at a level closer to government, on the basis of a balance of scientific advice and the needs and priorities of the NHS, industry and other stakeholders.

Accountability for spending decisions

5.56 The second key issue in deciding the form of the CCM is the extent to which it might take over responsibility and accountability for health research spending, as opposed to simply providing a mechanism for coordinating strategy and decision-making. The key questions here must be:

- whether the CCM will need such control over expenditure on health research in order to deliver its remit of improving the translation of research into health and economic benefit; and, if so
- whether the accountability issues that this would raise can be overcome without creating extra layers of management that are likely to lead to confused accountability and possibly less efficient decision-making, as arguably happened as a result of the Rothschild reforms of the 1970s.

5.57 The Review believes that, on the balance of evidence currently available, it is not necessary for the CCM to directly control expenditure on health research. Rather, decisions on the balance of expenditure between basic, translational and applied research can be made at the time of Spending Reviews, based on a joint submission put together by the CCM on the basis of input from all stakeholders. This means that the current lines of accountability for spending can remain in place. To achieve this, it is crucial that DH and NIHR, OSI and MRC work effectively both with the CCM and with each other.

5.58 Given these arguments, and those above regarding the necessary level of independence for the CCM, **we recommend that the CCM should be created as a jointly-staffed and funded Office of DH and OSI.** This has the advantage of not only being the simplest and least bureaucratic mechanism available, but also one that will provide an adequate basis for the operation of the Single Fund for health research based on a joint strategy and Spending Review settlement.

PROPOSED NEW ARRANGEMENTS

The Office for Strategic Coordination of Health Research—OSCHR

5.59 The Review's key proposal is to create a new, light-touch organisation to ensure a more strategically-coherent approach across publicly-funded health research in England and the UK, with the Devolved Administrations joining in as appropriate. We propose that this organisation should be called the Office for Strategic Coordination of Health Research (OSCHR). OSCHR's Mission should be: to facilitate more effective translation of health research into health and economic benefits in the UK.

Key functions 5.60 The key functions of OSCHR will be to:

- work with officials from DH, OSI and the Devolved Administrations to set the government's health research strategy, taking into account the advice, priorities and needs set out by NIHR and its equivalents in the Devolved Countries, MRC and the NHS;
- set the budget required to deliver the strategy and the objectives for DH and MRC, including the distribution of the budget between NIHR and MRC;
- submit to the Treasury a single funding bid for the agreed strategy;
- monitor delivery of the strategy against objectives, to report to ministers and Parliament on its progress, and to advise ministers on the effectiveness of maintaining two separate public research bodies; and
- to encourage a stronger partnership with the health industries and charities.

Structure 5.61 Chart 5.1 illustrates the recommended new arrangements. Key facets include:

- **OSCHR should be jointly-staffed by DH and OSI.** It should have between five and ten permanent staff, but with access to further resources from DH or OSI on a temporary basis if and when needed. It should report to both the Secretary of State for Health and the Secretary of State for Trade & Industry, who may, of course,

delegate oversight to other ministers and, on a day-to-day basis, to the Director-General of Science & Innovation at OSI, and the Director-General of Research & Development at DH;

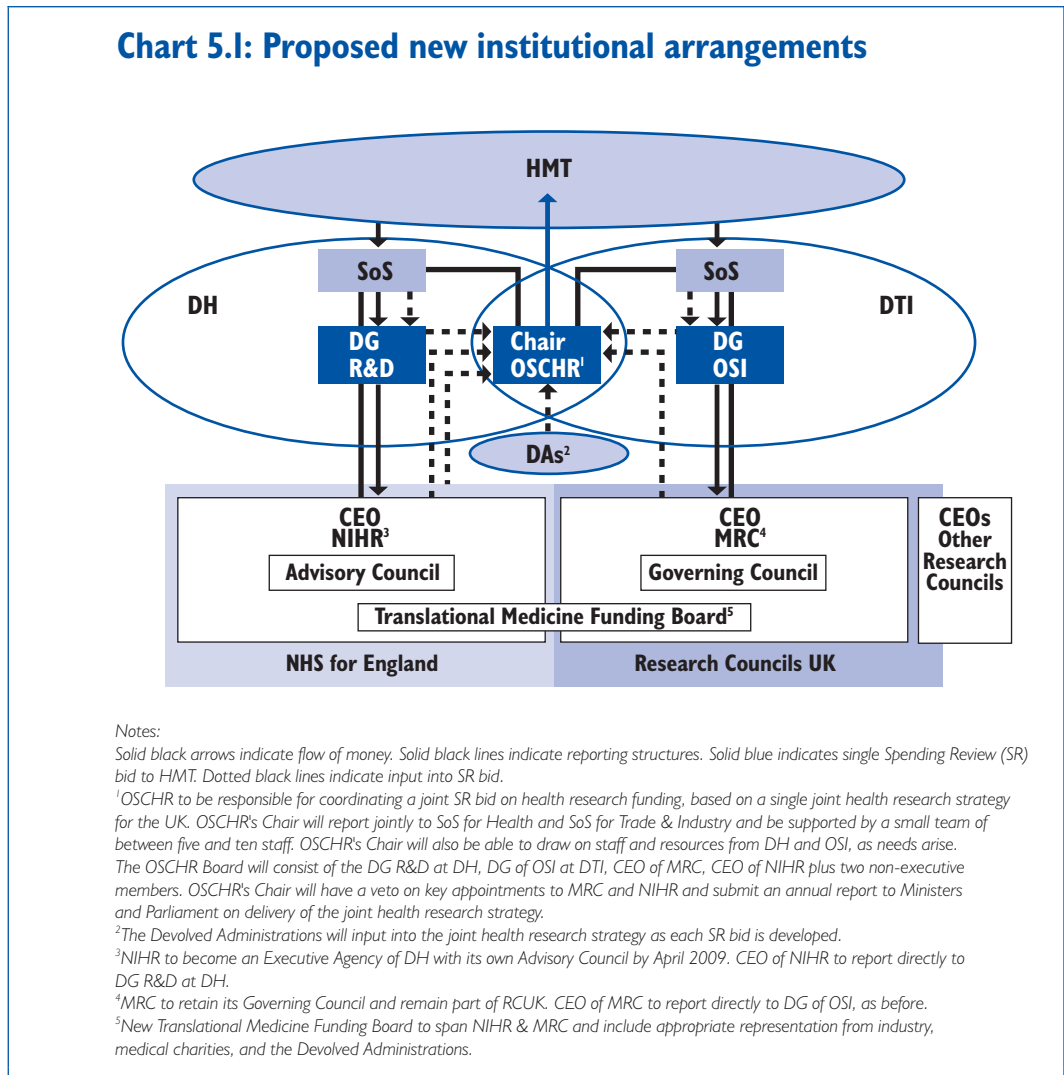
- **OSCHR should be headed by a non-executive Chair**, who should be jointly appointed by the Secretaries of State for Health and Trade & Industry. The Chair should, ideally, have experience of health research in both the academic and industry fields;
- **OSCHR should be led by a small governing Board**, which, as well as the Chair, should comprise the Director-General of Research & Development at DH and the Director-General of Science & Innovation, the CEOs of both MRC and NIHR, and three non-executive members (e.g. with senior experience gained in industry, the City, the NHS or from a major medical charity, and one representative from the Devolved Administrations²⁰). Whilst, clearly, it is crucial that wider stakeholders are consulted with regard to the single health research strategy, we do not believe that this requires the creation of a representative Board for OSCHR. This would be unwieldy, and risk the creation of a ‘lowest common denominator’ strategy; and
- **funding should continue to flow through DH and OSI directly to NIHR and MRC respectively**. This avoids creating difficulties in regard to accountability for spending, which should continue to rest with the current Accounting Officers. This is also why OSCHR should be constituted as a joint DH-OSI Office, the creation of which does not require legislation, rather than as a separate legal entity. For this reason the single fund can also encompass the entirety of the MRC and DH R&D budgets (currently around £1.3 billion per year).

Powers 5.62 Whilst this means that OSCHR will not have an executive role, its powers should, nonetheless, be sufficient to ensure that publicly-funded health research in the UK is properly coordinated under a joint strategy. These powers should include:

- **coordinating the joint health research bid and concomitant proposed joint health research strategy in Spending Reviews**. Input will need to come from a wide range of sources: ‘bottom-up’ from MRC, NIHR and the NHS; and ‘top-down’ from OSI and DH. OSCHR will have a crucial role in amalgamating and prioritising proposals into a single, coherent and cost-effective strategy. The Health Research Spending Review bid will need to be tensioned against other science priorities (by OSI) and other health priorities (by DH) at an earlier stage in the Spending Review cycle, in order to reflect this new process;
- **overseeing the Translational Medicine Funding Board proposed in Chapter 7**. More broadly, OSCHR will have a **key role in change management and effecting cultural change**, helping to bring NIHR and MRC closer together and ensure effective cross-working on a day-to-day, as well as strategic basis;
- the Chair of OSCHR should also be involved in key appointments, including the CEOs of NIHR and MRC, as well as to the MRC’s Governing Council and NIHR’s Advisory Council, and to the Translational Medicine Funding Board. In particular, **no recommendation for appointment to these roles should go to ministers unless it has been agreed by the Chair of OSCHR**; and

²⁰ With the DAs agreeing amongst themselves who is to be their joint representative

- preparing an annual report to the respective Secretaries of State and to Parliament on progress under the joint strategy, which should be placed in the libraries of both Houses of Parliament.



5.63 OSCHR will need the right skills to deliver its remit. These will include not only knowledge and understanding of medical research and stakeholder needs and priorities, but also ‘soft skills’, such as communication and facilitation skills, where much can be learned from the successes of the UKCRC in its role as a facilitator of change.

5.64 The Performance Management System currently used by OSI to monitor the performance of MRC will ensure that the single joint strategy for health research is translated into specific aims and objectives for MRC, which should be agreed between OSI and OSCHR. DH will need to develop a similarly robust system, again agreed with OSCHR, to monitor the performance of NIHR. We understand that this is currently being developed by DH. Both MRC and NIHR should send quarterly updates to OSCHR on their progress against deliverables, in addition to the report they send to their respective Departments.

Ways of working

5.65 The work of OSCHR will by its very nature be ‘lumpy’:

- preparing Spending Review bids will create peaks of work every couple of years;
- in the initial period, budgets will have to be adjusted relating to the newly agreed remits of the constituent parts of the Single Health Research Fund delivery system;
- once stable, the Board’s role should be more about monitoring and offering developmental advice, whilst continuing to hold the constituent parts to account;
- the Chair and Board should commission work from the constituent parts as required, including relating to Spending Review bids; and
- the Board would, on a regular agreed basis, review a performance scorecard from the constituent parts.

5.66 Other work will need to be supported either by submissions from the constituent parts (DH R&D, OSI, NIHR, MRC, and the Translational Medicine Funding Board²¹) generally as a result of a commission, or by working across the appropriate organisational parts in project teams to deliver commissioned projects. In this way, people with the right expertise and influence will contribute where needed.

5.67 The constituent parts will want to work effectively with OSCHR and to support its work, as otherwise they are unlikely to see a bid for CSR funding going forward as they would wish, or to receive the funding that they feel is required.

Other Institutional Changes

5.68 In order to fully deliver against the Government’s vision, the Review is recommending some further institutional changes:

- **MRC should retain essentially the same institutional structures as it has now.** It is, however, crucial that the MRC Boards become more representative of the broad spectrum of health research, and more streamlined, particularly if the MRC is to become more effective in the sphere of translational research. MRC should also remain part of RCUK as it is crucial that it retains, and builds upon its current links with other Research Councils, to ensure that research at the boundaries of health research and other disciplines receives adequate funding and attention. This would also ensure continued access to the Research Councils’ large facilities operations, avoiding any unnecessary disruption;
- **the NIHR should become a real, rather than a virtual institute, established as an Executive Agency of the Department of Health by April 2009,** when the reforms set out in Best Research for Best Health (BRfBH) will have been fully implemented. The Chair of OSCHR should agree the NIHR’s governing structure with DH;

²¹ See Chapter 7 for more details.

- **both NIHR (in its terms of reference) and MRC (in its Charter) should have a duty to cooperate closely with OSCHR and to work to deliver the joint strategy for health research. Both should report to the OSCHR Board on a quarterly basis against objectives, targets and milestones set under the joint strategy. A ‘balanced scorecard’ approach should be used to assess the performance of both organisations;**
- **in order to achieve greater clarity of objectives, more efficient decision making and allocation of resources, there should be a much clearer allocation of responsibilities between MRC and NIHR under the new arrangement outside the areas covered by the Translational Medicine Funding Board.** This will also ensure that each organisation focuses on its research strengths rather than both trying to cover the whole spectrum of research. One of the aims of the Review was to align research priorities more closely with wider health objectives. In some areas where both MRC and DH currently fund research (such as HTA or clinical research instigated by clinicians or other health professionals), the Review feels that DH is in a better position to do this. Box 5.2 sets out the details regarding the new relative responsibilities of MRC and NIHR. In practice, this clearer allocation will mean that the MRC will no longer fund research in areas where NIHR currently provides funding and, in the opinion of the Review, is better placed to lead, i.e.:
 - Health Technology Assessment (HTA) and Phase IV clinical trials;
 - Health Services Research (HSR);
 - Applied Public Health Research, including research carried out by the Health Protection Agency²² (HPA) to support their core business (but MRC should continue to fund fundamental research in this area, e.g. in developing better understanding of the biological contributions to behaviours);
 - Social care research; and
 - Clinical research conducted by NHS staff, contributing to the better care of patients.

OSCHR should ensure an orderly transition between the existing and new funding arrangements in the next spending review period, to prevent significant shifts in overall funding between basic, applied and translational research during this transitional stage, and should lead in ensuring the appropriate changes of responsibility are clearly allocated and implemented; and

- **translational research should be a joint MRC-NIHR responsibility**, with strategy overseen by the Translational Medicine Funding Board set out in Chapter 7 and joint working facilitated by OSCHR. MRC Technology, which has had real success in helping to translate MRC research into health and economic benefits, should continue to have a key role here.

²² MRC has already announced that it will no longer fund this.

Box 5.2 Roles and responsibilities of MRC and NIHR

Under the new arrangements, there should be a much clearer demarcation of responsibilities, reflecting the problems caused by overlapping responsibilities and the cultural barriers to applied research that exist in the MRC.

Under the new arrangements, the **MRC** should be responsible for all aspects of commissioning, funding and managing basic / underpinning research, including not only biological research but also the underpinning science and methodologies for public health (e.g. in understanding biological contributions to behaviours, in biostatistics, etc.) and underpinning methodologies for clinical research. It should also retain some other key roles outside these areas, most notably its role in international health, working in partnership with DFID and DH.

The **NIHR** should be responsible for research infrastructure in the English NHS, including the Centres of Excellence ('NIHR Research Centres'), NIHR faculty and NIHR infrastructure proposed in Best Research for Best Health; and on the research programme side, all Health Technology Assessment (HTA) including relevant Phase III/IV clinical trials, Health Services Research (HSR), health policy, social care and applied Public Health research programmes, whether commissioned or investigator-led. In addition, the NIHR should have enhanced functions to commission research, including clinical trials, where there are market failures, e.g. trials of new uses for off-patent medicines, comparative trials (such as the Allhat trials for statins), where there are few or no commercial incentives for companies to fund such trials.

Translational research should be a joint MRC-NIHR responsibility, with strategy set by the **Translational Medicine Funding Board**.

Relationships with the devolved Administrations

5.69 Clearly, given that MRC has UK-wide responsibilities, whereas NIHR is an England-only organisation (although it may commission research from elsewhere in the UK), further mechanisms are needed to ensure that the single fund for health research takes account of the health needs and priorities of the Devolved Administrations, which may differ in some respects from those of England. At the same time, however, we are anxious to avoid creating significant new bureaucratic structures. Given that we are not recommending that OSCHR should have a representative board, we have not recommended that Scotland, Wales and Northern Ireland should have their own, individual representatives on it, which would add significantly to the size of the Board, but that they should have a joint Board member. This reflects the fact that each country will retain its own NHS R&D budget and allocations, as well as representation within the MRC. In addition, we recommend that Devolved Administration interests should be reflected:

- through the inclusion of a specific objective in OSCHR's remit to reflect the needs and priorities of the Devolved Administrations and allow for collaboration with their NHS R&D programmes where there are common objectives;
- through the creation of a UK-wide Health Research Strategy Board, comprising the UK Departments of Health and Trade & Industry together with the Chair of OSCHR, which would meet once or twice a year, at either ministerial or senior official level, to discuss issues relating to health research. This will have a particularly

important role in ensuring that the viewpoints of the Devolved Administrations are taken into consideration in the run-up to Spending Reviews, or at other times where budgets and strategies are being set; and

- through ensuring that the Devolved Administrations are informed at an early stage, and on a strictly confidential basis, of new initiatives developed by NIHR, which will allow them to respond more effectively to concerns amongst researchers in the devolved countries that English-based researchers have an unfair advantage. This arrangement should be reciprocated by the Devolved Administrations with regard to England and each other.

TACKLING PRIORITY HEALTH CHALLENGES: A NEW PARTNERSHIP WITH INDUSTRY

5.70 Key to a successful partnership approach between the public research base and industry in tackling the health challenges of the future is to:

- identify health research priorities clearly, determined on a transparent and logical basis; and
- supporting this with effective institutional and procedural reforms that reward value-added research in these areas.

Identifying health priorities

5.71 As set-out above, OSCHR will be responsible for setting the UK's health research strategy based on both 'top-down' advice from DH and OSI, and 'bottom-up' advice from the NHS and the wider health research community. The 'top-down' approach will require OSCHR to understand the UK's health priorities. The Review recommends that the Department of Health, in conjunction with the other UK Health Departments, should undertake a review urgently to understand the impact of diseases and illnesses on the UK population and economy, and thereby determine the UK's health priorities. This review should report to the acting head of OSCHR, ideally in time for the findings to inform the Comprehensive Spending Review process.

Identifying health research priorities

5.72 OSCHR will combine this 'top-down' and 'bottom-up' input to set the strategic direction for research into particular disease areas, setting the vision and long-term objectives for the UK in each disease area, and it will plan how that vision is to be realised. For example, where our understanding of how to diagnose, treat or prevent a priority disease is inadequate, greater investment should be made into basic and / or clinical research; and where our understanding is more advanced, greater investment should be made into the translation of the basic or clinical science into clinically proven diagnostics and treatments. The Review recommends that OSCHR should use this information to establish an agreed and understood set of **health research priorities for the UK**, that target the biggest and most important health challenges for the UK over the coming decade.

5.73 OSCHR will use its understanding of the UK's health priorities to inform its industrial engagement activities. The research strategy set by OSCHR should send a very clear signal to the life sciences industries as to where the UK would like to see progress made on unmet health needs. Whilst the UK market for the pharmaceuticals industry is relatively small, with only 3.5 per cent of the global market, the role of NICE has resulted in the NHS becoming a relatively effective buyer. Further, ensuring that investment in our excellent basic science better supports UK health priorities should encourage commercial R&D activity in the UK to reflect those priorities.

UK Priority Health Research Projects 5.74 A key challenge for the UK is to connect its publicly funded research with companies and clinicians who can translate research findings into effective treatments and medicines. The Review believes that increasing demands on health spending means that greater priority should be given to research that tackles these identified UK health research priorities. The Review believes that research into priority areas (that fulfils defined criteria that protect the integrity of the drug development and oversight process) should be given a degree of priority status with regard to various institutional and procedural mechanisms. The Review therefore recommends that the Department of Health work with the National Institute for Health and Clinical Excellence, and the National Institute for Health Research (and their equivalents in the Devolved Administrations) to establish a new **‘UK Priority Health Research Project’ (PHRP) status** that can be conferred on projects deemed of national importance in tackling the health research priorities identified by OSCHR. These could be publicly funded research projects or programmes, or could be projects funded by charities or the life sciences industries. As stated above, the status will reflect a set of suitable criteria to be developed by government, which could include for example:

- the relevance of the project to contributing to an identified health research priority in the UK;
- the quality of the research being undertaken; and
- the likelihood of the research resulting in a finding that could have a significant impact, including a positive value for money / affordability assessment at later stages.

5.75 PHRP status should confer institutional and procedural advantages for health research that adds real value in tackling the UK’s identified health needs. There are a number of possible methods for conferring such advantages on PHRPs that should be explored by the government, including those set out below.

Clinical trials approval 5.76 First, PHRP status should ideally confer on priority research the advantage of faster approval for clinical trials in the NHS. The Review therefore recommends that the Government explore options for ensuring PHRP status is recognised by all those authorities responsible for the clinical trials approval process.

Regulatory approval 5.77 Second, PHRP status should ideally also confer on priority research the advantage of faster regulatory approval (this does not mean lower standards or burdens of proof). This might include priority selection into pilots for earlier conditional licensing, explored further in Chapter 8 of this report. However, the Review recognises that many of the procedures and requirements in this area are a European competency. Therefore, the Review recommends that the government explore with the European Medicines Evaluation Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) the possibility of creating a fast-track approval process for projects that have been officially recognised as UK PHRPs.

NICE process 5.78 Third, PHRP status should ideally also confer upon priority research an expedited route through NICE approval. Essentially, this will mean inclusion as an additional criterion when deciding which medicines should be assessed by NICE (and its equivalents in the Devolved Administrations) and which of the available processes should be applied. The Review therefore recommends that PHRP status is also included as a criterion by NICE when deciding which medicines should be assessed.

5.79 However, it is important to make clear here that PHRP status would not be designed to confer automatic commercial certainty for biomedical and pharmaceutical firms, who would still be required to produce effective therapies that represent proper value for money and are assessed as such by NICE in the usual manner. Rather it would confer upon them preferential *procedural* treatment, making the processes involved quicker and more efficient, recognising the degree of importance that the government attaches to health research that explicitly tackles health research priority areas.

IMPROVING COORDINATION OF RESEARCH EFFORTS ON DEVELOPING COUNTRY HEALTH ISSUES

5.80 In recent years, the UK, primarily through the Department for International Development (DfID), has played a key role in international efforts to address health issues in developing countries, a major issue in addressing global poverty. This reinforces the importance for the UK of maintaining and strengthening its position in international health research, where the MRC (which has two international units based abroad, in the Gambia and Uganda) and DfID work well together under an existing concordat-based relationship. Clearly, the UK's research interests in developing country health issues do not only arise in government. Commercial and charity funders, especially the Wellcome Trust, also have key interests here.

5.81 The Review has found that the impact of health research in the international development context is constrained by a lack of coordination between funders. The Government's Chief Scientific Adviser has recommended that a forum is set up to facilitate collaboration on development research in the UK, bringing together DfID, DH, Research Councils, and other funders of research, including charities and international funders. **The Review supports the establishment of this forum, but it believes that in the case of health research that there should also be an initiative to accelerate translation and enable delivery in the field. This could be provided as an additional responsibility of this forum but it would only be effective if it includes representatives of NIHR as experts in clinical, applied and health services research, as well as MRC, in order to engage the NHS in enabling delivery.**

CONCLUSION

5.82 The Review believes that, whilst institutional changes alone will not deliver the Government's objective of increasing the health and economic benefits arising from the UK's world-class health research base, the changes recommended in this chapter will be crucial to delivering a step-change improvement in performance. The following chapters examine a series of related areas where further proposed changes will help to create a reform package that will ensure that that step-change, and the desired increase in health and economic benefits, is delivered in practice.

6

Creating a research-friendly culture in the NHS

Chapter overview

While the principal task of the Cooksey Review has been to consider the most appropriate institutional arrangements for the Single Fund for health research created by bringing together the budgets of the MRC and the DH R&D programme in England, these changes alone will not bring about the greater translation and exploitation of publicly funded health research and innovation that the Government is seeking.

As discussed earlier, cultural changes are needed in both the MRC and DH to deliver on the Government's vision for deriving greater economic and health benefits. In this chapter, we focus on the cultural changes needed in the NHS, supported by new and reformed incentives and other reforms, to ensure greater translation and uptake of research and innovation driven either from publicly-funded sources, like the MRC, NIHR and the NHS itself, and / or from the private and charity sectors. We also consider the roles of the clinical researchers who deliver the evidence for, and are often the leaders of change.

The areas considered include:

- ensuring the health R&D ring-fence is effective;
- creating a more positive overall culture in the NHS for research and innovation;
- the removal of barriers to closer working with partners across the public, private and charity sectors;
- creating positive incentives for the NHS to undertake R&D;
- creating incentives for the spread and uptake of best practice;
- implementing new ideas in the NHS;
- more effective exploitation of Intellectual Property (IP) generated by the NHS; and
- procurement and innovation.

Many of the proposals for change look to build on the system reforms being introduced in the English NHS, as well as work taken forward in *Best Research for Best Health* (BRFBH) and by the UKCRC. They may, therefore, be less immediately applicable in Scotland, Wales and Northern Ireland. Nonetheless, it is important to consider whether alternative mechanisms can be found to address the concerns raised, which are more appropriate to the NHS systems being adopted by the Devolved Administrations

INTRODUCTION

6.1 The consultation identified issues related to the culture of, and incentives in the NHS that are key factors in limiting translation of health research into health and economic benefits. The issues raised included the need for:

- more incentives for both NHS organisations and employees to carry out and participate in research. This refers not only to financial incentives (e.g. clinical excellence awards), but also in terms of recognition in other reward mechanisms (e.g. Healthcare Commission assessment and government targets) and in terms of having the time and opportunity to take part in research-related activities;
- fewer disincentives to carry out research, e.g. financial disincentives;
- a less conservative approach to new ideas and technologies;
- more standard routes into the NHS for new technologies, particularly for smaller, non-pharmaceutical companies; and
- a more positive culture of innovation to disseminate best practice beyond existing NHS ‘islands of excellence’. Some institutions, benefiting from the persistence of particular individuals who push research and innovation, rapidly implement the latest ideas and technologies, while others are much slower.

6.2 The picture is mixed. Some parts of the NHS are very research- and innovation-friendly, particularly where there are strong university-hospital links, as the Review found in Manchester, Edinburgh, Glasgow, Oxford and Cambridge. These centres of excellence, however, are not generally representative of the wider NHS. Equally, the NHS’s capacity to take up new ideas and technologies is unclear. First, there is evidence that, although the NHS can be slower to adopt new technologies than health systems in some other countries, this varies between technologies^{1 2} and, once a technology is accepted, uptake tends to accelerate rapidly, particularly where it is covered by a National Service Framework (NSF). The Review believes that assessment processes for cost-effective new technologies could be improved, to make their take-up faster if possible, although there may also be limitations, given the time that is needed to assess new technologies in practice. The Review’s recommendations on the Critical Path for new technology development (see Chapter 8) attempt to address these issues. Second, it is important to distinguish between fast uptake of new technologies per se and fast uptake of cost-effective new technologies. It is the latter, which is consistent with the Wanless ‘fully-engaged’ scenario³, that the NHS should be looking to achieve, meaning that processes and incentives need to be put in place to enable this to happen as efficiently and as quickly as possible. The people, capacity and ability to carry out health research effectively are crucial to making this happen.

¹ The Review has seen early work prepared for the Ministerial Industry Strategy Group (MISG) for the pharmaceutical industry which suggests that rates of uptake of new medicines in the UK relative to other European countries vary hugely depending on the medicine, and does not support the notion of the UK as a relatively ‘slow uptaker’ per se. It may be, however, that the UK is a relatively slow uptaker for more expensive medicines — we would need to see more data to disprove or support this hypothesis.

² It is also important to remember that the statistics on uptake following marketing authorisation may be distorted by the different pricing/reimbursement systems in different countries. The UK is one of the few countries that will allow immediate launch and reimbursement of a medicine following receipt of a marketing authorisation, allowing less time for pre-launch preparations (e.g. marketing), whereas the launch of new medicines in other countries can be delayed by pricing discussions, allowing time for pre-launch preparations and therefore creating the conditions for faster uptake after launch.

³ *Securing our future health: Taking a long-term view, an interim report*, Derek Wanless, November 2001 — see http://www.hm-treasury.gov.uk/consultations__and__legislation/wanless/consult__wanless__interimrep.cfm.

6.3 Given these factors, the required reforms to the way the NHS works and changes to the NHS's culture are not a straightforward matter of changing procurement practice and culture simply to increase uptake, but rather need to be carefully designed to encourage better, faster uptake of cost-effective technologies and ideas, without introducing undesirable side-effects, such as greater uptake of technologies which are not cost-effective.

6.4 More widely, it seems that the devolved nature of the NHS, by which we refer to the delegation of management responsibility to individual NHS organisations, rather than the political devolution to the constituent countries of the UK, provides challenges to the promotion of R&D and innovation. Individual NHS organisations have considerable freedom to determine their own approaches⁴. Whilst the structure of the NHS should clearly be determined by the most effective way to deliver healthcare, the devolved structure does present problems to private companies and others who want to work with the NHS, particularly when it comes to running clinical trials or introducing new technologies. The consequence is lost opportunities or sub-optimal approaches to new cost-effective technologies.

6.5 The following proposals suggest how these issues might best be tackled, with the overall objective of achieving a position where research and innovation are 'hardwired' into the NHS as a core objective alongside service provision and teaching, within an NHS that remains, as now, highly devolved.

ENSURING THAT THE R&D RING-FENCE IS EFFECTIVE

6.6 Ensuring that the NHS R&D budget is spent on R&D is a pre-requisite for developing an NHS culture which is more 'R&D friendly'. Trusts will not be prepared to invest in R&D unless they have some certainty about the availability of funding, albeit funding allocated on a competitive basis. The announcement in Budget 2006 that the DH R&D budget will now be ring-fenced was extremely welcome, and provides a robust basis on which NHS research can be used to develop health and economic benefits. However, it is critical that this ring-fencing at national level is matched at local level, and that there is full accountability for R&D spending within NHS Trusts, particularly as Trusts may be under pressure to divert R&D monies to frontline services. The reforms developed in Best Research for Best Health (BRfBH) in England will help ensure this, by more closely linking research awards to research performance. Nonetheless, clear processes, including audit, will be needed to ensure that monies allocated for research are not spent on other activities.

6.7 However, whilst the DH R&D budget is now protected by a ring-fence, there are still some related funding streams which remain outside the ring-fence. Clearly, this creates some potential concerns, particularly given that the proposals in BRfBH for establishing an NIHR Faculty depend on these funds.

Clinical Academics

6.8 A particular issue has arisen in the consultation process around the funding for the salaries of the Academic Clinical Fellows, Clinical Lecturers and GP Fellowships, which, in England, is currently held within the Multi Professional Education and Training (MPET) Budget. This budget is allocated from the Department of Health to Strategic Health Authorities, and is not ring-fenced for education and training. This year, the MPET budget has been substantially reduced, placing the funding for Academic Clinical Fellows, Clinical Lecturers and GP Fellows at serious risk. **The**

⁴ Clearly, the precise position will vary between the four countries which comprise the UK; not all issues raised here and below will apply equally, or sometimes at all, to all four countries.

Review recommends that the component of the MPET budget that is used to support the training of clinical academic staff⁵ should be transferred to the DH R&D budget, ring-fenced, and used specifically for this purpose.

Training the leaders of cultural change

6.9 Equally, changing the NHS's culture to make it more open to research and innovation requires clinical researchers to lead the efforts to make those changes. The Review's research of the systems in the UK, North America and Sweden has identified the crucial role here of the relatively few medical doctors who also hold a PhD qualification.

6.10 The Walport report⁶ made a series of key recommendations for training the health researchers of the future, accepted by DH and included in BRFBH. A central component was the provision of competitively-awarded Fellowships to train Clinical Fellows to MD/PhD level to meet this leadership need. It was expected that these would be provided by existing training fellowships funded, for example, from the Medical Research Council, Wellcome Trust, British Heart foundation, NHS R&D and other research funders. However, the number of such Fellowships has been found to be considerably lower than had been thought. The MRC funds approximately 150, including basic laboratory science; CRUK currently funds approximately 100 and the NHS R&D currently funds ten. To compensate for this shortfall, a further 50 applied Fellowships per year may be needed to support the Walport Academic Clinical Fellows. **The Review recommends consideration should be given in the Comprehensive Spending Review to funding additional applied clinical fellowships.**

Clinician Scientist Awards

6.11 A further central component of the recommendations of the Walport report is the provision of competitively-awarded Clinician Scientist Awards for the post-doctoral training of Clinical Lecturers. The DH funding for Clinician Scientist Awards is the responsibility of the MPET Budget, and historically this budget has supported these posts. However, more recently these posts have been funded by the DH R&D Budget without any budget transfer from MPET. The Review believes there is merit in transferring this funding from MPET to the DH R&D budget where it will be ring-fenced to support these posts. **The Review recommends that the £8 million of MPET funding should be transferred to the DH R&D budget where it will be ring-fenced to support the Clinician Scientist awards that are essential to the success of the Walport recommendations.**

Capital for NHS research

6.12 Health services research has long been constrained by limits to the NHS research infrastructure, contributing to the widespread feeling in the NHS that research is a secondary activity. While there has been sustained investment in the research infrastructure needed for academia to drive forward basic science, this has not been matched in the infrastructure in the NHS to translate scientific discoveries into better services for patients.

⁵ The funding for the research training element through MPET is 25 per cent of the salary cost for Academic Clinical Fellows and 50 per cent for Clinical Lecturers. This comes to £20.5 million per year. The total salary cost through MPET (i.e. for both the 25 per cent research training element and the 75 per cent clinical training element) comes to £58.4 million. We believe it is essential to transfer the 25 per cent which funds the research training. However, since it is not possible to deliver the research training if the funding for the clinical training is removed, we recommend that the entire salary cost for the Academic Clinical Fellows and Clinical Lecturers is transferred from the MPET Budget to the R&D Budget – i.e. £58.4 million.

⁶ *Medically- and dentally-qualified academic staff: recommendations for training the researchers and educators of the future*, Report of the Academic Careers Sub-Committee of Modernising Medical careers and the UKCRC, March 2005

6.13 Between 2002 and 2005, the Department of Health invested £26million from the NHS R&D revenue budget to develop the research infrastructure in the NHS to support new medical schools. This addressed serious deficiencies that would otherwise have prevented the new medical schools playing a role in the nation's health research. But there is much more to do. In recognition of the need for infrastructural development, for the first time in 2006–07 a capital allocation of £50 million was agreed as part of the Department of Health's R&D programme budget.

6.14 In implementing BRfBH, prospective biomedical research centres were invited to bid for capital to develop as world-class research centres. The DH R&D Directorate has told the Review that robust and compelling proposals for over £60 million in 2006–07 have been received, and also that other research infrastructure is needed in the NHS fully to realise the aims of the new strategy and ensure the service plays its role in delivering the nation's health research. **We therefore recommend that the Comprehensive Spending Review examine the case for a sustained capital budget for DH R&D.**

A MORE POSITIVE APPROACH TO INNOVATION

6.15 The consultation process identified the NHS's 'conservative' approach to innovation as a barrier to uptake of new technologies and ideas. A number of reasons were cited as being at the root cause of this, including:

- a tendency by managers to see innovation primarily as a cost pressure, without looking to the full potential for efficiency gains;
- impediments to change, such as additional costs and professional reluctance to adopt new practices;
- the way R&D has been driven in the NHS, as 'push' from above or from inventors of a new product or process, rather than 'pull' from clinical need;
- gaps in clinicians' awareness of innovations or alternatives to current practice, either because
 - i) information about them is in a form that is not easily understood; or
 - ii) implementation requires specialist knowledge which can only be gained through direct contact with others who have implemented the innovation⁷.
- the incentives for research to achieve an impact on health and health needs are not as strong as those to achieve academic excellence; and
- the thoroughness, and therefore relative slowness, of systematic reviews, which are required to implement evidence-based medicine in the NHS.

⁷ Source: Internal DH paper on diffusion of technologies (the Review would like to thank DH for sharing this with us). The literature on diffusion differentiates between the 'hardware' and 'software' aspects of new technology. The former is the physical object that embodies the technology, whereas the latter is the information needed to use it effectively. It is this 'software' knowledge which cannot effectively be broadcast from a central source, and so requires contact with experienced users. This might explain, at least in part, the important role attached to 'thought leaders' by pharmaceutical companies, given that they are both trusted by their peers and in a position to share information gained from experience with a particular drug.

6.16 It is important to distinguish between genuine issues of unjustified conservatism on the one hand, and, on the other, the NHS's need to implement evidence-based medicine. Further, as resources are finite, there is a need to control the use of, and access to new technologies based on relative clinical- and cost-effectiveness. Many of the suggestions outlined below are crucial aspects of changing the NHS's culture where there may be undue conservatism and where that culture has, in part, developed as a result of unintended (dis)incentives

6.17 The Review has concluded that there appears to be a problem in the implementation related to the unsystematic way in which new technologies and interventions appear to be introduced into the NHS. This might contribute to the creation of a culture that is conservative even with regard to the use of clinically- and cost-effective new technologies, ideas and processes. This approach to introducing new technologies and interventions can make assessment of their efficacy and cost-effectiveness problematic, preventing their systematic adoption. Addressing this will be vital to delivering the vision of the NHS set out in the Wanless 'fully-engaged scenario'⁸: an NHS which is both as cost-effective and as efficient as possible, with an integral part of that being the rapid uptake of cost-effective new technologies. **We recommend a more systematic approach to the adoption of new technologies and ideas should be developed, to apply across the whole of the NHS, based on clearly mapped-out processes. We recommend that this should be taken forward by a project team bringing together the Department of Health, the National Institute for Innovation and Improvement / the National Innovation Centre, NICE and NHS clinician and commissioner representatives⁹.**

6.18 Other approaches that might help create an NHS culture that is more positive about innovation include:

- extending still further the involvement of doctors and other clinical staff in change processes in the NHS, at national, regional and local level. This should maximise the engagement of those most likely to be affected by change but also most likely to have ideas about how processes might best be changed. Success should be recognised, for example through bonuses or prizes, but also through opportunities to share knowledge developed in this way with other NHS institutions. New methods of engaging with clinicians could be piloted, perhaps using a small amount of seedcorn central money through an organisation like the National Institute for Innovation and Improvement (NIII);
- centres based around hospitals and their partner universities which better 'combine' the work of researchers and users of research, based on greater R&D 'pull' from users, i.e. giving them a much greater say in setting the R&D agenda, based on health needs. The Weatherall Institute of Molecular Medicine¹⁰ at Oxford University is a good example of this (see Chapter 7 for more details);
- better training for NHS managers and clinical staff to improve understanding of the benefits of research and how it can be used to drive clinical and cost improvements in service performance. An example of how this might be done can be seen in

⁸ See footnote 3

⁹ Chapter 8 builds on this idea in relation to the development and introduction into practice of new drugs, devices and diagnostics.

¹⁰ <http://www.imm.ox.ac.uk>

Canada, where the Canadian Health Services Research Foundation (CHSRF) has created a training programme which gives health system managers the skills to make better use of research findings in service delivery;¹¹

- more widely, there is a need to ensure better links between clinical researchers, both medical and non-medical, and clinicians, nurses and AHPs who are not active researchers, as well as commissioning managers, in order to ensure better uptake of findings from research. This could involve institutional changes, such as linking clinical networks more closely with research networks, but clearly also involves cultural change, particularly breaking down barriers between ‘researchers’ and practitioners’, as DH R&D are already aiming to do. Evidence-based medicine should be an integral part of everyone’s role: whilst for some, this might mean carrying out research, for others it might mean identifying and encouraging patients to take part in clinical trials or ensuring that they implement research findings in their everyday practice. This cultural change needs to be supported in the training, performance assessment and reward systems for NHS staff on both the management and clinical side, and for NHS organisations (e.g. through Healthcare Commission ratings); and
- training for researchers in entrepreneurship. One respondent cited the Medici collaboration in the Midlands¹² as a good example of this.

6.19 Together with the changes to incentives outlined below, these reforms begin to create the conditions in which research is no longer seen as an ‘extra’ part of what the NHS does, but an integral part of service delivery. This will help to make the NHS a more effective partner in the translation of health research into patient and wider economic benefit.

WORKING MORE EFFECTIVELY WITH PARTNERS

6.20 The Research for Patient Benefit Working Party (RFPBWP)¹³ identified incentives as a key issue in trying to encourage the development of an NHS which is more open to R&D and innovation. The changes needed to current incentives fall into two categories: the removal of current disincentives; and the development of new, positive incentives to create such a culture.

6.21 Looking first at the removal of disincentives, it is clear from the consultation that major concerns remain about processes, including ethical, safety and governance processes. These need improvement and rationalisation (a good example being the need to replace multiple criminal records checks for the same researcher with one check that is shared across organisations) involving a higher level of expertise, shorter turnaround times and a single approvals process for all NHS Trusts.

Working with industry

6.22 DH and the UKCRC have made good progress in tackling some of the ‘disincentive issues’, or ‘blocks in the system’, which delay research in the NHS, as can be seen in the UKCRC’s recently-published *Two Year Progress Report*. Amongst other things, this sets out progress in tackling incentives identified by the RFPBWP, for example including:

¹¹ For more details, see www.chsrf.ca/extra/overview__e.php

¹² For more details, see <http://www.midlandsmedici.org>

¹³ The RFPBWP was a multi-stakeholder group established following the BIGT ‘Biosciences 2015’ and AMS ‘Strengthening Clinical Research’ reports, to consider how best to implement their recommendations. The creation of the UK Clinical Research Collaboration (UKCRC) was one outcome.

- the creation of a suite of model agreements between research funders and NHS organisations, to reduce bureaucracy and facilitate faster initiation of research projects;
- plans to roll-out a ‘Research Passport’ for honorary contracts across the NHS, so that a researcher does not need multiple honorary contracts, as demonstrated in a successful pilot in Manchester; and
- streamlining the research ethics system.¹⁴

6.23 These developments are extremely welcome, and the momentum and commitment shown by the UKCRC partners so far need to be maintained.

6.24 In addition to the issue of bureaucracy, several pharmaceutical companies have also raised concerns about the cost of conducting clinical trials in the UK, and in particular concerns about the variability of costs charged by different Trusts and universities. This variation, they argue, cannot be justified by varying costs to the Trusts, and leads to the NHS losing clinical trials to rival centres abroad. They argue for a standard costing framework to apply across the whole of the NHS to overcome this issue, which the Review understands is already under development.

6.25 Given the complexity of the issues involved, the Review has not been able to carry out an economic analysis of the costs and benefits of attracting clinical trials to the UK. There is a general lack of rigorous analysis of costs and benefits in this area. However, given the potential health benefits for participants in clinical trials, and the potential economic benefits, it would seem a missed opportunity if the NHS were to run fewer trials than it is capable of because of issues such as variability in charging.

6.26 While progress has been made in tackling the bureaucracy surrounding clinical trials, we believe that it is also crucial to tackle these cost issues, including what appear to be some difficulties around the introduction of Full Economic Costing in the NHS and university sectors. We therefore welcome efforts to develop a standard costing framework for such trials that are carried out in the NHS, and would urge the adoption of such a framework across the UK as soon as possible.

Working more effectively with universities

6.27 Barriers to successful research activity can also arise where there are weaknesses in working relationships between NHS Trusts and their partner universities. While the Review found many examples where NHS Trusts work well or extremely well with their partner universities (see Box 6.1 for one example, in Manchester), in many cases more effort could be made to overcome the bureaucratic hurdles that can impede effective joint working.

6.28 There is no recommended relationship model to which an NHS Trust and its partner university should work. In some cases, existing structures could be made to work better. In others, universities and Trusts might follow the US Academic Medical Centre model, as Imperial College and St. Mary’s and Hammersmith NHS Trusts are doing with their plan to create the UK’s first Academic Health Sciences Centre¹⁵. This proposal, which promises to deliver greater integration of not only research strategies, but vital underpinning human resources and capital assets, should make for a more effective approach to health research and patient care at these institutions.

¹⁴ UKCRC, *2 Year Progress Report*, October 2006, <http://www.ukcrc.org/PDF/UKCRC&percent;20PR&percent;202004–2006.pdf>

¹⁵ See <http://www1.imperial.ac.uk/medicine/news/ahsc/>

6.29 NHS organisations and Universities should also work together more effectively in their appraisal of jointly-appointed clinical academic staff. Presently, this tends to be a dual, rather than a single process: this is unnecessarily resource intensive, given that it involves unnecessary bureaucracy and that a clinical academic's work cannot be neatly divided between 'clinical', 'education' and 'research' duties. **We recommend the UKCRC should develop a 'model framework' for partnership working, to improve university-NHS collaboration.**

6.30 Current VAT rules mean that the construction of new research facilities, which are often funded by charities, can only benefit from VAT zero-rating if use other than for a 'relevant charitable purpose' is not more than 10 per cent of the total use. In this instance, use for a relevant charitable purpose is 'use by a charity otherwise than in the course or furtherance of its business'. This has the potential to limit the scope for collaboration with industry on commercially undertaken research, which is crucial to the translation agenda. EU rules governing the application of VAT reliefs mean that, whilst the UK can maintain the existing zero rate for new charity buildings, an extension of this VAT relief is not possible, for example to cover the construction of all research premises, regardless of for what purpose and by whom the premises are used. **It is therefore important that an alternative means of addressing this issue is found.** Tackling this issue will play an important role in supporting greater collaboration between universities, the NHS and industry, and therefore furthering the translation agenda.

POSITIVE INCENTIVES FOR THE NHS TO UNDERTAKE RESEARCH

6.31 Incentives for NHS institutions to undertake research can take a number of forms:

- financial, ranging from central payments to payments from the beneficiaries of research (e.g. other NHS institutions);
- targets, ranging from those set and monitored by central government to those agreed and monitored locally; and
- recognition as part of performance assessment, especially that carried out by the Healthcare Commission¹⁶ (HCC) in England and the alternative performance assessment systems used in Scotland¹⁷, Wales¹⁸ and Northern Ireland¹⁹ (see below).

6.32 The RFPBWP made a series of recommendations to positively incentivise R&D in the NHS. Work on this has been taken forward under the auspices of the UKCRC, and progress is outlined in its *Two Year Progress Report*²⁰.

¹⁶ For more information on the Healthcare Commission's assessment process, see their website, www.healthcarecommission.org.uk

¹⁷ NHS Quality Improvement Scotland, www.nhshealthquality.org

¹⁸ Healthcare Inspectorate Wales, www.hiw.org.uk (although some responsibilities remain with the HCC)

¹⁹ HPSS Regulation and Quality Improvement Authority, www.rqia.org.uk

²⁰ UKCRC, *Ibid.*, pgs 26–28

Box 6.1 The Greater Manchester Research Alliance

There is a long tradition of partnership working in Greater Manchester. Three years ago there was a growing recognition that collaboration needed to increase if the conurbation was to respond effectively to pressure to deliver better quality and value research in the NHS. The Pharmaceutical Industry's Competitiveness Task Force Report and the new EU governance requirements also contributed to this thinking.

Following a consultation exercise, all 25 Greater Manchester NHS Trusts, its then Strategic Health Authority and The University of Manchester came together into a formal Greater Manchester Research Alliance supported by those Trusts at Chief Executive level. The central aim of the alliance is to encourage world-class research across the city region and to create synergies between the research endeavour and improvements in clinical care and the health of the population.

The success of the Alliance to date is built on two key foundations. The first has been the establishment, with strong SHA support, of a Strategy Board chaired by a research-committed Primary Care Trust Chief Executive, with NHS Trust management, research leaders, University, industry and Science City membership. The second has been the energy released by the formation of the new University of Manchester and its enthusiastic support of the Alliance. At operational level, close day-to-day working between Trust Research Managers, Research Directors and University Research leadership has been critical. The appointment in 2004, as Research Director, of a part-time senior clinical academic without allegiance to any one Trust has helped to maintain coherence and defuse potential conflicts of interest between organisations.

Successes since the Alliance's establishment in 2003 include:

1. More effective, light touch governance – the Greater Manchester Research Passport.
2. Considerable movement both towards stronger and new collaborations across and between research areas and between them and NHS service.
3. Better co-ordinated and successful bids for external funding (e.g. success in all rounds for establishment of UKCRC Local Research Networks).
4. Increased Chief Executive level involvement and interest from NHS and Universities alike.
5. Better understanding of the needs of strengthened collaborations with external stakeholders notably:
 - industry — underpinned by an innovative environment which benefits from strong University and NHS management of Intellectual Property and excellent facilities for incubation of commercial developments; and
 - city leaders — Manchester's nomination as one of the country's Science Cities has provided the opportunity for the Greater Manchester Research Alliance to work with Manchester Knowledge Capital/Science City to develop the Health Innovation element of the City Strategy. Support from the North West Development Agency and its Science Council has also been important

6.33 These measures will not, however, be sufficient to achieve the necessary changes on their own. The Review believes that further incentives would be helpful in supporting cultural change in the NHS, and in turn allow the NHS to undertake more R&D. In terms of new mechanisms, it might be possible, in theory, to match targets for service provision with new ones for R&D objectives, milestones and metrics. Targets have been effective in tackling some aspects of NHS performance (e.g. waiting lists). However, we are not convinced that targets would be a particularly effective mechanism for encouraging more R&D. Apart from question marks around their efficacy in all cases ('successful' targets were backed up by strong support from Central Government) and the desirability of such a centrally-driven system of managing R&D performance, it is not at all clear which aspects of R&D could be targeted. The Review has therefore rejected this approach.

The role of the Healthcare Commission 6.34 Nevertheless, the Review believes that the other two options, HCC performance assessment and financial incentives, could play a useful role in creating an NHS culture that is more supportive of R&D.

6.35 In terms of HCC assessment, we believe that this should be used to monitor and reward:

- research activity, ideally measured in quality-adjusted terms, rather than just based on, say, numbers of patients in clinical trials or research articles;
- research quality, measured not only by bibliometric analysis, but by real-world impact, e.g. which other organisations have taken up a new technology or technique as a result of a particular piece of research; and
- NHS organisations that create products and ideas that are commercially exploited or used elsewhere in the NHS.

6.36 The Review understands that there have been ongoing discussions between the UKCRC and the Healthcare Commission regarding the inclusion of R&D indicators in their assessment. In order to improve R&D performance in the NHS, **the Review recommends research should be regarded and treated as a priority, given its role in underpinning service delivery performance. We therefore urge the use of these indicators either in the HCC's performance assessment system, or in a mechanism with a similar level of influence on NHS performance, as soon as practicable.**

Financial Incentives 6.37 In the absence of HCC indicators to support R&D, financial incentives take on an even greater level of importance. The financial aspects of research are crucial. Changes to the NHS, including the introduction of Payment by Results (PbR) and Practice-Based Commissioning (PBC), the creation of Foundation Trusts that need to be run on ever more business-like lines, and the greater use of private contractors, such as Independent Sector Treatment Centres, as well as the large numbers of existing independent contractors working in the NHS (including a large proportion of GPs), mean that it is more crucial than ever that funding covers the full costs of research, and that research activity does not rely on cross-subsidy from elsewhere.

6.38 Currently, the costs of non-commercial research in the NHS are divided into three categories:

- the direct costs of carrying out research, e.g. researchers' salaries – these are paid by the research funder, e.g. the MRC or a charity like the Wellcome Trust;
- the indirect costs of research, including NHS infrastructure costs – these are met from the NHS R&D budget; and

- the costs of treatment of patients taking part in research – these are usually covered by Primary Care Trusts (PCTs) on the basis that the vast majority of costs would have arisen even if a patient were not taking part in a research project.

‘Excess costs’ 6.39 The issue of the costs of treatment in research projects arose in a number of responses to the Review, with some submissions arguing that, in certain circumstances, this can create significant difficulties in funding research, where the costs of treatment of a patient taking part in a clinical trial or other research project exceed those that would occur for an existing treatment, so-called ‘excess costs’. These may fall outside the scope of the PbR National Tariff, and so, unless PCTs voluntarily agree to pay for these ‘excess costs’, hospital Trusts will not be reimbursed for them. This creates two potential challenges:

- in practice, PCTs often fund the excess costs of research, on the basis that the research may not only benefit the particular patient involved, but may lead to improvements in the quality and / or reduction in the costs of treatment for all their patients in the longer-term. But PCTs are under increasing financial pressure, and, combined (in England) with the increased transparency of NHS costs under PbR and PBC, this may lead to fewer PCTs being willing to fund such excess costs; and
- given the concentration of NHS research activity, in England in particular, these financial issues may particularly affect PCTs in certain regions. But the PCT funding formula does not take account of this extra burden, creating financial disadvantages for some PCTs.

6.40 These issues have, until now, been relatively obscure amongst the NHS’s financial flows. But the increasing transparency means that they now need to be addressed, and positive incentives for R&D created, if the NHS is not only to remain a place where excellent research is undertaken, but the aims of BRfBH in England are to be met. **The Review recommends that a working group, involving DH’s policy leads for PbR and PCT allocations alongside DH R&D and representatives from across the NHS, is set up to investigate:**

- what reimbursement for excess R&D costs is needed and how best this should be implemented. One option to be explored is whether adjustments to national funding systems offer an appropriate solution, without undermining wider goals, or whether this would be better done with targeted R&D support. Whatever mechanism is used, this would clearly require careful moderating to ensure that the costs involved are genuinely R&D-related, and are not associated with inefficiencies or other cost problems facing particular Trusts;
- whether existing funding mechanisms are adequate to ensure that PCTs are not disadvantaged financially by having a research-intensive hospital in their area. If not, the working group should investigate whether this would best be rectified by adjustments to national formulae or by a more targeted R&D-specific intervention; and
- that financial constraints arising from funding systems do not create undue difficulties for hospital Trusts or other NHS employees, contractors and organisations (including GPs, dentists, allied health professionals, and ISTCs) which have previously carried out little research but would like to carry out more.

Support for research from NHS patient care funding 6.41 While the main source of funding to support the costs of research in the NHS is provided by NHS R&D funding allocations to NHS providers, local arrangements in the NHS also provide funding from other NHS sources to support research, in particular, people doing research employed by both the NHS and universities. It is estimated that this could amount to about £90 million per annum. This money is currently included in the patient care budget and not the DH R&D budget. With the introduction of Payment by Results this funding is being placed under intense pressure and, as a consequence, high-quality clinical research is at risk and individuals have been placed under threat of redundancy. **The Review recommends that DH conduct an exercise to identify the NHS patient care funding that is currently used to support research, and transfer it to the ring-fenced DH R&D budget.**

Incentives for GPs 6.42 In terms of incentives for GPs, there are flexibilities within the contract (such as developing an Enhanced Service) that offer the opportunity to directly influence and provide financial rewards for GPs who are research active, either in terms of participating directly in health research or in helping to recruit patients to clinical trials. Clearly, incentives here would need to be drawn very carefully, for example it is important that such incentives are not seen in terms of GPs being paid to recruit patients to trials, which would be perceived as a conflict of interest. Rather, a framework might be drawn up which rewards GPs who are ‘research active’, with the definition being carefully designed to avoid such conflicts, and being based upon a set of measures rather than single targets.

Building on Best Research for Best Health 6.43 The implementation of the strategy set out in BRfBH is a very welcome development, which will make a huge difference to research in the NHS, particularly in terms of ensuring quality and excellence. But further work to build on these reforms is needed if the NHS as a whole, rather than only the major centres which will develop under BRfBH, is to be an organisation which is much more open to both carrying out and implementing the findings of research.

6.44 Under the reforms, funding for the major biomedical centres which will become ‘Centres of Excellence’ in translational medicine will be awarded every five years. This will sustain a cadre of world-class health research centres in the UK, against a backdrop where the costs of clinical research necessitate concentration of resources in key centres. However, there needs to be scope for other centres to develop, in order to provide a challenge to the established centres in the quinquennial funding competitions, and thus help to drive excellence in the system. There is a case for further funding to support more centres that may be capable of challenging for the award of Centre of Excellence status. Equally, funding might be set aside, to be awarded on a fully-competitive, peer-reviewed basis, in order to support high quality research to flourish in smaller centres. This will be particularly important in areas such as health services and public health research, which are less dependent on access to specialist infrastructure. **We recommend that the Comprehensive Spending Review considers the case for money to be allocated to new NIHR programmes in this area.**

6.45 The introduction in BRfBH of an element of funding for investigator-led research is a welcome development, providing an opportunity for NHS organisations which have supported the establishment of research teams in particular areas to continue to do so, even when the main calls for research shift to other areas, driven by changing priorities. Such assurance of long-term opportunities is an important incentive for NHS organisations to consider it worthwhile to support the establishment of such teams. Some respondents to the consultation suggested that the level of investigator-led funding should be increased. **We recommend that this matter is kept under review.**

INCENTIVES FOR THE NHS TO SPREAD BEST PRACTICE

6.46 Whilst it is clear that parts of the NHS are at the cutting edge of ideas in implementing new ways of working, the consultation process highlighted that the NHS as a whole can be characterised in terms of ‘islands of excellence’ in implementing best practice, surrounded by a ‘sea’ of moderate to poorer performers in this area. Some potential underlying reasons for this were set out above.

6.47 In recent years, the NHS Modernisation Agency has taken the lead in trying to spread best practice in health service management and delivery around the NHS. This role has now been taken over by the National Institute for Innovation & Improvement (NIII). Despite significant progress in some Trusts and in some areas of practice, the lack of widespread progress has led some commentators to conclude that it is not possible to drive such changes from the Centre. Instead, they argue that there is a need to change the incentives applying to hospital Trusts and PCTs in order to really have an impact in driving take-up of best practice.

6.48 It has been suggested that these incentives could take two broad forms: incentives to take-up cost-effective new ideas and technologies; and incentives to promote take-up by other institutions of ideas, techniques and technologies that an institution has developed.

6.49 While the Review does not believe that the evidence supports the replacement of a centrally-led approach with an entirely incentives-led one, it would seem sensible to consider the case for additional incentives for NHS researchers and organisations to engage in peer-led dissemination of best practice. It is open to the NIII to employ leading exponents of new working practices and techniques to help spread best practice. However, the Review believes it is also important to allow researchers the opportunity to combine such dissemination activities with continuing their ‘day-job’, especially given that the dissemination task is likely to be a short-term one.

6.50 The Review has considered the case for funding or rewarding researchers to play a key role in dissemination. Here, for example, BRfBH is adopting a similar approach to that taken by ZonMW in the Netherlands, which builds dissemination of research findings into its programme grants and provides additional administrative and expert support for that dissemination²¹. Whilst the Review was not able to find conclusive evidence supporting any particular incentive system, it would seem sensible for a range of approaches to be piloted, if resources allow, such as:

- the approach adopted by ZonMW;
- providing funding to researchers’ employers to free up some of their time to disseminate research findings (e.g. by buying consultants’ clinical sessions, as happens under BRfBH for clinical sessions to carry out research);
- directly rewarding researchers for successful dissemination of research findings, e.g. through clinical excellence awards²²; and
- rewarding NHS organisations which allow their researchers time to disseminate research findings. This might involve buying out clinicians’ time, payments from a

²¹ For more details, see Ravensbergen, J and Lomas, J, *Creating a culture of research implementation: ZonMW in the Netherlands*, Global Forum Update on Research for Health. WHO, 2005:64–66. There is clearly also a strong argument for adopting this approach for much of the research funded by MRC – the exception being perhaps the most ‘blue-skies’ elements of its portfolio.

²² We understand that there have been ongoing discussions between the UKCRC and the DH regarding the use of clinical excellence awards to reward excellent research carried out by NHS researchers. We would strongly support their use in this way.

fund set aside to reward NHS organisations (and / or their partner universities) for successful implementation in other locations of ideas they have developed, or other similar mechanisms (prizes, other forms of public recognition).

6.51 **We recommend the incentives outlined above should be piloted, as resources allow.**

IMPLEMENTING NEW IDEAS AND TECHNOLOGIES IN THE NHS

6.52 In addition to incentives to spread best practice ('push' incentives), the NHS needs support and possibly further incentives to implement new ideas and technologies in practice ('pull' incentives). One of the disincentives to implement new technologies and new ways of working is that, while in the longer-term they might be cost-saving, the short-term transition costs associated with implementation are often unfunded, making it difficult to implement change in the NHS where budgets are usually tight.

6.53 Another disincentive is that the benefits of changed ways of working sometimes accrue to a budget holder who is separate from the funder of the costs of the new technology / way of working. This was seen, for example, in the issue of delayed discharge from secondary care, where the costs of change fell to social services budgets, but the benefits fell to hospitals. As a result, extra financial incentives were given to holders of social services budgets to ensure that change happened. In England, the introduction of PbR and PBC should help here, as both costs and benefits should fall to PCTs and commissioning practices. But it will be important to ensure that mechanisms are found to resolve transition costs of implementing changes to practice.

6.54 The idea that funding needs to pay due regard to diffusion and adoption of new techniques and technologies was also a frequent comment in submissions to the Review. It was argued that a lack of funding to embed evidenced-based interventions into NHS practice had led to an imbalance between research and practice. Additionally, research results also need to be expressed in a clearer language to have impact, and the original investigators need closer links with others focussed on dissemination. It has been suggested that the role of 'research disseminator' should be developed as a specialist role, rather like the role of 'research translators' being piloted by MRC and King's College / Guy's & St. Thomas' hospital to deal with the 'first gap in translation'²³. **We suggest that this approach should be piloted by the NIHR to address implementation of research in areas of service delivery.**

MORE EFFECTIVE EXPLOITATION OF INTELLECTUAL PROPERTY DEVELOPED IN THE NHS

6.55 NHS Intellectual Property (IP) issues are increasingly debated, driven in part by initiatives such as the Healthcare Industries Task Force (HITF) and the establishment of nine regional NHS Innovation Hubs and now the National Innovation Centre (NIC). The primary role of the Hubs is to help turn ideas into reality and manage intellectual property emanating from activity within the NHS, with all NHS staff with potential intellectual property being encouraged to go, in the first instance, to their local Innovation Hub for advice. The NIC takes the overall lead for IP management

²³ This is discussed in more detail in Chapter 7, below.

for technology innovations emanating from the NHS. Its primary aim is to advise and support the NHS, industry and academics to accelerate the process by which technologies which can be applied to healthcare are successfully identified, developed and translated into use.

6.56 The launch of the NIC in September 2006 is a very welcome development. The skills and experience in IP that it offers should enable the NHS and the Innovation Hubs to build on early successes to address not only the need to more effectively exploit IP, as set out in the 2002 DH Framework and Guidance on the Management of Intellectual Property in the NHS, but also to respond to the finding of the 2002 Wanless Review that the NHS was slow to take up cost-effective new ideas and technologies.

6.57 A clear message emerging from the Cooksey Review consultation was that the NHS needs a clear path for funding the development of an idea through to implementation, in the case of the best ideas, around the whole of the NHS and not just in a few Trusts or PCTs. Many respondents believed the current development path is not straightforward, with successful development and translation into practice of an idea relying largely on serendipity. It is also unclear how the needs of the NHS locally and nationally for technological solutions to problems might best be articulated and addressed. There does not appear to be a process in place to ensure that such needs are tackled. However, it does appear that at least some of the NHS Innovation Hubs are having a substantive impact, generating non-commercial process innovations and hard Intellectual Property (IP). Given the difference of views that emerged during the consultation, a useful step might be for the NIC to map out how this process currently works in different areas of the country, and then to establish and communicate best practice. This might then provide a basis for a bid for renewed funding for the Innovation Hubs, which the Review understands is not guaranteed beyond March 2007, a position that clearly needs to be clarified as soon as possible.

6.58 In tackling this agenda, there may be lessons to learn from other technology transfer organisations, most notably Cancer Research Technology (CRT) and MRC Technology (MRCT), as well as the experience of the Wellcome Trust. Given that they have broadly complementary portfolios with little overlap, there is also an opportunity for NIC and the Innovation Hubs to work in a closer partnership with MRCT, whose expertise and experience, as a more established organisation, could be extremely helpful. Equally MRCT may be able to learn from the Hubs' greater experience with devices. We understand that there have been some exploratory discussions around formalising an arrangement along these lines in some form of partnership agreement, and would strongly support such a move. Additionally, the Review was also very impressed with the progress Scottish Health Innovations Ltd (SHIL) had made in exploiting IP developed in the Scottish NHS (see Box 6.2). As with MRCT, there may well be opportunities here for partnership or to learn from SHIL's experiences.

6.59 In improving the NHS's approach to IP management, it will also be necessary to resolve IP ownership issues, which in many cases remain unclear. In particular, it is often unclear whether ownership falls to the NHS or its employees. The most straightforward approach would be to adopt a shared ownership approach, along the lines of that used in universities. However, this may be complicated by the reality that much research in the NHS and universities is carried out across boundaries, e.g. by university employees in hospitals and vice-versa. It is, therefore, just as important that the NHS agrees an approach to IP with universities that addresses this issue. **Crucially, such arrangements must not add further barriers to the effective exploitation of IP. Given the**

potential for this to happen, it might be sensible for these issues to be worked through at a national level (e.g. through the UKCRC, under the arrangements for developing a framework for cooperation suggested above).

6.60 A final issue was with regard to what appears to be a dual, and somewhat conflicting, role of Innovation Hubs and the NIC, in that they not only provide routes into the NHS for products developed by SMEs, but also ensure proper and appropriate exploitation of IP developed in or by the NHS. Whilst there are clearly links to be made here, given, for example, that the two functions both involve the use of local R&D networks, it is unclear to the Review whether there is a conflict of interest or indeed whether hubs are staffed to fulfil both roles effectively.

PROCUREMENT AND INNOVATION

6.61 Most of the issues outlined above relate to local decision-making around R&D, innovation and take-up of new technologies and processes. It is clearly right that most decisions in this area (with the exception perhaps being for very high-cost technologies which have the potential to severely unbalance local budgets) are taken at a local level, consistent with the accountability for spending decisions and financial balance, which lies with PCTs and hospital Trusts (in England)²⁴.

6.62 It is also clear that, in order for NHS organisations to be properly accountable for their decisions, the strategic decision-making processes around the use of healthcare technologies and processes need to be clear and transparent, and related to national guidance (e.g. National Service Frameworks and NICE guidance) and priorities (e.g. as set out in PSA targets), where these exist (e.g. NICE guidance only covers a small proportion of NHS activity). The need for a more systematic approach to new ideas and technologies nationally has already been noted. Equally, it would seem sensible for local commissioners in PCTs, working with clinical staff (both from primary and secondary care) and healthcare providers, and supported by expertise from the DH Commercial Directorate and the NIII, to develop strategic plans to guide the procurement, and support for the introduction of new technologies and processes, based on assessments of clinical- and cost-effectiveness, local needs and priorities, and local budget constraints.

6.63 'Local strategic procurement strategies' along these lines would have a number of benefits, including:

- enabling the costs and benefits of various new technologies and processes to be weighed against each other and prioritised accordingly;
- providing a mechanism for planning the uptake of NICE and other central guidance, which was raised as an issue for some parts of the NHS in a recent Audit Commission report²⁵;

²⁴With health boards and hospital Trusts in Scotland and Northern Ireland, and local Health Boards and hospital Trusts in Wales.

²⁵ Audit Commission Report: managing the financial implications of NICE guidance. www.audit-commission.gov.uk.

Box 6.2 Scottish Health Innovations Limited

Scottish Health Innovations Limited (SHIL) was established in 2002 to support the development and commercialisation of innovations arising within the NHS in Scotland. With funding from the Scottish Executive's Chief Scientist Office, NHS Scotland, Scottish Enterprise, Highlands and Islands Enterprise, the Department of Trade and Industry and the European Regional Development Fund programme, SHIL seeks to identify and develop new technologies which can be exploited through partnerships with the private sector. In so doing SHIL seeks to:

- improve quality and value for money of patient care throughout NHS Scotland;
- increase the generation of income to the NHS;
- stimulate economic wealth in Scotland through the creation of new jobs and enterprises; and
- deliver new market opportunities for businesses interested in licensing NHS Scotland technologies.

SHIL provides high quality advice and assistance on market application and intellectual property (IP) protection to inventors and researchers throughout NHS Scotland. Not only does this help increase the level of awareness in innovation and IP, but it provides a point of contact for new inventors to bring forward their ideas. It is already quite noticeable how attitudes to commercialisation have changed within NHS Scotland since the company was established, as more and more staff begin to realise how important innovation is to the provision of better healthcare for patients and to a more effective Health Service. In addition, SHIL also ensures that good ideas that cannot be commercialised are shared so that efficiencies are achieved or costs saved.

The criteria used by SHIL to select projects for commercialisation are based on an assessment of their novelty and clinical usefulness, the commercial opportunity they offer, and the funding which will be needed for each product's development. Since its formation, SHIL has received over 400 disclosures of innovations from staff working in NHS Scotland, of which approximately one in ten have been taken forward for commercialisation.

By acting as an early risk investor, it is SHIL's intention to add as much value as possible to each innovation by providing managerial and funding support during their development prior to their licensing to commercial partners.

In most cases, it is the funding and development requirements for a product which will dictate at which stage SHIL will look to license it to a commercial partner. For example, where the funding requirement is high and/or the development programme lengthy and complex—as would be the case if regulatory studies were going to be required in the major markets such as the USA—SHIL will usually look to either secure a co-development agreement or to license the product, after the concept has been proven, to a company with a strong market presence in the field. Alternatively, if there were sufficient investor interest, a spin-out company might be created to take the project forward. Projects with a lower risk profile, simpler regulatory requirements and a national rather than international market prospect can be taken much further by SHIL. Whatever the decision, the aim is always to add as much value as possible to a product before offering it to other parties.

- providing a mechanism for explicitly considering not only the cost effect of new technologies (i.e. whether a new technology is more or less expensive than an existing one), but also the volume effect (enabling more people to be treated), which was identified by Derek Wanless as a key issue around the NHS's relatively slow uptake of cost-effective new technologies²⁶; and
- allowing local consultation on the procurement strategies, and therefore creating the potential for greater public and patient understanding of, and involvement in decisions which tend to provoke a great deal of public interest (for example, as seen in many cases where the use of new drugs has been restricted). Clearly, such local consultation will need to be as broadly-based as possible, in order to avoid the risk of capture by special interest groups.

6.64 **We therefore recommend that this approach should be piloted in several health economies across the UK to ascertain whether such an approach can help both provide a more strategic approach to procurement of new technologies and greater local accountability for procurement decisions.**

²⁶ *Securing our future health: Taking a long-term view, an interim report*, Derek Wanless, November 2001 — see http://www.hm-treasury.gov.uk/consultations_and_legislation/wanless/consult_wanless_interimrep.cfm.

7

More effective translation of research into health and economic benefits

Chapter overview

In this chapter, the Review makes recommendations to address the gaps in translation that the Review has identified: the first gap arises in the translation of basic and clinical research into ideas and products; the second gap relates to introducing those ideas and products into clinical practice.

The key recommendations outlined in this chapter are:

- OSCHR should establish a joint MRC / NIHR Translational Medicine Funding Board to take the lead in developing a translational research strategy which aims to increase translation into health and economic benefit. This Board will be responsible for allocation of both response mode and targeted calls for research relating to the translational research strategy, with joint MRC / NIHR sub-boards assessing research proposals based on peer review. The Board should also seek to address the skills gaps in the drug development pipeline. The Board will develop a system of matrices to monitor its own performance and demonstrate its impact on translational medicine.
- DTI and DH should carry out an analysis of the entire range of public / charity funding streams which are applicable to the translation of health research, to create a coherent picture of the support available and identify any gaps in that support. Information on publicly-funded support should be available, in an easily accessible format, to SMEs and individuals involved in innovation.
- The Small Business Research Initiative (SBRI), which is designed to increase the success of smaller businesses in obtaining contracts from government bodies, clearly has the potential to benefit both the government and SMEs. The Review recommends that the Chair of OSCHR, together with the Director-General of DH R&D, and the CEO of the MRC and DH Commercial Directorate set up a working group to develop a strategy and implementation plan for the SBRI that crosses the MRC / DH boundary.
- OSCHR should set targets for the MRC and NIHR to allocate an increasing proportion of funding, over time, to research that involves working across disciplinary boundaries, or takes place in institutions that have demonstrably implemented strategies to adopt a model of partnership between basic and clinical scientists.
- Since 1993, the NHS Health Technology Assessment (HTA) programme has been very successful in its role of Knowledge Production, by providing NHS decision-makers with a high quality evidence base, in meeting needs created by 'R&D market failure' and for its innovation and flexibility. The Review finds that a substantial proportion of the escalating information needs of the NHS could be met by expanding the HTA programme to enable delivery of large improvements in the quality and efficiency of healthcare in the NHS.

INTRODUCTION

7.1 As has been clear throughout this report, the consultation for the Cooksey Review has pointed to a widely-shared belief and consensus that the UK is a world leader in basic research, but the UK is not as successful as it could be at taking the results of that research along the pathway to new innovations, products or health care practices. Having looked at the high-level institutional reforms needed to build a more coherent approach to government-funded health research, and then considered changes to incentives and culture in the NHS, this chapter considers the wider factors which impact on the UK's ability to more effectively translate health research into practice.

7.2 We have identified two gaps in translation:

- the first gap arises in the translation of basic and clinical research into ideas and products; and
- the second relates to introducing those ideas and products into clinical practice.

THE FIRST GAP IN TRANSLATION

7.3 The first gap in translation relates to the process of taking ideas developed either by basic scientists working in the laboratory or by clinician-scientists working in a clinical environment, or, increasingly, by a mix of the two, and developing them into products that can either be commercialised or in some other way disseminated into wider healthcare practice. The key issues raised during the consultation process for the Review here include:

at a national level:

- achieving more effective strategic coordination of efforts to translate health research to a stage where it can be commercialised and / or generate health benefits for patients;
- ensuring that the skills base needed to ensure that health research in the UK continues to be world-class, and that we have the skills to translate it into greater health and economic benefits;
- the availability of capital for SMEs in the healthcare sciences sector that are looking to commercialise ideas developed in healthcare research, especially in the biotech sector; and
- whether research procurement can be used more effectively as a tool for driving translation by the private sector, and particularly by SMEs.

at the level of individual Higher Education Institutions and NHS Trusts:

- making translation happen in practice. How to link the direction of basic research to health priorities and needs more effectively;
- strengthening Knowledge and Technology Transfer in Higher Education Institutions (HEIs);
- building more effective links between research, entrepreneurs and sources of finance.

Sources of support for translation – achieving greater strategic coherence

7.4 Whilst most of the submissions to the Review recognised the need to increase the level of translation of health research, the importance of partnership with industry and the need for multidisciplinary environments in this process, the majority did not go into detail as to how such improvements could best be achieved or identify what was needed to create the right environment. Several suggested that there should be a clear strategy to support translation, whilst others suggested that there should be dedicated funding streams to support applied or translational research. Some sought the establishment of a separate Translational Medicines Strategy Board, along the lines of DTI's Technology Strategy Board.

7.5 There appears to be a consensus that there needs to be more support to get research to the state where it is implementation-ready. In other words, there is a need to ensure that a clear and straightforward pipeline for translation of health research exists in the UK, that the funding and skills base needed are available, and that information and advice is easily obtainable. We agree that there is a need for a more coherent approach to translating health research into concrete health and economic benefits. Such a strategy would have two aspects.

7.6 First, there is a need for a more coordinated approach between the MRC, the NIHR and its equivalents in the Devolved Administrations with regard to translational research, involving the health charities and industry in developing a strategy for translation and partnerships to tackle particular issues. **The Review recommends that OSCHR should establish a joint MRC/NIHR Translational Medicine Funding Board** as set out in Box 7.1 to address these challenges.

7.7 Second, there needs to be a clearer picture as to the support available to translate the results of research and take ideas through to commercialisation. Much of this support is concentrated in DTI schemes, but there are also other important funders, such as the Wellcome Trust.

7.8 Indeed, while widely accepted as a reality, the gaps in support for effective translation have not yet been systematically mapped out. A separate paper highlights areas of public funding which relate to the translation of research across a wider range of organisations¹. While this should provide a flavour of the variety and complexity of the funding available, more work needs to be done to accurately map out the entire landscape of funding available for the translation of health research and product development, and to clearly identify where gaps exist.

¹ Available on www.hm-treasury.gov.uk/independent__reviews

Box 7.1: The Translational Medicine Funding Board (TMFB)

The **Chair** of the TMFB should be someone with knowledge and experience in translating research into health and economic benefits – perhaps with a combined academic / pharma industry background.

Members should include the MRC, NIHR, the healthcare industries, DTI, DH, HEFCE, clinical and basic researchers, the healthcare charities, the NHS, and the DAs. OSCHR should have an observer seat on the Board. Clearly, the size of the Board should be limited to ensure its effectiveness, ideally to no more than 12 members.

Budget: Allocated funding from both MRC/NIHR as agreed with OSCHR and set out in the Joint Health Research Strategy.

Reporting /Accountability: It will report jointly to MRC and NIHR as they have accountability for budgets used, but in addition will submit a half-yearly progress report to OSCHR.

Functions: The Board should:

1. Take the lead in developing a translational research strategy which aims to increase translation into health and economic benefit, including:
 - commercialisation of the outcomes of research funded by MRC / NIHR;
 - developing a skills strategy to facilitate more effective translation, e.g. building on the MRC/Kings pilot to create research translators;
 - considering new funding mechanisms to ensure that there is adequate funding across the translational pipeline, including follow-on and seed funding, and funding for development of prototypes;
 - working with industry and the medical charities in a variety of ways (e.g. public private partnerships, co-funding of projects) to meet needs such as: pre-competitive drug development tools (e.g. biomarkers) and technology development (e.g. using stem cells in predictive toxicology). It should also have specific responsibility for R&D to support the redesign of drug development proposal as set out in Chapter 8; and
 - feeding in priority areas for funding of clinical trials.
2. Oversee allocation of both response mode and targeted calls for research relating to the translational research strategy, with joint MRC / NIHR sub-boards assessing research proposals based on peer review. Given the expectation that there will be more good proposals than can be funded, good proposals will also need to be considered against wider criteria which will be developed by the Board and agreed with OSCHR. These criteria could include issues like: potential to meet unmet need, potential impact on health, and the importance to the NHS, but should not include criteria that could undermine selection on the grounds of excellence.

The Board should have a joint MRC/NIHR secretariat, which will be responsible for day-to-day administration of the Board's responsibilities. In the first instance, the head of the secretariat should come from the OSCHR team to help support changes to culture and working practices. The secretariat will have appropriate skills and experience to be able to assist applicants to build up proposals where they are deemed by the Board to be of interest but where they are lacking in specifics (following either a specific call for interest or in applications received under response mode calls).

The Board will be responsible for developing a system of matrices to monitor its own performance and demonstrate its impact on translational medicine.

7.9 The Review recommends that OSI and DH, with input from DTI, should carry out an analysis of the entire range of public / charity funding streams which are applicable to the translation of health research, to create a coherent picture of the support available and identify any gaps in that support. This should be conducted with the objectives of:

- **addressing any gaps;**
- **considering simplification of publicly-funded support (in line with current cross government efforts led by the DTI to consolidate funding streams); and**
- **ensuring information on the publicly-funded support is available in an easily accessible format to SMEs and individuals involved in innovation.**

7.10 It is, however, important to recognise that the need to translate research findings is not limited to health research, but is an issue for all areas of research. Care needs to be taken to ensure the mechanisms put in place to aid the translation of health research are compatible with, and build on other more general mechanisms currently available or being developed to aid translation more generally. Otherwise, there is a risk of adding further to the confusion that already surrounds the multiplicity of government schemes in this area.

Skills For Health and Medical Research

7.11 Many of the submissions to the Review consultation raised concerns about the lack of specialist skills in areas such as bioinformatics, clinical pharmacology, biostatistics, quantitative methods, knowledge transfer and entrepreneurship. Some suggested that not enough was being done to support research as a discipline within the allied health professions. In the case of nursing, for example, it was argued that nurses were not being given the opportunity to develop research and evaluation skills.

7.12 It is clear from the comments received, and from reviewing systems here in the UK and abroad, that the skills needed to ensure successful translation are unique and that the UK needs to build up the skills base in these areas.

7.13 In recent years, there have been a number of reviews and reports that have highlighted skills and careers issues related to research more widely. These include the Roberts Review², the BIGT Report³, two reports from the Academy of Medical Science⁴, and the ABPI report, Sustaining the Skills Pipeline⁵. The Leitch Review of Skills⁶ is also currently considering the wider skills profile which will be needed by 2020 if the UK is to maximise economic prosperity and productivity.

7.14 Some action has already been taken to address the particular skills issues facing health research. Most important of these has been the work on academic medical careers carried out by the joint Academic Careers Sub-Committee of Modernising Medical Careers and the UKCRC, and chaired by Dr. Mark Walport, which published its report in March 2005⁷. This described a flexible pathway through which junior doctors and dentists could combine research and education with a clinical career. The recommendations set out within that report are currently being implemented and progress is discussed in the UKCRC's Two Year Progress Report⁸. Another subcommittee chaired by Professor Janet Finch is undertaking a similar process aimed at developing clinical research career structures for nurses.

7.15 Evidently, a wide range of funders have a role in ensuring the UK has the right skills to translate health research into health and wealth benefits. This extends to ensuring that there are well-structured career paths for researchers and translators. However, given the wide range of interested parties, there is a risk of fragmentation in the UK's approach to skills for health research, and therefore a need to bring these different groups together to ensure a common strategy is developed and taken forward.

7.16 **The Review recommends that DFES, HEFCE, DH and OSI, together with their counterparts in the DAs where appropriate, establish a working group with a remit to develop a strategy to ensure that the UK has the right mix of skills, experience and career structures across the whole spectrum of health research, including ensuring more effective translation of research.** Membership of this working group should include representation from across DFES, HEFCE, DH, OSI, MRC/RCUK, NIHR, UUK, industry and healthcare charities. The strategy should complement initiatives already underway, such as the RCUK strategy and UKCRC's initiatives. The working group should be responsible for implementing the strategy and monitoring progress.

7.17 **The Review recommends that, in addition, given its specific remit to oversee translational medicine, the joint Translational Medicine Funding Board should seek to:**

- **work with the UKCRC to coordinate the development and funding of MD-PhDs in order to ensure that skills gaps are eliminated;**
- **work with the higher education sector and industry to pilot new qualifications to provide experience in research, e.g. Masters in Research (lessons here might be learned from the Karolinska Institute's licentiate degrees⁹); and**

² <http://www.hm-treasury.gov.uk/documents/enterprise—and—productivity/research—and—enterprise/ent—res—roberts.cfm>

³ <http://www.bioindustry.org/bigtreport/>

⁴ *Strengthening Clinical Research*, , and *The Freedom to Succeed: a review of non-clinical research fellows in the biomedical sciences*, <http://www.acmedsci.ac.uk/images/project/AcdMedSc.pdf>

⁵ <http://www.abpi.org.uk/publications/pdfs/2005-STEM-Ed-Skills-TF-Report.pdf>

⁶ <http://www.hm-treasury.gov.uk/independent—reviews/leitch—review/review—leitch—index.cfm>

⁷ <http://www.ukcrc.org/pdf/Medically—and—Dentally-qualified—Academic—Staff—Report.pdf>

⁸ <http://www.ukcrc.org/PDF/UKCRC&percent;20PR&percent;202004—2006.pdf>

⁹ More details are set out in Chapter 3, above.

- **identify skills gaps in the drug development pipeline and ensure that steps are taken to address these, considering the potential for matched private/public funding where appropriate.**

Access to Capital

7.18 Many small companies face difficulties attracting investment to develop and commercialise their products. Whilst larger pharmaceutical companies often buy smaller companies that are developing pharmaceutical products or other technologies, it is argued that this is leading to potentially-useful technologies being left undeveloped.

7.19 In recognition of the difficulties faced by small companies more generally in attracting the capital they need, the Government has developed a number of initiatives including:

- R&D tax credits, which are more generous for SMEs than for larger companies;
- the Enterprise Investment Scheme¹⁰, which helps certain types of small higher-risk unquoted trading companies to raise capital by providing a range of tax reliefs for individual investors in qualifying shares in these companies.
- Venture Capital Trusts¹¹, which are designed to encourage individuals to invest through collective schemes in a range of small higher-risk trading companies whose shares and securities are not listed on a recognised stock exchange; and
- the Enterprise Capital Fund (ECF) scheme, where the Government leverages venture capital (VC) with debt in funds managed by the private sector¹². This was specifically designed to fill an ‘equity gap’ for investments of up to £2 million.

7.20 However, the biotech sector has argued that, in practice, these initiatives, whilst welcome, have not fully addressed their difficulties in attracting capital. In particular, with regard to the ‘equity gap’, it is argued that there are significant differences between the biotech sector and many others:

- in most technology sectors, such as IT and communications technologies, an investment of up to £4 million will usually enable a company to develop a product and to introduce it to the market, thereby starting to generate cash. At this point start-up companies will be able to raise further capital; and
- biotech companies, on the other hand, cannot develop a positive cashflow until a product is cleared by the regulatory bodies. On average, this occurs after between 8 and 11 years of development work, with significantly higher levels of investment than is usually required in other sectors. This problem is magnified by the high risk of a negative outcome at any stage of the clinical trials process. This frequently precludes VC financing at the early stages. Similar difficulties appear to face SMEs in the medical devices and ‘traditional’ pharmaceutical sectors.

7.21 When comparisons are made between the US and UK VC markets, it appears that the relative underdevelopment of the UK VC market further contributes to the difficulties faced by small biotech firms in the UK in attracting investment – UK venture capitalists appear to be inclined to invest less and are more risk-averse than their US counterparts.

¹⁰ http://www.hmrc.gov.uk/eis/chapter1/eis-chapter1__1.htm

¹¹ <http://www.hmrc.gov.uk/guidance/vct.htm>

¹² <http://www.sbs.gov.uk>

7.22 Some have argued that this is evidence of a market failure that the Government should address, for example through public investment in the biotech sector. Whilst discussions during the Review have suggested the possibility of market failure, it has not been established clearly that a market failure exists, nor has it been shown that the economic benefits of government intervention would exceed its costs. In terms of market failure, for example, it may be that the market is, in fact, acting rationally in not investing in the sector, given that it is argued that returns do not match the risks of investment. Furthermore, in making any comparison with the US, it is important to understand the underlying dynamics of US VC investment in the biotech sector, where very high returns appear to be concentrated in a small number of investment firms, and where returns may also be effectively subsidised by high levels of public investment in clinical trials (in which the US NIH invests \$4.2 billion a year, including some Phase III trials). We have seen no evidence of the economic costs and benefits of such investment, although this may well generate health benefits through the development of new treatments.

7.23 At this stage, therefore, the Review has been unable to reach any conclusions as to the need for further support for small firms in this area. It will be important for the sector to work with the government, through the Capital for Enterprise Board, to develop an understanding of the extent of any market failure that may require expansion of current government provision for support in this area, and to establish whether the benefits of such intervention would exceed its costs.

Procurement from SMEs – the Small Business Research Initiative (SBRI)

7.24 Government procurement practice is also generally recognised to influence SMEs' ability to innovate. The Small Business Research Initiative (SBRI) was announced by the Government in 2000, and is designed to increase the success of smaller businesses in obtaining contracts from government bodies to conduct research and development. In particular, it aims to:

- provide opportunities to those existing small firms whose businesses are based upon providing R&D, by increasing the size of the market;
- encourage other smaller businesses to increase their R&D capabilities and capacity, to exploit new market opportunities; and
- create opportunities to start new technology-based or knowledge-based businesses.

7.25 The consultation process highlighted concerns that the SBRI had not been implemented effectively in the health area. A number of reasons have been cited for this, amongst which the most important seem to be that:

- it was unclear how the SBRI fitted with the R&D budgets of DH (NHS R&D and the Policy Research Programme) and the MRC; and
- as currently organised, DH has no locus to systematically identify procurement needs for technologically-related R&D, and carry these forward through commissioning and on to evaluation and uptake within health and social care services.

7.26 The SBRI clearly has the potential to benefit both the government and SMEs. On the one hand, government and the public sector have a range of significant and pressing needs for R&D that SMEs in the bioscience, healthcare, and other industries could address. On the other, SMEs often struggle to obtain R&D funding. A renewed health SBRI could help improve R&D procurement opportunities for SMEs that address the major health-related needs of government.

7.27 One of the main challenges would be to identify accurately and specify research needs. For example, DH is already flooded with commercial offers of technology solutions to healthcare associated infections, but many of these fail to address the real needs (e.g. for equipment that can be cleaned easily, quickly and effectively).

7.28 **The Review recommends that the Chair of OSCHR, together with the Director-General of DH R&D, the CEO of MRC and the DH Commercial Directorate, set up a working group to develop a strategy and implementation plan for the SBRI that crosses the DH / MRC boundary.**

MAKING TRANSLATION HAPPEN

7.29 Success in making translation happen in practice ultimately rests on individual organisations involved in research, whether they be NHS Trusts, universities, units run by the MRC or the medical charities. Aside from the issues relating to the NHS, respondents to the Review consultation raised four issues with regard to translation activities within and between institutions:

- the importance of linking research priorities to clinical needs and priorities in local settings (thereby matching the national priority setting for health research to be led by OSCHR);
- the vital role played by certain types of staff, again acting in local settings, in facilitating translation of research into practice;
- the need to develop the roles and skills of university Technology Transfer Offices (TTOs), learning from best practice both in the UK and abroad; and
- the potential to foster closer links locally between researchers and universities, entrepreneurs, and finance and legal firms.

Translation in Higher Education Institutes and the NHS

7.30 In Chapter 5, we set out proposals to change the way in which the strategic direction of health research is set in the UK, maintaining the key ‘bottom-up’ role of scientists in advising on where the science is going and on what is possible, but ensuring that this is balanced by ‘top-down’ input on the health, economic and science priorities of the nation as a whole. We believe that these changes at the national level should be matched by changes along similar lines at a local level if the Government’s ambition is to be realised in practice.

7.31 This is already happening in practice in some institutions, for example at the Weatherall Institute of Molecular Medicine (IMM) at Oxford example (see Box 7.2) and, as noted earlier, at Duke University. The partnership between basic and clinical scientists in these institutions and in others around the world provides a framework for practice that should be more widespread in the UK.

7.32 **The Review recommends that OSCHR should set targets for the MRC and NIHR to allocate an increasing proportion of funding, over time, to research that:**

- **involves working across disciplinary boundaries (e.g. basic and clinical research, or health research and engineering, etc.); or**
- **takes place in institutions that have demonstrably implemented strategies to adopt this model of research partnership.**

This could include, for example, joint strategies between Higher Education Institutes, NHS Trusts and MRC and charity-funded research units. These targets should be included in the performance management frameworks for MRC and NIHR.

Research 'Translators'

7.33 In delivering translation in practice, the importance of the interface between pre-clinical and clinical activities is well-recognised, and many pharmaceutical and biotechnology companies have 'research translators', whose role is to liaise between pre-clinical and clinical groups to facilitate development of ideas and therapies, through the phases of development to early proof-of concept studies in humans. As noted in Chapter 6, MRC and Guy's & St Thomas' are co-funding a pilot scheme where 'research translators' at King's will provide a bridge between pre-clinical and clinical sciences, facilitating communication and collaboration by acting as a point of contact between pre-clinical and clinical researchers. They will be responsible for identifying existing scientific opportunities suitable for exploitation, as well as identifying new areas for collaboration. The Review supports this initiative, and recommends it is expanded to other institutions if it proves successful.

Technology Transfer in Higher Education Institutes

7.34 Universities have a responsibility to ensure that knowledge is used for maximum economic and social impact. Technology Transfer is an important subset of knowledge transfer, but revenue generation for the academic institution should not be the only goal of knowledge transfer: in some cases, allowing free transfer of knowledge will have a greater benefit to the wider economy and society. Indeed the biomedical sciences has a greater focus than most other disciplines on the commercial exploitation of intellectual property. In many other fields, collaborative problem-solving or the movement of people between universities and business are more prominent parts of the knowledge transfer agenda.

7.35 University TTOs have been established by individual universities to facilitate the commercialisation of the knowledge they generate. They have been established in a variety of ways: some such as the University of Oxford's Isis Innovation Ltd, are wholly-owned subsidiaries of the University; whilst the Technology Transfer Office of Imperial College, London (Imperial Innovations Group plc) has recently been floated on the Alternative Investment Market of the London Stock Exchange. Other TTOs are partnering with companies that specialise in intellectual property commercialisation. The Review Team's visit to Sweden also suggested that there might be lessons for UK HEIs from the successes of the Karolinska Institute in Stockholm in attracting commercial investment into start-up companies founded on the basis of IP developed at the Institute. Karolinska Institutet Innovations AB has developed two specific funding vehicles, in order to support two different portfolios of such start-up companies. These funds have attracted significant external commercial capital by allowing investors to spread their investment risk across dozens of research discoveries and innovations, rather than having to take the significantly higher risks involved in investing in individual start-ups.

Box 7.2: Weatherall Institute of Molecular Medicine, Oxford

In the 1980s, molecular biology was still an emerging discipline, and the application of the methods of molecular and cell biology to clinical research posed problems that had not been encountered before. There were few centres where clinicians could be trained in direct application to the kind of problems that interested them, particularly in UK medical schools. The Institute of Molecular Medicine was established by Sir David Weatherall in the Clinical School of the University of Oxford in 1989 to foster research in the field of molecular and cell biology with direct application to the study of human disease. The Institute was developed as a partnership with the MRC and several medical charities.

What particularly marks out the IMM from other similar institutions is that its approach to research is driven by clinical problems, rather than the classic 'curiosity-led' approach followed elsewhere.

Within the Institute, there are thirty-six independent groups, all of which are attached to a clinical department within the University and are responsible for raising their own research funding. In addition, there is a core administrative service at the Institute to maintain a high quality environment. The groups remain in the building as long as their research is productive and attracting funding support. The research teams are independent and remain attached academically to their parental University clinical departments. In this way, the Institute has successfully encouraged close integration of basic and clinical scientists, generating a critical mass of scientific expertise and facilities that has attracted both non-clinical scientists and young clinicians who wished to train in this new field and tackle problems of particular interest, working across disciplines.

Notable successes from the Institute include:

- the discovery of the molecular basis of several monogenic diseases and different kinds of mental retardation;
- major progress towards an understanding of the inherited components of common diseases such as diabetes and rheumatoid arthritis and genetic factors that make individuals more or less susceptible to common infections such as malaria;
- progress towards an understanding of the function of the protein that is defective in children with cystic fibrosis;
- development and trials of vaccines for meningitis in children;
- trials of a new type of AIDS vaccine for developing countries; and
- identification of genes involved in controlling the life span of lymphocytes.

In addition, the Institute has several patents, and a number of start-up biotechnology companies have been started by Institute scientists, including Avidex, Oxagen and Oxxon Pharmaccines.

7.36 The Higher Education Business and Community Interaction Survey¹³ suggests that the UK higher education sector appears, in general, to be improving its KT performance. The survey shows that universities are achieving greater income generation and more substantial output, and that a larger number of staff are involved with interactions with industry, through collaborative research or consultancy activity. But the experience of the USA shows that building KT capability is a long term activity, and these efforts must continue if economic and societal value from publicly-funded research is to be realised.

7.37 Comments from consultation respondents on TTOs included:

- TTOs need to have a greater understanding of their customers' needs;
- the emphasis of TTOs should change, with a greater weight being put on getting treatments into use in healthcare, rather than on creating revenue. Over-valuation of Intellectual Property (IP) was seen as a major block to translation, not only in individual cases but even more so in cases where IP from different universities needed to be combined to create a commercially-viable proposition;
- there is too much competition between different university TTOs and a lack of mutual understanding and trust between universities and business; and
- lessons should be learned from the success of MRCT and Cancer Research Technology.

7.38 Some aspects of technology transfer and commercialisation are very specialised, and need inputs from a range of experts, such as lawyers, patent offices, as well as high level Technology Transfer skills. It may be unrealistic to expect all HEIs to generate sufficient Technology Transfer activity to support the establishment of a TTO with this range of expertise, suggesting that pooling or sharing of some specialist capacity should be a viable option to in-house capability. **The Review recommends that HEIs consider pooling resources for Technology Transfer and that the Government consider the case for giving such pooling activity further emphasis through existing mechanisms to support HEI knowledge transfer activities.**

7.39 As universities build their KT capacity, KT professionals need support to develop the appropriate skills and experience for their role. Some development training courses for KT are in place, such as training and CPD from AURIL, Praxis and others, the UNICO survey and Good Practice work supported by HEFCE. The emerging Institute for Knowledge Transfer (IKT) potentially adds the standards for professional training and development. As IKT involves most major bodies involved in KT it could also act as a forum where standards can be established between industry and Higher Education; it also potentially provides the basis for a more coherent and strategic framework for identifying and supporting KT activity in Higher Education.

7.40 Whilst it is evident that a single model for Technology Transfer Offices will not work across the whole of the HEI sector, **the Review recommends that HEFCE and OSI should review the current technology transfer activities across the HEI sector so that strengths and best practice can be identified and promulgated across the sector.**

7.41 In addition, support for KT professionals and academics needs to be taken forward in the context of holistic workforce development for HE (across academics and administration), including

¹³ www.hefce.ac.uk/pubs/hefce/2006/06—25/

support for strategic leadership in the third stream. One option that was suggested during the consultation process was for MRCT, Cancer Research Technology and other successful TTOs to also provide mentoring and training services.

7.42 It is clear from discussions during the Review consultation and from written responses received that both MRC Technology (MRCT) and Cancer Research Technology Limited (CRT) are highly regarded by both the research and business community. CRT is the commercialisation arm of Cancer Research UK. As discussed in Chapter 2, MRCT manages the commercial development of IP arising from basic research carried out in MRC's institutes, centres and units. There are several common themes that contribute to the success of these two organizations. They both have strong links with their scientists and staff who are knowledgeable in both the science and commercialisation. They both have facilities and resources to help drug development and can do this in a variety of ways. They both highlight the need to have dedicated staff with the right experience and skills, who know about the research and have the ability to communicate effectively with scientists, clinicians and those involved in commercialisation. They both consider the long-term benefits of developing products to improve health rather than generating the greatest short-term revenue.

Building links between researchers, entrepreneurs and finance

7.43 It is clear from the comments received in the Review consultation process and from reviewing systems here in the UK and abroad that the skills needed to ensure successful translation are highly specialised, and that the UK needs to build up the skills base in these areas. This relates to a wider requirement to ensure that the UK has the right skills to meet the needs of a knowledge-based economy. The process highlighted examples of best practice both in the UK and abroad that could be used to help build up these skills, and therefore to help deliver translation at the local level.

7.44 In 2005, the MaRS Discovery District opened in Toronto (see Box 7.3). It brings together all the pieces of the translational jigsaw, in an environment which connects and fosters collaboration between the science, business and banking / investment communities. It has a dedicated resource centre where advice and a variety of programmes are managed by skilled and experienced staff. Its early success highlights the importance not only of co-location, but of actively bringing different communities together to create a single, new community focussed on supporting effective translation of research into commercially-viable businesses. The vision shown by MaRS' leaders, who include people with experience of building successful businesses from start-up stage, has been key to delivering this.

Box 7.3: MaRS

MaRS is an independent, not-for-profit corporation formed by leaders from Canada's business and public sectors to enhance Canada's competitiveness by supporting innovation and accelerating commercialisation. MaRS is specifically focused on improving commercial outcomes from Canada's foundation of science and technology innovation. MaRS does this by connecting and fostering collaboration between science, business and capital through co-location in the MaRS Centre and more broadly through catalytic programs, structured networks and the MaRS web portal.

The MaRS Centre is located in Toronto's renowned 'Discovery District' – Canada's largest concentration of biomedical research, spread across major teaching hospitals, the University of Toronto, and more than two dozen affiliated research centres. Phase I of the MaRS Centre (700,000 sqft) opened in May 2005, and construction on Phase II is scheduled to commence in early 2007.

The MaRS model is to use place and partnerships to build a community in which innovators, entrepreneurs, scientists, professionals and investors can exchange knowledge, share best practices, and expand their networks. The 65 organizations that currently reside in the MaRS Centre represent researchers, technology transfer specialists, business associations, professional service providers and venture capital firms, as well as technology firms ranging from start-ups to multinational companies.

Two key components of the MaRS Centre are: a 35,000 sqft Incubator, home to 25 emerging companies in the life sciences and information technology sectors; and the Collaboration Centre, a series of conference and networking rooms. The MaRS Centre facilitates physical and virtual collaboration by integrating the latest communication technologies, and MaRS extends its reach beyond its physical location using webcasts and other accessible collaboration tools.

In addition to facilities, MaRS offers a broad range of educational programs and business services to address the needs of emerging and growth-oriented companies. Through the MaRS Venture Group, a team of experienced investors, entrepreneurs, technology experts and advisors, companies can access expertise in everything from protecting their intellectual property, to managing a board of directors, to mapping a competitive landscape, to obtaining and structuring financing.

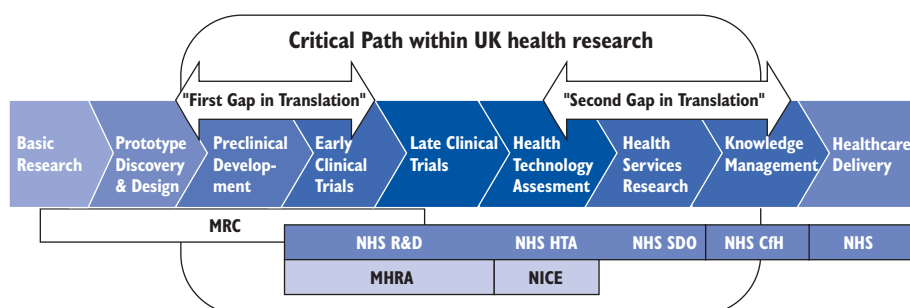
7.45 While the creation of clusters or incubators of businesses is not new the vision and the active facilitation of translation at Mars is a different approach to that normally adopted, and it is this particular aspect that makes it an interesting case study that it will be worth following as it develops in order to draw out lessons for similar approaches in the UK.

THE SECOND GAP IN TRANSLATION

7.46 An equally crucial stage in translating research into practice is the evaluation and identification of those new interventions that are effective and appropriate for everyday use in the NHS, and the process of their implementation into routine clinical practice. In clinical trials, the eligibility of patients is rigorously predetermined and experimental conditions are carefully controlled. However, once shown to be effective in a clinical trial, evidence is also required to establish the benefit of using an intervention amongst the broader patient population in routine

clinical practice. Given the finite resources available to the NHS and, indeed, all health systems, data is also required to evaluate the clinical- and cost-effectiveness of new and pre-existing interventions. Moreover, research into the organisational structures that deliver those interventions can highlight where improvements and efficiencies might be made. All of the above processes, or, indeed, deficiencies in these processes, can themselves generate a gap in the translation of new medical interventions into everyday practice, in what is referred to here as the ‘Second Gap in Translation.’ In this context, Knowledge Management, from research observation to routine clinical practice, can be broken down into four discrete activities: Knowledge Production, Knowledge Transfer, Knowledge Reception and Knowledge Use.

Chart 7.1: Pathway for Translation of Health Research into Healthcare Improvement



Blue boxes below parts of pathway correspond to specific responsibilities of public sector bodies supporting research. MRC: Medical Research Council. NHS R&D: National Health Service Research and Development. NHS HTA: NHS Health Technology Assessment programme. NHS SDO: Service and Delivery Organisation research programme. NHS CfH: Connecting for Health. Light blue boxes below parts of pathway correspond to the specific responsibilities of statutory regulatory agencies. MHRA: Medicines and Healthcare products Regulatory Agency. NICE: National Institute for Health and Clinical Excellence.

7.47 There are four key NHS and NIHR organisations involved in these areas:

- the Health Technology Assessment (HTA) programme;
- the Service Delivery and Organisation (SDO) programme;
- the National Institute for Health & Clinical Excellence (NICE); and
- NHS Connecting for Health.

The HTA programme

7.48 The NHS Health Technology Assessment (HTA) Programme provides the scientific information on clinical and cost-effectiveness that is required to determine whether technologies should be encouraged into, or discouraged from, routine clinical practice. The HTA programme is coordinated via the National Coordinating Centre for Health Technology Assessment at the University of Southampton and funded by the Department of Health. The programme is recognised as a global leader in this area. It aims to ensure that high quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage, provide care in and develop policy in the NHS. Technologies assessed by the HTA programme include medical devices, equipment, drugs, procedures, talking therapies and rehabilitation measures. Its principle customer is the NHS including the National Institute for

Health and Clinical Excellence (NICE), but it also carries out research for the National Screening Committee, the National Clinical Directors ('Czars') for Cancer, Heart Disease and Mental Health, the Chief Medical Officer and the Chief Dental Officer. It is accountable to, but scientifically independent from, the Department of Health. Thus, day-to-day decisions on the funding of research are taken at 'arms-length' from ministers and civil servants.

7.49 The programme is grounded firmly in the NHS, so that the content, speed, iteration and scientific quality of its work are driven by the information needs arising from patient care. Its studies, which are aimed at reducing uncertainty by using large numbers of patients, are internationally important, and of policy and practical relevance. Indeed, given its needs-led approach, the HTA programme has actively ensured that research funded addresses relevant questions via strategic input from patients and the public. The programme operates via two types of analyses: Evidence Synthesis, where primary data is re-analysed from multiple, previously performed studies, and Primary Research, where new data is gathered, typically via clinical trials. It has addressed an important 'R&D market gap' by occupying a research niche that the commercial and public sector previously tended to avoid, such as head-to-head comparisons between different brands of drug or clinical trials with patient-relevant, rather than surrogate, outcomes.

The NHS Service & Delivery Organisation Programme

7.50 Established in 1999, the aim of the NHS Service Delivery and Organisation (SDO) Programme is to consolidate and develop research evidence about the organisation and delivery of health services to enable practitioners, managers and policy-makers to improve the quality of patient care, the efficiency of health services and, ultimately, the health of the nation. It operates from a coordinating centre based at the London School of Hygiene and Tropical Medicine and is governed by the Programme Director who is responsible to the Director of R&D at the Department of Health. A Programme Board advises the Director on SDO Programme strategy, research priorities and commissioning topics, and is comprised of NHS managers, academics, health and social care professionals, service user representatives and eight *ex-officio* members.

7.51 The SDO programme formulates a set of general topics of research to address the cost-effectiveness of healthcare delivery. These topics are identified in a number of ways, including direct requests from the Department of Health Clinical Directors, policy groups and the NHS chief executives' forum, and as responses to government policy. Workshops are used to bring together practitioners, academics and policy makers to identify research themes and topics to inform the SDO Programme about future research. Consultation and listening exercises as well as workshops have identified several research issues, such as nursing research.

7.52 The areas of research funded by SDO, by their very nature, rarely produce Intellectual Property that can be protected and exploited as a commercially-viable proposition. Consequently, and unlike the translation of research into new drugs, devices, diagnostics, or other healthcare products, the commercial sector tends not to have an interest in investing in health services research. In addition, the research councils and charities have not supported this kind of research to anything like the same extent as they have basic research¹⁴. Thus, like the NHS HTA programme, the NHS SDO programme has specifically addressed an 'R&D market gap'. As highlighted in the Wanless Report,¹⁵ which examined the long-term resource requirements for the NHS, health services research

¹⁴ *UK Health Research Analysis*. UK Clinical Research Collaboration. May 2006

¹⁵ *Securing Our Future Health: Taking A Long-Term View*. Report from Derek Wanless to the Chancellor of the Exchequer, HM Treasury, London. April 2002.

is, and will continue to be fundamental to the performance of the NHS. Consequently, it will therefore be important for the UK economy as a whole, given that healthcare accounts for a significant, and growing, percentage of GDP. The SDO Programme, therefore, plays a highly important role in establishing the evidence base for the effectiveness, quality and safety of the health service, and, in turn, delivering the Wanless agenda.

The National Institute for Health and Clinical Excellence

7.53 The National Institute for Health and Clinical Excellence (NICE) was established in 1999 as an independent organisation to provide national guidance on the facilitation of access to promising treatments and the encouragement of innovation in the NHS, whilst ensuring the efficient use of resources. Since 2005, NICE has also had analogous responsibilities to the wider public health community and has started to provide guidance on preventing ill health and maintaining good health for the population as a whole. Although the HTA programme generates evidence based on the scientific assessment of health technologies, the task of NICE is to issue guidance to the NHS following appraisal of those technologies based on both (i) the independent data analysis supplied from HTA-commissioned research and (ii) assessments of the fiscal resources available to the NHS.

7.54 NICE interacts with both the NHS R&D function and the MRC. NICE's interactions with the NHS R&D programmes have been extensive. As mentioned previously, it relies on the HTA programme to undertake the production of assessment reports for the technology appraisals programme. The NHS HTA and SDO programmes (see above) have also been able to commission research addressing some of the evidence gaps identified during the development of NICE guidance. NICE's interactions with the MRC have largely been as a consumer of its primary research, whilst individual members of the MRC staff make important contributions to the work of the Institute as members of its advisory bodies.

NHS Connecting for Health

7.55 NHS Connecting for Health was established in 2005 to enhance Knowledge Reception and Use in the NHS via the National Programme for Information Technology (NPfIT). This will bring modern computer systems into the NHS to improve service delivery, patient care and research opportunities. Together with its National Knowledge Service, the NPfIT will play a central role across the entire spectrum of Knowledge Management within the NHS. It is thus key to addressing effectively the Second Gap in Translation.¹⁶

Addressing the Second Gap in Translation

7.56 Since its inception in 1993, the NHS HTA programme has been extremely successful in its role of Knowledge Production by providing NHS decision-makers with a high quality evidence base, in meeting needs created by 'R&D market failure' and for its innovation and flexibility. Under the new institutional arrangements proposed in this report, the HTA programme should benefit significantly from a greater proportion of support for clinical research, quality and safety research and public health intervention research within the overall portfolio of UK health research. There is

¹⁶ Specific recommendations on NHS Connecting for Health are made in a separate section of this report.

a crucial need for improved Knowledge Transfer, Reception and Use of HTA findings through the NHS. A substantial proportion of the escalating information needs of the NHS could specifically be met by expanding the HTA programme to:

- strengthen the commissioned workstreams for primary research, clinical trials and themed call programmes;
- generate a more systematic approach to the evaluation of diagnostic tests;
- follow up on research recommendations from NICE;
- improve the assessment of medical devices, in collaboration with the NHS Purchasing and Supply Agency;
- improve Knowledge Transfer via joint developments with the National Knowledge Service of Connecting for Health; and
- augment HTA clinical trials infrastructure.¹⁷

7.57 The Review believes that this agenda will substantively increase the effectiveness, and lead to more effective use, of the NHS HTA Programme. **To enhance the evidence base informing decisions on the effectiveness and cost-effectiveness of technologies in the NHS, the Review therefore recommends an expansion of the NHS HTA programme to fund these developments, which, for a relatively modest investment, could deliver large improvements in the quality and efficiency of healthcare in the NHS, and will be crucial to delivery of the Wanless ‘fully-engaged’ scenario. To inform future spending decisions and to ensure that this extra investment achieves the intended outcomes, it will be important from the outset to develop a system of metrics that can accurately evaluate the impact of this expansion of the HTA programme.**

7.58 With the increasing recognition of its importance and continued success, the NHS SDO Programme budget has expanded steadily, reflecting the growth in the amount of research commissioned, from £167,000 in 2000–01, to £3.7 million in 2002–03 and £7 million in 2006–07. There are plans to substantially increase the SDO programme research funding over the next three years and to allocate additional funding to new research areas, such as public health research. These plans to enlarge the programme should be developed in parallel with those for further expansion in the capacity of the NHS for Knowledge Transfer, Reception and Use. The National Programme for Information Technology, operated by NHS Connecting for Health, may be an important first step in the evolution of decision-based software systems that healthcare professionals will need in order to manage effectively the growing scale of our knowledge base and thus improve the care of patients. However, this programme is not likely to be operational at such a level for some time. Nor has it been designed specifically for the purpose of Knowledge Transfer. In any event, the uptake of new knowledge, particularly complex information, often depends the direct communication of new potential users with those familiar with that new technology, so that solutions involving Information Technology are unlikely to be entirely sufficient. Likewise, direct marketing or information campaigns are unlikely to adequately support the spread of these types of knowledge within the health services.

¹⁷ Estimates are based on evidence submitted to the consultation for the ‘Cooksey review’ by the NHS HTA programme.

7.59 **The Review recommends the establishment of a pilot programme, under the joint auspices of the NHS SDO programme and the NHS' Connecting for Health 'National Knowledge Service', to examine the effectiveness of employing a small number of full-time 'Knowledge Transfer Champions' to disseminate the findings of health services research and facilitate early adoption of those findings into routine practice in the NHS.** It will be important to develop an appropriate system of metrics from the outset to accurately assess the effectiveness of this pilot programme. Should it prove successful, the programme could be extended to include wider knowledge transfer functions within the NHS, such as the dissemination and implementation of NICE guidelines.

7.60 NICE sits at the interface between health technology assessment and clinical practice. As part of its process to develop guidance, NICE routinely identifies priorities for research that reflect important gaps in the evidence base. NICE increasingly reviews technologies closer to the stage when they will be granted a marketing license. At this stage of development, there is often only preliminary evidence on costs or effectiveness, particularly for specific disease indications and subgroups. In these cases, NICE can make recommendations for an intervention to be used “in the context of research,” so that the necessary evidence can be generated to inform a future decision on its use. In other words, as a body concerned with Knowledge Transfer, it also has a pivotal role in identifying future needs in Knowledge Production.

7.61 Moreover, as part of its recently expanded remit, NICE has also issued recommendations for the use of an intervention in the context of Public Health research. For example, in recent guidance on interventions to encourage physical activity, NICE recommended the use of pedometers and exercise referral schemes only in the context of well designed trials. The guidance describes the type of research needed to assess these interventions that already take place within the NHS and the broader public sector. NICE has also, on occasion, recommended the use of an intervention in conjunction with prospective collection of information on side-effects, efficacy or costs. Such recommendations can propose the use of existing registers or clinical databases or, alternatively, the establishment of a new register or clinical database. In order to take full advantage of these NICE recommendations, it would be useful to identify resources to support this type of research and establish formal arrangements between NICE, the NHS and the commercial sector, so that the output of this research could be fed more systematically back into the NICE review process and inform future NICE recommendations.

7.62 In addition, the delivery of robust scientific appraisal for new technologies is coming under increasing challenge as a result of its reliance on methodologies that, it is widely recognised, need further development, given that HTA is a relatively new science. Appropriate research is required to address these challenges. In particular, research into methodology for:

- biostatistics;
- indirect comparisons between treatment options;
- economic evaluation of public health;
- appraisal of evidence derived from clinical trials;
- disinvestment methods;
- behavioural research; and
- the assessment of the impact of NICE guidance

should strengthen the ability of NICE to deliver its remit in the future.

The Review recommends that funding be identified and formal arrangements be established between the NHS HTA Programme, NHS SDO Programme and NICE in order to:

- **Implement NICE recommendations calling on the NHS to use health interventions in a research context; and**
- **Investigate improvements in methodologies for use in both NICE appraisals and assessments of the impact of NICE guidance on the NHS.**

7.63 It will be important from the outset to develop a system of metrics that can accurately assess the impact of this research in the implementation of NICE guidance.

8

A new drug development pathway

Chapter overview

Chapter 4 noted that the private sector and, in particular, the pharmaceutical industry, is the largest single investor in health research in the UK. This Chapter looks at some of the challenges facing the pharmaceutical industry, and the health industries more widely, in ensuring that this investment delivers new medicines, diagnostics and devices at a price that both rewards innovation and is affordable to increasingly financially-stretched health systems around the world. It then proposes a new partnership between the public and private sectors to tackle some of the underlying issues through investment in R&D to support the drug discovery process, and potential changes to the regulatory system to support faster up-take of new cost-effective medicines and technologies (as distinct from all new medicines and technologies).

INTRODUCTION

8.1 It has become increasingly clear during the Review that a major challenge to the agenda of increasing the translation of health research into clinical practice is increasing the take-up of cost-effective medicines in a way that rewards innovation but is also affordable to increasingly stretched healthcare systems around the world. Respondents to the Review have pointed to three barriers in particular in the UK:

- an NHS culture that tends to be cautious, rather than supportive of innovation. At the same time, many in the NHS would argue that the marketing approach of pharmaceutical companies has contributed to this problem;
- regulatory barriers, particularly in terms of safety and efficacy, where it has been argued that regulation has failed to keep pace with both changes in the science underlying the drug discovery and development process, and patient and public perception of individual and social risk; and
- some sections of the healthcare industries have argued that uptake of new medicines and technologies has been limited unduly by the use in the NHS of Health Technology Assessment (HTA), e.g. by organisations such as the National Institute for Health and Clinical Excellence (NICE), to assess the clinical- and cost-effectiveness of medicines, devices and technologies.

8.2 This chapter seeks to examine the issues raised in these areas, i.e. what has been described as the ‘Critical Path to new medical products’¹. Its underlying contention is that it is increasingly clear that the current model for drug development is unsustainable in the long-term. Drug development appears to be becoming ever more expensive, and, as new drugs are increasingly targeted at smaller populations (sometimes referred to as more ‘personalised medicine’), the reality is that they will either not repay the investment needed to develop them, or they will be too expensive for health systems to afford. We therefore propose some new approaches, involving a ‘new

¹ See ‘Challenge and opportunity on the critical path to new medical products: view from the US Food & Drug Administration’, FDA, March 2004

partnership’ between industry, Government and regulators (of both safety and clinical- and cost-effectiveness), to try to tackle these issues and create wins for all stakeholders: industry, Government, the wider economy and, most importantly, patients.

WHAT IS THE ‘CRITICAL PATH’?

8.3 The US Food and Drug Administration describes the ‘Critical Path’ to new medical products as involving the following stages:

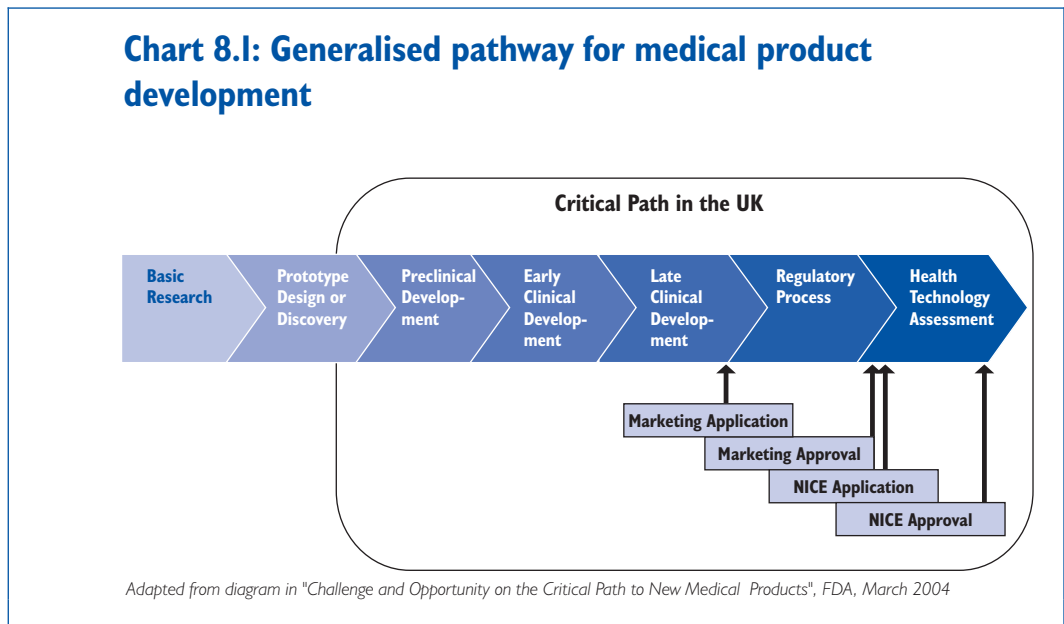
- prototype design or discovery;
- preclinical development;
- clinical development (i.e. Stage I – III clinical trials), at the end of which a company will file for market authorisation; and
- filing approval and launch preparation.²

8.4 To this, we would add the further stages of assessment of clinical- and cost-effectiveness by NICE (using HTA) or comparable bodies working elsewhere in the UK³; Stage IV clinical trials, which can either be used to address particular issues raised by a regulator, or to assess clinical- and cost-effectiveness and how new products are used in practice; as well as ongoing safety monitoring. These processes are not unique to the UK or Europe. Stage IV clinical trials are commissioned by regulatory authorities worldwide, and HTA is commissioned by purchasers globally, including in the US.

8.5 The regulation of healthcare products can, therefore, currently be characterised as a very linear process, but also one with uncertain end-points: a new product with potential for tackling a particular disease is developed in a laboratory; and then tested on increasing numbers of volunteers and then patients for safety and efficacy, at which point it is given a licence; in the UK, it is then assessed by NICE (based on work by the Health Technology Assessment Programme) for cost-effectiveness, as well as by Area Prescribing Committees, PCTs and hospitals; at this point guidance is given to the NHS as to how and when it may best be used. This guidance to the NHS may or may not then be implemented in full.

² Ibid., pg 4.

³ Throughout this chapter, references to NICE should also be read to include those comparable bodies.



8.6 Clearly, this is an extremely complex and long process. One estimate is that a new drug typically takes 12 years to reach the stage of being given a marketing authorisation⁴ (although device development is typically shorter and more incremental). Given that patent life lasts 20 years⁵, this clearly raises challenges for pharmaceutical companies in terms of recovering the cost of developing the new drugs and making a profit. This perhaps makes it unsurprising that many companies are worried about developments such as the increasing use of technology assessment processes, not only because it makes judgements about clinical- and cost-effectiveness that could reduce access to markets, but also because of the time involved in reaching even a positive judgement (this is just as true for manufacturers of medical devices, even though patents are not always as crucial an issue as they are for pharmaceuticals). This can also be frustrating for patients who, understandably, want access to new treatments as fast as possible, particularly when existing ones are of limited effectiveness. This has underpinned recent moves by the DH and NICE to introduce a faster initial assessment for some new treatments⁶.

8.7 During the consultation for the Cooksey Review, two particular issues have been raised regarding the ‘Critical Path’ process in the UK where the Review believes improvements could be made to the benefit of all stakeholders:

- regulations around the healthcare product development process have been getting ever more complex, increasing the time it takes to develop a new drug or device and therefore increasing the cost in two ways: directly because of higher costs associated with more complex processes, and indirectly by reducing real patent life. Given the introduction of new types of product, based on advances in understanding of genetics, etc., some increase in regulation may be inevitable, at least until the technologies involved are better understood. However, it has also been argued that regulation has increased too much, owing to an ever-increasing concern about safety, and a perceived failure to balance this properly with potential benefit. Whilst, as a result of discussions with many stakeholders, the Review’s judgement is that there is at least some truth in this, it is also true that part of the cause of this issue

⁴ DiMasi et al, Journal of Health Economics 22 (2003), pg 164 & pg 181. NB This is the time taken to develop a new molecular entity (NME)—around 35 per cent of new drugs fall into this category.

⁵ Plus potentially an extra four years under Supplementary Protection Certificate (SPC) arrangements

⁶ The ‘Single Technology Assessment’ (STA) process – see <http://www.nice.nhs.uk/page.aspx?o=278616>

has been the reluctance of pharmaceutical companies to release all of the data from clinical trials. It is therefore very welcome that new arrangements to address this have now been put in place. As regulation in this area is now largely driven by the EU and the European Medicines Evaluation Agency (EMA), tackling these issues will require cross-EU working; and

- Health Technology Assessment (HTA) arguably comes too late in the process, at least for some categories of medicines⁷. If the NHS's HTA Programme and NICE were involved earlier in the testing of a drug, and were able to influence the questions asked, the outcome measures, and the design of studies, NICE might be more comfortable with making interim judgements on new medicines, which would allow limited earlier adoption of those thought to be cost-effective. The NHS will also need changes to its dissemination strategies for guidance about cost-effective use of medicines to ensure more rapid and certain implementation. But a cultural change would also be required in pharmaceutical companies, for example allowing organisations like the NHS HTA programme to be more involved in designing efficacy studies and outcome measures; and possibly some changes in their marketing strategies, ideally to align them more closely to NHS objectives.

Why is this important?

8.8 A number of interlinked trends have raised concerns amongst key stakeholders around these issues. First, some have argued that the pharmaceutical industry could face a future financial crunch, caused by falling numbers of new medicines, a weak pipeline, and the rising costs of drug development. It has been claimed that the number of new drugs being produced has fallen⁸, although the latest statistics from the FDA do not show a clear trend⁹. It could be argued that the mid-1990s – from where a ‘drop’ in new drug approvals is generally measured—was a period of exceptional productivity, and that the current level of new drug development is simply a return to an earlier, more sustainable trend. But equally, drug company expenditure on R&D has risen by almost 80 per cent between 1995 and 2004¹⁰, perhaps driven by the higher cost of developing biologics as opposed to more ‘traditional’ chemical-based medicines. It will be important to see whether this leads to an increase in new drug launches as the results of this investment come through over the next few years (remembering that there is a time-lag owing to the long lead times in producing a new drug). It has also been claimed that the cost per new drug developed has increased substantially over time, and this will clearly be affected by the results of the increased drug expenditure, but also the introduction of new technologies (e.g. automated screening), the increased focus in the last decade or so on finding new ‘blockbusters’ (drugs with annual sales of over \$1 billion) and other trends – but, again, the trends here are unclear¹¹.

⁷ We recognise that it may not always be possible to reach anything other than a broad judgement at earlier stages in the drug development cycle, at least using current HTA methodologies (this reinforces the need for greater investment in research in this area). But, equally, earlier HTA / NICE involvement should enable faster progress in getting the data needed.

⁸ FDA, *ibid*, pg2

⁹ <http://www.fda.gov/cder/rdmt/>

¹⁰ CMR International 2005 Pharmaceutical R&D Factbook

¹¹ It is by no means clear that drug development costs have risen by as much as is sometimes claimed. First, as noted above, only around 35 per cent of new drugs are genuinely new molecular entities (NMEs) – the type of new drug for which average development cost are usually cited. Second, the methodology for developing the cost estimates has been challenged, e.g. it is based on self-originated NMEs, which cost more than other types of NME (e.g. those that are licensed in), and appears to include (substantial) costs that are met by R&D tax credits (i.e. are effectively met by taxpayers in various countries that operate such credits). Third, it is unclear that all R&D costs reported are genuinely for R&D necessary to obtain a marketing authorisation for a new drug or to inform HTA, i.e. some R&D costs are more marketing-related.

8.9 Perhaps more importantly, it does appear that new drugs are likely to become more expensive, given the likelihood that an increasing proportion of new drugs will be ‘personalised’ medicine¹², and will therefore require a higher return per patient treated in order to cover their development costs. Whilst, previously, ‘blockbuster’ drugs, with their huge potential markets and therefore huge income-generation potential, could provide pharmaceutical companies with growing profits and effectively cross-subsidise the lower returns generated by drugs with smaller, more niche markets, the number of such drugs looks likely to reduce in favour of more ‘personalised’ drugs targeted at particular disease sub-groups. A recent, well-publicised example is Herceptin, which is targeted at about 20 per cent of patients who have a particular form of breast cancer.

8.10 This has already had a knock-on effect on drug prices: given both higher costs and smaller target populations, an increasing number of medicines coming onto the market are priced in the many thousands of pounds. For example, the cost of Herceptin has been estimated at over £20,000 per patient per year. This comes on top of recent trends in NHS drugs expenditure, which rose by around 50 per cent between 2000 and 2005¹³, and look set to return to this ‘trend growth’ after a brief interlude following the 2005 Pharmaceutical Price Regulation Scheme (PPRS) agreement.

8.11 This presents real financial challenges, especially if principles such as equal access to treatment are to be maintained. As we have seen recently with Alzheimer’s drugs¹⁴, the NHS’s ability to control costs by carefully limiting access to treatments, especially those that are more expensive, is increasingly being challenged by patients and campaigners. A recent IPPR survey found that one-third of people questioned believed that there should be unlimited access to new drugs irrespective of cost¹⁵, further illustrating the growing difficulty in trying to control drugs budgets, even using ‘rational’ systems of access based on assessment of costs and benefits.

8.12 There are problems with the incentives created by many drug reimbursement schemes as they do not distinguish between drugs in terms of efficacy or improvement over existing treatments. Nor do they tend to reward improvements in productive efficiency. This has led to the rather startling conclusion in one review, looking at data over 13 years, that only 6 per cent of new drugs actually represent significant clinical improvements, defined as being ‘the first drug to treat effectively a particular illness or which provides a substantial improvement over existing drug products’ upon existing ones¹⁶.

How should Government respond to these issues?

8.13 There are a number of potential responses to these challenges. Some pharmaceutical companies have argued that access to medicines should be much less restricted so that companies can be more certain of recouping their investments in R&D. This is clearly unrealistic, both

¹² Although the reality may be that, perhaps with the exception of treatments for cancer, where this is just starting to happen, true ‘personalised medicine’ is still some way away, in part because of the difficulties and costs of implementing such an approach. For a fuller discussion, see the Royal Society’s report, *Personalised medicines: hopes and realities* — <http://www.royalsoc.ac.uk/document.asp?id=3780>

¹³ For branded drugs, i.e. those that fall under the Pharmaceutical Price Regulation Scheme (PPRS). The increase was split 60:40 between increases in volume and price (i.e. the price of newly-released medicines being higher than those they replaced). Overall spend, i.e. including non-branded medicines, rose by 60.7 per cent from 1999/00 to 2004/05.

¹⁴ <http://news.bbc.co.uk/1/hi/health/6036519.stm>

¹⁵ *Public ‘expect too much from NHS’*, BBC News website, 2 September 2006. See <http://news.bbc.co.uk/1/hi/health/5298824.stm>

¹⁶ S G Morgan et al, *‘Breakthrough drugs’ and growth in expenditure on prescription drugs in Canada*, *BMJ*, 2005;331:815–816. Another, higher estimate of innovation could be deduced from the fact that the US FDA classifies around 15 per cent of drug candidates as priorities for urgent review because they might represent a clinical advance.

politically and economically. For example, the US, which most closely correlates with this model, spends 16 per cent¹⁷ of GDP on healthcare, of which higher drug prices and drug consumption constitute a significant proportion. But it is far from clear that this expenditure generates additional health or economic benefits. The US does not have greater life expectancy than other Western countries, and any economic benefits from increased R&D have to be offset against (and could well be outweighed by) economic rents paid for drugs of limited clinical value (i.e. such an approach is allocatively inefficient, as it leads to wasteful spending on medicines).

8.14 The opposite response would be simply to ‘crack down’ on ‘wasteful’ drug expenditure and seek to prevent alleged rent-seeking¹⁸ behaviours, especially by substantially reducing prices for those drugs that are not of significant additional economic benefit and by changing rules around marketing. To a certain extent, this has been done in countries like New Zealand and Australia. Australia has introduced therapeutic pricing, rewarding high value-added drugs more than low value-added ones¹⁹. This may well bring benefits in terms of cost savings (at least in the short-term) from a taxpayer / funder point of view, but is an insufficient approach on its own, in that it fails to address some of the underlying causes of the rising costs of medicines. This approach may carry costs in terms of missed opportunities to bring therapies to market, as well as the loss of potential wider economic benefit from R&D investment, which is clearly important to countries like the UK, with a significant pharmaceutical industry base.

8.15 A more productive approach, therefore, might be to look to combine some of the incentives involved in therapeutic pricing (and basing access to new treatments on cost-effectiveness) with reforms to expedite the ‘Critical Path’ process of developing those treatments outlined above. This would encompass both EMEA / MHRA regulation and Health Technology Assessment, which lead to NICE evaluation recommendations. This should generate wins for:

- patients (in terms of faster access to new, high value-added medicines);
- health funders (given better assurances that new medicines will add significant clinical value); and
- industry (which should benefit from shorter lead times for drug development and assessment of both clinical and cost-effectiveness, and lower costs, as well as more certainty that high value-added medicines will be purchased at a price that covers their costs, including a risk-based return on investment).

8.16 Reforms to pricing are out of the scope of the Cooksey Review, and indeed are currently being considered in detail by the Office of Fair Trading (OFT), and so we do not consider those here. Rather, the rest of this Chapter explores potential reforms to the ‘Critical Path’, which are clearly linked to both the health research agenda and improving translation of basic research into health and economic benefits.

¹⁷ NB Figure for 2004. Various forecasts suggest that, if current trends continue, US healthcare costs could exceed 20 per cent of GDP within the next decade.

¹⁸ ‘Rent-seeking’ takes place when an entity seeks to extract uncompensated value from others by manipulation of the economic environment, especially involving regulations or other government decisions. A ‘rent’ is therefore a return in excess of the cost of production (which includes an appropriate, risk-adjusted return on capital).

¹⁹ In a globalised market the impact of such incentives depends on how many countries adopt them and the proportion of the market they represent.

Putting a ‘Critical Path’ reform programme into practice in the UK

8.17 The Review believes that consideration should be given to alternative drug development models that ensure wins for all stakeholders: funders/taxpayers and patients, as well as industry and shareholders. In order to achieve this ‘win-win’ position, reforms to the UK ‘Critical Path’ would need to enable:

- more rapid discrimination between potential new therapies, at earlier stages of drug development, thereby reducing the failure rate at each stage of the drug development process, hence reducing cost and allowing attention to be focussed on those therapies most likely to be successful. This may be essential to ensuring that a new generation of drugs which are targeted at smaller numbers of patients (and hence generate less revenue than the ‘blockbusters’ on which the pharmaceutical industry currently relies) are affordable to purchasers and economic to develop. A side-benefit might be that potential therapies which are currently seen as more marginal because the end market for them might be relatively small, may become more viable if there is greater certainty about their potential success and their development costs are reduced;
- earlier ‘conditional licensing’ of new drugs. The Review believes that conditional licensing should apply at an earlier stage in the drug development pathway (e.g. at the end of Phase II testing). This should not be confused with current arrangements for conditional licensing where a drug has been through significant Phase III testing. Conditional licensing at the end of Phase II would allow clinical use much earlier, under strict controls, including ensuring that patients are fully aware of the risks and properly informed to make such decisions in partnership with their doctors. Some submissions to the Cooksey Review suggested that patients are often far less risk-averse than is assumed by regulators, citing examples of drugs which have been withdrawn from the market on safety grounds but reintroduced after patient campaigns;
- involving NICE at this earlier stage to enable faster assessment of clinical and cost-effectiveness. This process could be improved further if the NHS IT programme (NPFIT) enables the use of real-world data rather than data from the controlled environment of clinical trials. This would ensure more rapid assessment of any emerging side effects and efficacy over longer time periods;
- more rapid uptake of those new drugs which are assessed as being cost-effective, therefore requiring processes and approaches which enable NICE to discriminate faster between these and less cost-effective new drugs;
- clearer processes for ensuring that NICE initial assessments and recommendations for further research are followed-up more rapidly and / or systematically.

8.18 The potential benefits of such an approach could be very large—not only reducing the costs of drug development, but also, by developing the UK system in this way, making the UK a more attractive place for pharmaceutical R&D investment. However, not least given that the UK regulatory system for drug approval is now part of a wider European system, moves in this direction would require engagement with the European authorities (both the EMEA and the Commission). Indeed, the Commission have already launched an Innovative Medicines Initiative (IMI), which

covers some of these areas²⁰, offering opportunities for collaboration across the EU, backed by a planned 440 million Euros per year, over seven years. We would also emphasise that earlier approval would also be a complex process, which might be better suited to some drugs than others, although this may change over time as testing technologies and methodologies evolve, emphasising again the importance of the R&D component of any changes.

New technologies in medicines discovery

8.19 In order to achieve these objectives, specific programmes need to be established to support the development of new technologies in medicines discovery. This is an area where pharmaceutical companies appear keen to collaborate with each other as well as other funders. The idea is to develop new technologies which will speed up the drug discovery and development process, right up to licensing. For example, this might involve identifying new ‘end points’ or ‘biomarkers’ in clinical trials which would act as a proxy for proof of efficacy and / or safety and therefore shorten the time needed to bring safe new drugs to market. A UK strategy here will need to take into account the relative strengths of the UK and other countries in this broad area, and focus on UK strengths. For example, the UK is in a comparatively strong position to develop tools to enhance predictive toxicology (e.g. using stem cells²¹), which could reduce drug attrition rates at the clinical trials stage, where costs to industry are highest.

8.20 The FDA Critical Path report set out a list of research topics, which would contribute towards the objective of a shorter drug development process²². Under these topics is a list of research areas that needed to be pursued:

- better evaluation tools – developing new technologies, biomarkers and disease models to improve clinical trials and medical therapy;
- streamlining clinical trials – creating innovative and efficient clinical trials and improved clinical endpoints;
- harnessing bioinformatics – data pooling and simulation models;
- moving manufacturing into the 21st century – manufacturing, scale-up and quality management;
- developing products to address urgent public health needs; and
- specific at-risk populations – unlocking innovation in paediatric products.²³

8.21 The impact of such a programme of research could be enormous. For example, the ability to determine better which patients will benefit from a particular drug will allow better targeting of drugs, not only improving efficacy and safety, but also ensuring that scarce healthcare resources are better targeted.

8.22 While the Review does not have the scientific expertise to comment on the specific proposals made by the FDA or in the IMI, these areas do correlate with issues raised by stakeholders during the consultation process for the Review. We believe that taking forward an agenda along these lines would be a key task for the new Office for Strategic Coordination of Health Research (OSCHR) and the proposed Translational Medicine Funding Board (TMFB). A Public-Private Partnership (PPP) model might provide the best way to ensure effective collaboration with industry.

²⁰ See http://ec.europa.eu/research/fp6/index_en.cfm?p=1_innomed

²¹ Development of this was one of the recommendations in the *UK Stem Cell Initiative Report*, November 2005

²² See also the EU's (http://ec.europa.eu/research/fp6/pdf/innovative_medicines_sra_final_draft_en.pdf), which sets out an agenda in similar terms for the Innovative Medicines Initiative.

²³ ‘Critical Path opportunities report and list’, FDA, March 2006

Supporting the development of a 'Critical Path' agenda in the UK

- 8.23 In addition there is a need for:
- a systematic programme of pilot studies of conditional licensing programmes for new drugs at an earlier stage, rather than insisting on full completion of exhaustive studies first, e.g. allowing initial use by specialists (in the context of a Randomised Control Trial), but not GPs. This mirrors somewhat existing practice for drugs where there are no or few effective existing treatments. EMEA and MHRA would clearly need to lead here, but the proposed Translational Medicine Board could play an important role, using the expertise in the NHS and MRC;
 - pilot studies for new approaches by the NHS HTA programme and NICE, involving earlier engagement in assessing new drugs, perhaps involving those pharmaceutical companies who are more open to such an approach. This may well need to be backed by more underpinning research into HTA methodology and health economic models;
 - a more systematic approach to and expansion of HTA, i.e. expanding it to cover a greater proportion of NHS activities, ensuring that key NICE recommendations for further research are followed up, and creating a system for following up initial assessments made at an earlier stage with full assessments on the basis of data emerging from post-launch use;
 - the establishment of disease registries by the HTA programme, to enable more effective tracking in practice of how new drugs are used (e.g. for which patients, or the extent of off-label uses), safety, and clinical- and cost-effectiveness. Using the future National IT Programme, this process could be automated and expanded to include a greater range of medicines and adherence to NICE and other NHS guidance, across both secondary and primary care; and
 - NHS Connecting for Health (CfH) and the UKCRC have already started work on ensuring that the new NHS National Programme for IT (NPFIT) has a strong research component. Good initial progress has been made. But it is essential to ensure that research is fully embedded in and integral to the NHS IT programme, and prioritised on a par with other service uses for the system.

8.24 These and other changes could help to reduce the time and cost of developing a new drug or intervention, and hence start to control the escalation in prices which is associated particularly with the development of new drugs targeted at relatively small populations. But, given the relatively small size of the UK market (3.5 per cent of global sales) and the importance of the US market (48 per cent of global sales), close collaboration with other governments and institutions in the EU and the US is needed if these issues are to be addressed effectively. It remains to be seen how this agenda will work alongside the EU's IMI, and this would need to be carefully worked-through.

8.25 Finally, it is worth adding that this agenda of reforms will probably need to be complemented by wider changes. Brief reference has been made to pricing. This will not only need to encompass Western countries, but also large emerging economies, particularly China and India, where economies of scale and affordability issues will be different, and might require a re-think about the pharmaceutical industry's pricing model. In turn, this might help to drive a re-think about the industry's approach to marketing. In particular whether current marketing expenditure²⁴, which

²⁴ See Consumers International, *Ibid*, pg 20, for a breakdown of declared marketing spend by company. Some commentators have noted that this may not encompass the totality of marketing spend, e.g. R&D expenditure typically includes studies which are marketing driven.

typically exceeds R&D expenditure is sustainable. The emergence of new markets therefore offers opportunities for spreading the costs of drug development over a wider patient population, perhaps making 'personalised' medicines more affordable in Western countries, but also challenges the existing approach to getting new medicines to market.

RECOMMENDATIONS

8.26 Clearly, the agenda outlined in this Chapter is ambitious and will probably require a sustained effort over many years if it is to be successful. But the issues raised are of such fundamental importance, and the potential benefits for all stakeholders so large, that they cannot sensibly be ignored.

8.27 In terms of first steps, **the Review therefore recommends that:**

- **OSCHR and the TMFB should work with the healthcare industries and other interested stakeholders (e.g. the medical charities) to develop proposals for joint public and private investment in new technologies for medicines discovery, along the lines laid out in the FDA's Critical Path programme and the European Innovative Medicines Initiative;**
- **the HTA programme and NICE should seek to work with the ABPI and individual pharmaceutical companies to identify new medicines under development that might be best suited to piloting the proposal made above for earlier HTA / NICE involvement (e.g. in agreeing the information they would need to see from Phase III clinical trials);**
- **OSCHR should work with DH, the MHRA and the ABPI to develop a strategy and timeframe for developing the idea of earlier conditional licensing, working with the EMEA and other European partners, as well as the FDA; and**
- **a coordination mechanism should be established to oversee these activities, involving key stakeholders including OSCHR, the DH Medicines, Pharmacy and Industry Directorate, the DH R&D Directorate and its counterparts in the Devolved Administrations, the Chair of the new TMFB, the MHRA, NICE, and the HTA programme.**



LIST OF ABBREVIATIONS

ABHI	Association of British Healthcare Industries
ABPI	Association of the British Pharmaceutical Industry
AHP	Allied Health Professional
AMRC	Association of Medical Research Charities
AMS	Academy of Medical Sciences
BHF	British Heart Foundation
BIA	BioIndustry Association
BIGT	Bioscience Innovation and Growth Team
BRfBH	Best Research for Best Health
CCM	Central Coordinating Mechanism
CEO	Chief Executive of an organisation
CIHR	Canadian Institute of Health Research
CRT	Cancer Research Technology
CRUK	Cancer Research UK
CSO	Chief Scientist Office –Scotland
DALY	Disability Adjusted Life Year
DFES	Department for Education and Skills
DFID	Department for International Development
DH	Department of Health
DHSSPS	Department of Health (Northern Ireland), Social Services and Public Safety
DTI	Department of Trade and Industry
ECF	Enterprise Capital Fund
EGF	Early Growth Funding
EMEA	European Medicines Evaluation Agency
EPSRC	Engineering and Physical Sciences Research Council
ESRC	Economic and Social Research Council
FDA	Food and Drug Administration (US)
FEC	Full Economic Cost
GDP	Gross Domestic Product
GP	General Practitioners
HCC	Healthcare Commission
HEFCE	Higher Education Funding Council for England
HEIs	Higher Education Institutions
HEIF	Higher Education Innovation Fund
HITF	Healthcare Industries Task Force
HIV	Human immunodeficiency virus
HPSS	Northern Ireland Health and Personal Social Services
HSPHR	MRC's Health Services and Public Health Research programme
HTA	Health Technology Assessment
IKT	Institute for Knowledge Transfer
IMI	Innovate Medicines Initiative
IMM	Institute of Molecular Medicine at Oxford
IP	Intellectual Property
IPR	Intellectual Property Rights
KT	Knowledge Transfer
LMB	Laboratory of Molecular Biology
MHRA	Medicines and Healthcare products Regulatory Agency

MPET	Multi Professional Education and Training Budget
MPI	Medicines, Pharmacy and Industry (DH Directorate)
MRC	Medical Research Council
MRCT	MRC Technology
NDPB	Non-Departmental Public Body
NEAT	New and Emerging Applications of Technology Programme
NHS	National Health Service
NIC	National Innovation Centre
NICE	National Institute for Health and Clinical Excellence
NIH	National Institutes of Health (US)
NIHR	National Institute for Health Research
NIII	National Institute for Innovation & Improvement
NPfIT	National Programme for Information Technology
NSF	National Service Framework
OCCMO	The Office of the Chief Medical Officer (Wales)
OFT	Office of Fair Trade
OSCHR	Office for Strategic Coordination of Health Research
OSI	Office of Science and Innovation
PBC	Practice-Based Commissioning
PbR	Payment by Results
PCTs	Primary Care Trusts
PICTF	Pharmaceutical Industry Competitiveness Task Force
PPP	Public Private Partnership
PPRS	Pharmaceutical Price Regulation Scheme
PSREs	Public Sector Research Establishments
QOF	Quality and Output Frameworks
RCC	Research Funders' Forum, the Research Careers Committee
RCUK	Research Councils UK
R&D	Research and Development
RDAs	Regional Development Agencies
RFPBWP	The Research for Patient Benefit Working Party
RVCFs	Regional Venture Capital Funds
RS	Royal Society
SBIR	Small Business Innovation Research (US)
SBRI	Small Business Research Initiative
SDO	Service Delivery and Organisation
SET	Science Engineering and Technology
SHIL	Scottish Health Innovations Limited
SMEs	Small and Medium Enterprises
SRIF	Science Research Investment Fund
TB	Tuberculosis
TMFB	Translational Medicines Funding Board
TT	Technology Transfer
TTO	Technology Transfer Office
UKCRC	UK Clinical Research Collaboration
UKCRN	UK clinical research networks
UK HE	UK Higher Education
UKHTF	UK High Technology Fund
UNICO	University Companies Association
UUK	Universities UK
VAT	Value Added Tax
VC	Venture Capital Trusts

WORD	Wales Office of Research and Development in Health and Social Care
WT	Wellcome Trust
ZonMw	The Netherlands Organisation for Health Research and Development

B

ACKNOWLEDGEMENTS

1.1 Sir David Cooksey and the Review Team are extremely grateful for the invaluable contributions received from a wide range of organisations and individuals. A full list of those who responded to the public consultation will be available on the HMT Website at www.hm-treasury.gov.uk/independent__reviews. We received over 280 responses, which will also be available on the website except for the few cases where they were provided in confidence.

1.2 The team visited research institutes both in the UK and abroad, and we would like to thank the Foreign Office staff in the US, Canada and Sweden for arranging very successful and illuminating discussions. We also visited research facilities in Cambridge, Edinburgh, Glasgow, Manchester and Oxford and would like to thank those who arranged these visits. Last, but not least, we would like to thank all those who gave up their valuable time to talk to us during our visits – they have made an enormous contribution to our thinking.

1.3 The team visited each of the Devolved Administrations, which gave us a greater insight into the different perspectives of each administration and their individual perspectives on the issues that the Review was considering. We also met with Government Ministers and / or Senior Officials from a number of Government Departments and NDPBs including DH, HEFCE, MRC and MRCT, EPSRC, BBSRC, ESRC, NICE, MRHA, NIC, DTI, and OSI. Again, we would like to thank all of the people involved for their time and input, and for their universally positive approach to the review.

1.4 Sir David Cooksey and the Review Team are particularly grateful to the Academy of Medical Sciences and the Royal Society who jointly hosted the stakeholder meeting, “Lost in Translation”, and those who gave such thought-provoking presentations. We are also grateful to those who attended the meeting and entered into the thought-provoking and lively discussions. A meeting report will be available on the HMT website at www.hm-treasury.gov.uk/independent__reviews.

1.5 Finally, we would like to thank all those from the stakeholder communities who met with the team during the review process. We are extremely grateful for the time you took to discuss the issues with us, and hope that we have reflected the broad consensus of opinion in our Report.



Published by TSO (The Stationery Office) and available from:

Online

www.tsoshop.co.uk

Mail, Telephone, Fax & E-mail

TSO

PO Box 29, Norwich NR3 1GN

Telephone orders/General enquiries 0870 600 5522

Order through the Parliamentary Hotline *Lo-call* 0845 7 023474

Fax orders 0870 600 5533

Email book.orders@tso.co.uk

Textphone 0870 240 3701

TSO Shops

123 Kingsway, London WC2B 6PQ

020 7242 6393 Fax 020 7242 6394

16 Arthur Street, Belfast BT1 4GD

028 9023 8451 Fax 028 9023 5401

71 Lothian Road, Edinburgh EH3 9AZ

0870 606 5566 Fax 0870 606 5588

TSO@Blackwell and other Accredited Agents

ISBN 0-11-840488-1



9 780118 404884