MRC Medical Research Council

Impact of MRC Research

October 2010

Executive Summary

The MRC has a proven track record of delivering impact since 1913

For almost 100 years the MRC has been improving the health of people in the UK and around the world by supporting the highest quality science possible. The MRC invests in world-class scientists, trains the research leaders of tomorrow and sustains a flourishing environment for internationally recognised research. The MRC has a proven international track record in delivering impact from its research portfolio, having funded the work that led to 29 Nobel Prizes[1], randomised clinical trial design (1940s)[2], the link between smoking and cancer (1950s, see Box 9), a major part of the dramatic reduction in mortality from childhood leukaemia (1970s)[3] and DNA fingerprinting (1980s)[4]. We continue to provide the financial support and scientific expertise behind key medical breakthroughs today.

MRC research delivers scientific knowledge of the highest quality and this work is effectively translated into new treatments that improve health and wellbeing

Recent analysis[5] has shown that the citation impact of publications attributable to MRC research is fully twice the world average, and higher than the remainder of UK medical research. This shows our selection and support of excellence over the long term which yields results for the UK: research which leads to new understanding, new products and processes, and strongly attracts expertise and inward investment.

Translating medical discoveries into new treatments requires selection of the right ideas, provision of the right support and facilities and coordination with other stakeholders to manage the 'push' and 'pull' of research into application. The MRC set out to contribute to a step change in translational medical research in the UK over this spending review period, and will have successfully supported an additional £130 million of work in this area. This money is being actively managed through new schemes aimed at maximising the impact from this investment. All indications are that we are meeting the goal set out in the Cooksey Review of 2006[6] to accelerate the translation of research from the laboratory to the clinic, with MRC funding supporting a larger and more expert capacity in the UK to take fundamental research into early phase clinical trials. However, the returns from such research are only realised over the long term and require sustained investment.

The MRC has a world-leading reputation for commercialising its research discoveries. Income from the MRC's intellectual property portfolio between 1998/99 and 2008/09 totals £450m, and is expected to have exceeded £500m at the end of 2009/10. Most significantly, MRC discoveries in the area of monoclonal antibody technology have created an entirely new therapeutic approach, and have led to the development of new drugs with a global market valued in 2010 at $40 billion[7]. These drugs are benefiting tens of thousands of patients in the UK, in major diseases such as arthritis and cancer.

The results of medical research contribute billions of pounds to UK GDP

This paper highlights evidence that the economic rate of return from medical research can be quantified, and is positive and substantial. The net value to the UK of health gains and 'spill over' benefits arising from medical research has been shown to wield a significant impact on the UK economy.

Examples of the many and varied ways MRC research is attracting inward investment and securing productive interactions with industry are outlined in this report. The MRC has sought to understand the volume of this activity so that it can better design strategies to maximise such interactions and continue to deliver world-class impact. Analysis[8] has shown that currently 13 per cent of MRC principal investigators actively collaborate with the private sector, and that MRC-funded research groups have secured over £550m of investment from industry or funding agencies based outside the UK since 2006. It is also clear that MRC funding provides skilled people, ideas and expert collaborations that help grow existing businesses and create new entrepreneurial opportunities. MRC research has resulted in the granting of over 200 new patents since 2006, 35 per cent of which are already actively licensed to others. MRC researchers have been active in the creation or growth of over 30 spin-out companies, which represent hundreds of high value jobs.

A healthy society is a productive society and public and charitable research in just one area – cardiovascular disease – was calculated to have led to UK health gains valued at £53bn while the overall rate of return on public and charitable investment was estimated to be 39 per cent[9]. In particular, the MRC-funded research that established the link between smoking and cancer has heavily influenced public policy, with the result that smoking prevention strategies are estimated to be saving the UK over £2bn a year[10].

There is strong support for sustained public investment in medical research

Recent reports by the House of Commons Select Committee on Science and Technology[11], the Academy of Medical Sciences[12], the Council for Science and Technology[13], the House of Lords Science and Technology Committee[14], Imperial College Business School (Haskell and Wallis)[15] and the Royal Society[16] have all emphasised the support that a strong science base will give to the economic recovery and the long-term competitiveness of the UK. Haskell and Wallis[15] recently argued that there is "strong evidence of market sector productivity benefits from public R&D spend on research councils" and that their findings "suggest that for maximum macroeconomic impact government innovation policy should focus on direct spending on research councils". In particular, public support for spending on medical research remains high: in 2010 the Wellcome Trust Monitor[17], a unique survey of 1,200 adults, found almost all respondents (95 per cent) thought that medical research should be supported and encouraged, even if a lot of public money would need to be invested.

The impact of MRC-funded research

There is compelling evidence that investment in medical research leads to significant improvements in both health and economic prosperity. The UK has a world-leading medical research sector, and research funded by the MRC is a vital part of this success. Maximising the impact of this research is a key element of the MRC strategic plan, and over the current spending review period the MRC can demonstrate substantial and positive impact from its research portfolio.

Publicly-funded medical research contributes to significant health gain for the world population. This health gain contributes tens of billions of pounds to UK GDP

Health gains achieved as a result of medical research will have a positive economic impact. A healthier population is more productive, people spend longer in the workforce, invest more in their education and save more for a longer life. Research published in 2008[9] highlighted the substantial health gains that have arisen from research funded by public and charitable research organisations. In this research two specific research areas (cardiovascular disease and mental health) were analysed. The health gain between 1985 and 2005, net of the incremental cost of delivering treatments through the NHS, was calculated. Using a modest estimate of £25,000[18] for each additional year of quality life gained per person, the benefit from medical research into cardiovascular disease (CVD) alone totalled a staggering £53bn. CVD, which includes coronary heart disease, stroke and other diseases of the circulatory system, remains the biggest killer in the UK, causing 34 per cent of deaths (almost 198,000 people each year) and has been estimated to cost the UK economy over £30bn a year (£14bn direct health care costs, £8bn in productivity losses, and £8bn on the informal care of people with CVD)[19]. With the cost of illness so high, research which delivers even modest improvements in health gain will lead to significant economic impact. Death rates from CVD have fallen by 40 per cent in the last 10 years, with reduction in risk factors such as smoking accounting for more than half of this (58 per cent), and improved medical and surgical treatments accounting for the remaining two fifths (42 per cent). MRC-funded research has made key contributions to both understanding major risk factors for CVD and discovering new therapies and improved approaches for treating these diseases.

MRC research addresses the major health challenges facing the UK population

Examples of other areas where the impact on the economy is highly significant and the MRC is responding strategically[20] include:

Ageing	As the age profile of the population shifts, an increased prevalence of neurodegenerative diseases such as Alzheimer's is expected. The Foresight Mental Capital and Wellbeing project[21] reported that over the next 30 years, the number of people affected by Alzheimer's in the UK could double to 1.4 million, and the annual cost to the economy of this has been estimated to be £50bn. See MRC achievements in Ageing research http://www.mrc.ac.uk/Achievementsimpact/Ageing/index.htm
Obesity	Rising levels of obesity within the UK population is increasing the burden of obesity-related conditions such as cardiovascular disease and diabetes. This is enhanced by more sedentary life styles. The Foresight report on obesity[22] stated that, based on current trends, levels of obesity will rise to 60 per cent in men, 50 per cent in women, and 25 per cent in children by 2050, with a further 35 per cent of adults and nearly 40 per cent of children overweight. The overall cost to the UK is forecast to reach £50bn per year by 2050 on current trends. See MRC Obesity research priorities http://www.mrc.ac.uk/Ourresearch/Priorities/Obesityresearch/index.htm
Lifelong Health and Wellbeing	The longer survival of individuals accompanied by a falling birth-rate alters the ratio of dependents to earners and wealth generators. This changing demographic will resonate both within families, with increased dependence of older family members, and across society as the needs of the older age group rest ever more heavily on the working population. This shift impacts significantly on the long-term management of chronic diseases. Recent UK Office of National Statistics figures[23] show that between 1981 and 2006 life expectancy, "healthy life expectancy" (HLE) and "disability free life expectancy" (DFLE) have all increased. However, as life expectancy has increased more than HLE and DFLE, this has reduced the proportion of life spent in favourable health states during this period. See cross-research council Lifelong Health and Wellbeing (LLHW) initiative http://www.mrc.ac.uk/Ourresearch/ResearchInitiatives/LLHW/index.htm
Mental Health	The social challenges of mental health and wellbeing are considerable at the individual, family and population level. The recent Foresight Mental Capital and Wellbeing project[21] estimated the cost of mental ill-health to be about £77bn per year for England, £49bn for economic costs alone. See MRC Brain and the senses http://www.mrc.ac.uk/Achievementsimpact/Brainsenses/index.htm
Addiction	The cost to society of addictions includes the health and economic impact of smoking, but also crime, harm to family, community and society (including impact on educational attainment), financial stability, homelessness, productivity, unemployment, absenteeism, family stability and family welfare. It has been estimated that the Government spends £15bn each year on meeting the costs of drug-related social and economic harms[24]. See MRC Addiction research strategy http://www.mrc.ac.uk/Ourresearch/ResearchInitiatives/Addictionresearch/index.htm

Infections	The threat of new infections is significant and the research base offers the opportunity to significantly increase the UK and global preparedness for pandemics. See MRC achievements in Infections research http://www.mrc.ac.uk/Achievementsimpact/Infections/index.htm
Global Health	Poor health in developing countries will have an impact on health in the UK, both in the area of major burdens of infectious disease and, increasingly, the global pressures of a rising tide of chronic non-communicable diseases. See Global Alliance on Chronic Disease www.ga-cd.org
Environmental Change	Unprecedented rates and magnitudes of environmental change together with population increase will not only put pressure on resources that support health and wellbeing but also produce new and unexpected social and health challenges. For example, in the UK, damage to human health from poor air quality costs each of us an average six months of life expectancy and is estimated to cost the nation some £20bn a year[25]. See cross-research council programme on Living with Environmental Change (LWEC) www.lwec.org.uk

The MRC has recently completed a major new survey of its researchers to assess the extent and to begin to measure the rate at which MRC research is leading to impact. MRC research has led to 24 new products and interventions being launched onto the market between 2006 and 2009. Among these products were monoclonal antibody therapies for nine different diseases, including treatments for common conditions such as rheumatoid arthritis, psoriasis and wet age-related macular degeneration. Each of these three conditions affects around 1 to 2 per cent of the world population (see Box 1).

Box 1 Humanised Antibody Technology, an MRC discovery which has revolutionised medicine

MRC research stemming from work done in the 1970s led to the development of monoclonal antibodies, and in particular discoveries that allowed the engineering of 'humanised' versions of these antibodies, suitable for therapeutic use. The invention of methods for producing therapeutic monoclonal antibodies has revolutionised biological research.

Antibody drugs have created a market forecast to grow to over $43bn by 2012[7] and these drugs are expected to be the most successful segment (in terms of compound annual growth rate) of the prescription pharmaceutical market over this period. This is particularly important when it is noted that the pharmaceutical industry faces expiry of many key patents on small molecule drugs around 2011/12. Antibody drugs now make up a third of all new drug treatments for a variety of major diseases, including cancer, arthritis and asthma. The following treatments owe their origin to MRC research:

Humira® is used to alleviate inflammation in autoimmune disease and is approved for treatment of patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, moderate to severe chronic psoriasis and juvenile idiopathic arthritis. Humira® was the first blockbuster monoclonal antibody therapy with $1bn in sales in 2005. By August 2009 Humira was being used in 80 countries in the treatment of 370,000 patients, and it is now estimated to be the world's top earning pharmaceutical product, expected to reach $10bn in sales by 2016[26].

Herceptin® targets the Her2 protein, which plays a role in 20 per cent of breast cancer cases. Trials have shown that Herceptin® alongside chemotherapy and surgery halves the risk of recurrence and may improve long-term survival rates in these patients. These data led to NICE recommending Herceptin® for women with early-stage, Her2 positive breast cancer. Since the product's launch in 1998, many thousands of women have benefited from treatment with this drug. Herceptin® earned $4.9bn in sales in 2009[26].

Lucentis® is the leading treatment for wet age-related macular degeneration. Macular degeneration is an eye condition that leads to a progressive loss of central vision. People retain some peripheral vision, but the ability to see well enough to recognise faces, drive and read is affected, and vision can deteriorate rapidly. Each year, 26,000 people develop the wet form of the disease in the UK[27].

Monoclonal antibodies are also key reagents used in all areas of biological research. Their binding properties are used to uniquely identify the distribution of specific molecules in cells and tissues, and to purify biological components.

MRC research is credited with establishing fundamental methods and techniques that continue to underpin world-leading medical research, diagnosis and treatment: for example, magnetic resonance imaging (MRI)[28], laser scanning confocal microscopy (MRC Laboratory of Molecular Biology in the 1980s[29]), and more recently optical projection tomography[30]. MRC research has discovered new diagnostic approaches and treatments, such as the recently publicised breakthrough in bowel cancer (see Box 2).

Box 2 Test cuts bowel cancer death rate by nearly half

In 2010 trials were completed that demonstrated that bowel cancer can be prevented with a simple, once-in-a-lifetime, five-minute screening test. Among 40,000 people screened, the test cut the incidence of the cancer by a third and the death rate by 43 per cent over a decade. Bowel cancer is the second biggest cancer killer in the UK, after lung cancer, claiming 16,000 lives a year. The test is so effective that incorporating it into the existing bowel cancer screening programme could potentially save twice as many lives as the estimated 1,400 deaths a year saved by breast cancer screening.

The study started in 1994 when the screening test was offered to men and women aged 55 to 64. The test uses a flexible tube inserted through the anus to examine the lower bowel for the presence of polyps (small growths), which are burnt or snipped off. Polyps occur in around one in five people over 55, and in one in 20 they develop into cancer. The procedure is safe, painless, needs no anaesthetic and is over in five minutes. Follow up over 11 years showed a long-lasting protective effect, so the test should never need repeating. The study, published in *The Lancet*[31], was funded by Cancer Research UK, the MRC and the National Institute for Health Research.

The MRC has a world-leading track record in selecting and supporting research which delivers major health impact in the UK and internationally

High-quality scientific output has helped the UK to maintain its position as second only to the USA with respect to its share of the world's highly cited scientific publications in clinical sciences, health and biological sciences[32]. Information provided by the research community via the MRC e-Val survey has shown that the research the MRC supports has particularly high impact. The average **citation impact of published work attributed to MRC funding is twice the world average**.

This excellence is the result of effective and efficient selection procedures. The MRC has applied these procedures to maintain quality while reserving the flexibility to invest strategically and, where appropriate, to be bold in supporting programmes that step into entirely new territory. Examples of initiatives that were considered at the time to be 'high risk' but are now accepted as 'mould-breaking' include:

- Setting up the MRC's commercial liaison office and collaborative centre in the mid-1980s. This initiative developed into MRC Technology[33], now the world's number one academic healthcare technology transfer organisation.
- The UK Biobank[34] is a visionary medical project aimed at improving the prevention, diagnosis and treatment of cancer, heart disease, diabetes and many other serious conditions. Funded also by the Wellcome Trust and Department of Health, the UK Biobank has now recruited 450,000 participants across the UK.
- The UK Centre for Medical Research and Innovation (UKCMRI)[35] is planned to accommodate 1,500 scientists and staff to create the critical mass to find new ways to tackle difficult biological questions in health and disease, and integrate transformative basic research programmes with world-leading clinical environments in the heart of London. UKCMRI is a partnership between Cancer Research UK, the MRC, University College London and the Wellcome Trust, and has won an additional £250m backing from Government.

The MRC is a good custodian of public money, exceeding targets for administrative efficiency[36] and recycling and re-prioritising resources appropriately. For example, MRC units represent significant long-term investments, and since 1990 the MRC has opened 18 and closed 38 units.

A thriving medical research base is crucial for inward investment, for improving the performance of existing businesses and creating new entrepreneurial opportunities

A healthy science base which provides skilled people, high quality ideas and facilities is crucial to attracting inward investment to the UK. In 2005 the pharmaceutical industry was the largest contributor to UK research and development, accounting for 25 per cent of business investment[37]. Estimates of the spill-over benefits from private sector investment as a result of public funding of medical research are only approximate, but studies have suggested that the economic value of these is significantly higher than that arising from the health gains from research. The MRC has made major contributions to creating and growing new businesses, has been active in promoting interactions between academia and the private sector, and can show how MRC-supported research has stimulated new inward investment to the UK.

Box 3 The MRC Protein Phosphorylation Unit, Dundee – a model of academic/private sector collaboration

Sir Philip Cohen, director of the MRC Protein Phosphorylation Unit (PPU) in Dundee, has been studying protein phosphorylation for 35 years, during which time it has emerged as one of biology's principal control mechanisms. Abnormalities in protein phosphorylation have been shown to be a cause of global diseases such as cancer, diabetes and rheumatoid arthritis, and it is now one of the largest areas of scientific research worldwide. The market for drugs that act on kinases was worth $15.2bn in 2009 and is projected to reach $20.2bn by 2014[38].

The PPU team has a history of successful cooperation with industry, notably its relationship with the US company Upstate, which led to the setting up of Upstate Dundee – a company with 65 employees. In 1996, Sir Philip and his colleague Peter Downes began to seek support from the pharmaceutical industry for a Division of Signal Transduction Therapy (DSTT) to help speed up the development of specific inhibitors of kinases and phosphatases.

The DSTT was established in 1998, initially with five-year support of £6.5m from Astra, Zeneca, Pfizer, SmithKline Beecham and NovoNordisk – later joined by Boehringer Ingelheim. This unique collaboration proved so successful that it was renewed for a further five years in 2003 at a greatly expanded level (this time supported by AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck and Co, Merck KGaA and Pfizer). With core funding of £15.2m plus add-ons, it is one of the largest research collaborations between the pharmaceutical industry and a UK research institution. At BIO99, Pfizer described the DSTT as their most important academic collaboration worldwide, while GlaxoSmithKline have stated that it is the model for how industrial-academic collaborations should work. With a further renewal of core funding in 2008, the DSTT has now raised over £40m of private sector investment to assist in the translation of research into potential new treatments for cancer, hypertension and Parkinson's disease.

The importance of the research focus of the MRC-funded groups in Dundee is highlighted by a recent decision by the Scottish Government to invest £10m to establish a new Scottish Institute for Cell Signalling, and the formation of a further spin-out company Ubiquigent Ltd to market the resulting reagents, assays, services and technologies. Ubiquigent Ltd received £3m funding from Stemgent, a US-based stem cell science reagent company, in 2010[39] and has now employed its first three staff.

The Dundee DSTT partnership (see Box 3) represents one of the largest private sector investments in academic research in the UK, however **13 per cent of all MRC-funded researchers (over 300 principal investigators) have productive interactions with the private sector** (over 250 private sector partners worldwide) in which staff, expertise, materials and funding were actively exchanged between 2006 and 2009[8]. Other recent major private sector investments include:

- A new clinical imaging centre at Imperial College which has attracted £50m of investment from GlaxoSmithKline (opened 2007)[40]. This resulted in part from the MRC's long-term funding of medical imaging at Hammersmith Hospital.

- The decision by Pfizer to invest $100m in its stem cell research programme[41]. This has already resulted in collaborative agreements with University College London and the establishment of a new research unit in Cambridge with the creation of 70 new jobs[42]. The MRC has continued to invest strategically in translational stem cell research throughout this spending review period.

By combining the value of health gains and spill-over benefits, a recent study[9] estimated that for every £1 that public and charitable funders invested in cardiovascular disease research between 1975 and 1992, a stream of benefits was created equivalent to earning approximately 39p each year thereafter over the long term.

Other econometric studies have estimated that investment in research-intensive universities and clusters of research organisations stimulate regional economies. Each year, the MRC invests considerable sums in each of the English regions, and in Scotland, Wales and Northern Ireland. These investments have an impact on the local economies. For example, a report commissioned by Cambridge University and others in 2004[43] showed that Cambridge's impact on the local economy was considerable, and included a large element attributable to life sciences research and development. The portion attributable to MRC funding would be well over £1bn based on an MRC investment in 2004/05 of £35m a year in research in Cambridge alone.

MRC research has been responsible for the creation or growth of around 30 spin-out companies since 2006 (see Box 4). Since 2006, MRC research has led to the granting of over 200 new patents, and by 2009 discoveries from 76 (35 per cent) of these had been licensed worldwide.

Box 4 MRC research has led to the growth and successful creation of new companies

Heptares Therapeutics Ltd[44]
MRC spin-out company Heptares Therapeutics Ltd was formed in July 2007. The company's focus is on the structural determination of G-protein coupled receptors (GPCRs), which are expected to be promising drug targets. Heptares raised over $20m venture capital funding in 2009 and expects to grow to between 30 and 50 staff this year. Interest in the work of Heptares has been significant and an agreement with Novartis was announced in October 2009 with potential milestone payments of over $200m.

Synairgen Plc[45]
Synairgen was formed by the University of Southampton in 2003 based on discoveries made by Professors Stephen Holgate, Donna Davies and Ratko Djukanovic (whose research has benefited significantly from MRC funding), with a focus on respiratory diseases (asthma and chronic obstructive pulmonary disease). The company raised second round funding in 2009, employs between 10 and 20 staff, and in 2010 announced commencement of a Phase II clinical trial of inhaled interferon beta for the treatment of exacerbations of asthma caused by respiratory viruses including influenza.

Summit Plc[46]
Summit, formed by Oxford University in 2003, has partnered programmes including a first-in-class Phase I trial of a compound for treating Duchenne Muscular Dsytrophy (DMD). The DMD programme is based on Professor Kay Davies's research, which has been significantly funded by the MRC.

Thiakis Ltd[47]
Professor Steve Bloom, an MRC-funded expert on metabolic medicine working at Imperial College, showed that administration of a natural peptide to human volunteers not only led to significant weight loss but also increased energy expenditure. The discovery was the result of over 20 years of research in this field. Thiakis Ltd, an Imperial College spin-out company, was formed in 2004 to develop this discovery for the treatment of obesity and associated conditions. Thiakis was sold in 2008 to Wyeth for £20m plus potential future payments of £80m, subject to meeting certain milestones.

- The MRC e-Val survey[8] information has provided an estimate of the inward investment to the UK resulting from the science base, where this is significantly funded by the MRC. Between 2006 and 2009, over £550m further funding was committed by agencies outside of the UK, or from the private sector, to research groups funded by the MRC.

- The first destination for 14 per cent of MRC-supported PhD students was reported to be the private sector in 2007/08[8], with most students (68 per cent) finding employment in the science and engineering base. The MRC supports approximately 1,400 PhD studentships at any one time, with approximately 400 completing their studies each year. The MRC e-Val survey has shown that 10 per cent of staff benefiting from an MRC-funded research position found their next post in the private sector (over 300 researchers between 2006 and 2009).

The MRC has successfully built up translational research capacity in the UK with innovative funding strategies that will bring more discoveries into the clinic

By the end of 2010/11, the MRC will have spent at least an additional £130m in order to grow translational research and the capacity for translational research. The MRC has sought to add value to UK academic science by creating new managed 'follow on' funding streams, which ensure that development paths, intellectual property (IP) and partnering plans maximise impact. These schemes include the Developmental Pathway Funding Scheme (DPFS – see Box 5), expansion of the MRCT Drug Discovery Group, and the Development Gap Fund, as well as a number of initiatives aimed at pump-priming work and capacity in MRC units and institutes and university laboratories, enhancing engagement with industry and targeting support for experimental medicine, biomarkers, stem cell medicine etc.

Box 5 The MRC Developmental Pathway Funding Scheme

The Developmental Pathway Funding Scheme (DPFS) is a new, rigorously-assessed funding scheme set up by the MRC to help strengthen the translation of fundamental research towards patient benefit. It does not fund discoveries of new causes or risk factors of disease, biomarkers, drug targets, biomaterials or research tools, but takes these as starting points and supports their application to improve healthcare and benefits for patients. The DPFS forms a key part of the MRC's Translational Research Strategy[48].

The MRC also recognised that there are opportunities for some universities to develop and manage portfolios of studies funded through the DPFS route and similar schemes. Five universities have been selected to receive funding to pilot such devolved portfolios. The DPFS has so far supported 68 new projects, 42 of which are part of the devolved portfolios. This devolution of the management of such studies should allow more efficient and effective use of underpinning resources and infrastructure, ensure continuity of skills, create a better environment for training and make the best use of project management and oversight systems.

One innovative aspect of the DPFS is the close management of the studies and the expectation that continuation of funding is dependent on meeting defined project milestones. Resources from unsuccessful projects will be diverted to support new work. Awards made so far are focused on 'high-risk, high payoff' projects, particularly those using approaches not yet being actively pursued by industry. Successful project proposals have clearly defined milestones, outcomes and evidence of future value[49].

These activities focus on the best way to maximise the rate of return from medical research: by reducing the time between investment and outcomes being realised. As was recognised in the Cooksey report[6], the UK is ideally placed to capitalise on its strong science base. The UK has to date discovered and developed more leading medicines than any other country, apart from the USA, and as many as the rest of Europe combined. In 2005, 15 of the world's 75 best-selling drugs had been discovered and developed in Britain. What is required is the expertise and support over the long term to accelerate translation of these discoveries to the clinic.

The MRC works from a strong position of successfully assisting products to market, with the MRC Technology Drug Discovery Group (DDG) having an involvement in the development of **over 10 per cent of the worldwide pipeline of therapeutic antibodies**. The pivotal contribution to the field made by MRC researchers has placed the UK at the centre of this industry. The DDG is now incorporated into the Centre for Therapeutics Development (CTD), and the formation of the CTD and further MRC investment has expanded the capacity for development work by more than 65 per cent (see Box 6).

Box 6 UK Centre for Therapeutics Development

The MRC is investing almost £10m through the Centre for Therapeutics Discovery (CTD)[50] to take cutting-edge MRC biology into the early-stage drug discovery process: building high-throughput assays and screening focused libraries. CTD is also doing 'hit to lead' chemistry, which takes 'hits' from a chemical screen and optimises them using medicinal chemistry to produce more refined 'lead' molecules.

The CTD includes the MRCT Therapeutic Antibody Group which has a proven track record of success in antibody humanisation extending over 20 years and has produced 10 clinical candidates and two regulatory approved humanised antibodies: Elan/Biogen Idec's Tysabri® and Chugai/Roche's Actemra®. The recent BIS report "Current and Future Role of Technology Innovation Centres in the UK"[51] emphasised the need for sustained investment in centres with a similar business focus built on elite research.

The CTD has undertaken a major collaboration with GlaxoSmithKline (GSK) and DiscoverX to identify ligands for up to 90 orphan G protein-coupled receptors (GPCRs). Lack of a ligand has proved a stumbling block in the efforts to associate a function with a given GPCR, and thus understand its potential role in disease. The aim of this venture is to identify ligands for some of the orphan GPCRs and associate them with diseases to assist future drug discovery programmes.

The MRC is internationally respected and trusted by global stakeholders in health research

Outputs from many areas of research include 'merit goods' which, without government intervention, the public would under-consume. Often the social benefit of consumption outweighs the private benefit: this is evident in the implementation of vaccination programmes. Examples of vaccination programmes with a significant MRC research input include the programme which eliminated ***Haemophilus influenzae*** type B (Hib) disease in The Gambia[52].

In addition, in the case of many tropical illnesses and other diseases that affect the poor, low income levels deter private investors. However, there is global support for public investments in healthcare research and development for these neglected diseases, for humanitarian reasons as well as for the globally shared benefits that arise from such research. Significant funding is deployed in this area by charitable and public sector funders, but the MRC has made substantial and distinctive impact on areas of global health, in partnership, and playing to its strengths, particularly in clinical trials. An example is the DART trial[53], which is the largest randomised trial of monitoring practice and structured treatment interruptions in the management of antiretroviral therapy (ART) in adults with HIV infection in Africa (see Box 7).

The MRC took a key role in the creation of the Global Alliance for Chronic Disease (GACD)[54] in 2009. The GACD was founded to support clear and coordinated research funding priorities in the battle against chronic non-communicable diseases (cardiovascular diseases, type 2 diabetes, chronic respiratory diseases and certain cancers). These largely preventable diseases are responsible for a total of 60 per cent of all deaths worldwide. Together the alliance members fund an estimated 80 per cent of public health research worldwide.

Box 7 HIV therapy in Africa – the DART trial

The six-year DART trial[53] was the largest randomised trial of monitoring practice and structured treatment interruptions in the management of antiretroviral therapy (ART) in adults with HIV infection in Africa. The DART findings[55] were voted as runner up 2009 *Lancet* paper of the year.

DART was coordinated by the MRC Clinical Trials Unit, funded by the MRC, Rockefeller Foundation and UK Department for International Development, and benefited from collaborations with organisations in Uganda and Zimbabwe. First-line drugs for DART were supplied by Boehringer Ingelheim, Gilead Sciences and GlaxoSmithKline. The trial aimed to establish the best way to deliver ART in resource-poor settings, and early data from the trial demonstrated the significant effect this treatment was having (after two years, 94 per cent of participants were still alive – a staggering 17-fold reduction in deaths compared with mortality rates among HIV-positive Ugandans before ART was introduced).

The trial found that regular laboratory tests to monitor side effects of anti-retroviral therapy (ART) in Africa offered little additional clinical benefit to populations when compared to careful clinical monitoring. Critically, it concluded that a third more people could be treated for HIV in Africa if expensive lab tests were abandoned.

Other findings included confirmation that a cheap and widely available antibiotic would save the lives of thousands of people starting ART in developing countries. Co-trimoxazole was found to cut the risk of death by 50 per cent in the first 18 months of treatment – meaning one in two deaths on antiretroviral treatment were preventable. Co-trimoxazole (trimethoprim-sulfamethoxazole) is a widely available, low-cost antibiotic used in resource-poor settings to treat and prevent pneumonia, *Isospora belli* – a human intestinal disease – and bacterial infections. The antibiotic also has anti-malarial properties and was found to reduce the occurrence of malaria by 26 per cent.

MRC strategy is to target the largest rising need with the largest research and development gap, in order to deliver both practical interventions and improved policy advice. Examples include insecticide-treated mosquito nets for prevention of malaria[56] (see Box 8).

Box 8 Prevention of deaths from malaria – insecticide-treated mosquito nets

Nets treated with biodegradable insecticides protect people from malaria in two ways: by physically preventing malaria-carrying mosquitoes reaching the skin and by killing the mosquito when it lands on the net. The MRC Laboratories in The Gambia first demonstrated this in 1984, and other MRC studies later showed that use of insecticide-treated mosquito nets resulted in a 63 per cent reduction in deaths in children under five years[56]. The use of insecticidal mosquito nets is now a leading part of the WHO global programme on malaria[57].

MRC research impacts on public services and public policy

Research in areas such as the relationship between health and diet, the environment and health, or other areas that result in public health interventions and policy changes rather than commercially exploitable 'products', is unlikely to find commercial market opportunities. In these areas it is vital that public funding is available to generate a sound evidence base. A significant example would be establishing the link between smoking and health. The scale of the health problem caused by smoking meant that smoking cessation programmes have proved to be one of the most cost-effective and high-impact public health interventions ever introduced (see Box 9).

Box 9 Medical research and public policy on smoking

MRC-funded research first published in 1956 showed that the death rate from lung cancer among heavy smokers was 20 times the rate in non-smokers, indicating beyond doubt that smoking causes lung cancer[58].

In 2004, follow-up results demonstrated that the overall risks from smoking were even greater than originally suspected and that, on average, smoking lowered life expectancy by 10 years[59] and around half of those who smoked were killed by their habit. Research also showed that stopping smoking at ages 30, 40, 50 and 60 increased life expectancy by around 10, nine, six and three years respectively. This work, predominantly led by the MRC, resulted in national public health campaigns and a dramatic reduction over the past 50 years in the number of people who smoke. According to 2000 data, 115,000 people a year died from smoking: half of the number in the early 1970s when twice as many people smoked as do now.

As well as influencing behaviour, research in this area has impacted on public policy. There were Government bans in England, Scotland, Wales and Northern Ireland on smoking in workplaces and public places after sustained exposure to passive smoking was also shown to be harmful (non-smokers who are exposed to second-hand smoke at home or at work increase their risk of developing lung cancer by 10-30 per cent[60]).

According to the Government's draft regulations, the England ban is estimated to bring in net benefits of up to £2.1bn a year due to the large number of lives saved. The effect of the Scotland ban was quantified in the first year after it came into force[61]: there was a 17 per cent fall in admissions for heart attacks, which compares with an annual reduction in Scottish admissions for heart attacks of 3 per cent per year in the decade before the smoking ban.

Other examples of the way MRC-funded research has informed the setting of policies which improve society and the economy include:

- **Stockings not effective at preventing venous thromboembolism**. MRC research at Edinburgh University published in 2009 has had significant impact on NICE and international clinical guidelines for the treatment of stroke patients. It is estimated that the NHS may save £7m and 320,000 hours of nursing time a year by cutting the use of stockings for approximately 80,000 stroke victims a year in the UK[62].

- **New UK screening programme aims to prevent 6,000 deaths a year from abdominal aortic aneurysms.** Researchers at the MRC Biostatistics Unit contributed to the case for a UK national screening programme for abdominal aortic aneurysms (AAA). The programme to detect AAAs early was launched in 2009. AAAs affect 4 per cent of men aged 65-74 (approximately 80,000), and results in 6,000 deaths a year[63].

- **National Prevention Research Initiative (NPRI) research informs new policy recommendations on alcohol.** The House of Commons Health Committee published a report on alcohol control in 2009[64], recommending the introduction of minimum pricing, increased duty on alcoholic drinks and better regulation of alcohol promotion. Research funded by the NPRI[65], a coalition of 16 funding partners including the MRC, made a key contribution to the report. Professor Gerard Hastings's NPRI-funded research project on marketing was cited by the report and Professor Hastings served as an advisor to the committee. This research also contributed to the British Medical Association's 2009 report "Under the influence - the damaging effect of alcohol marketing on young people"[66], and an NHS Confederation and Royal College of Physicians report "Too much of the hard stuff: what alcohol costs the NHS"[67].

- **MRC research reduces the number of radiotherapy visits for women recovering from breast cancer.** Lower total doses of radiotherapy, delivered in fewer, larger treatments was shown by MRC research in 2008 to be as effective as the international standard of a higher total dose delivered over a longer time to treat women with early stage breast cancer[68]. Breast cancer is the most common cancer in England and the second most common cause of death from cancer for women. In 2005, over 38,000 new cases of breast cancer were identified. This work has provided valuable evidence to help refine the treatment for these patients.

- **Protecting newborns.** At the MRC Clinical Sciences Centre in London, Professor David Edwards and collaborators have shown that 'hypothermic neural rescue therapy' – controlled cooling of the brain – reduces the risks of death and disability in infants suffering birth asphyxia and reduces cases of cerebral palsy in survivors. This is the first practical and cost-effective treatment for this serious condition, providing not only a clinical therapy but also proof of principle that neural rescue is possible[69]. NICE has already given preliminary guidance that the treatment should become part of normal NHS practice. Through the Experimental Medicine funding call, the MRC has supported further developments of this therapy, including new imaging biomarkers and early phase studies of related treatments.

MRC research findings are frequently cited in UK clinical guidelines, which collate the evidence base in key areas and are relied upon in clinical practice. The MRC e-Val survey collected evidence of MRC research having been cited in over 70 international clinical guidelines since 2006, including 15 guidelines issued by the National Institute for Clinical Excellence (NICE).

MRC selects and trains the research leaders of tomorrow

The MRC aims to sustain the UK's ability to attract the most talented graduates to careers in medical research, and to attract high achievers from other sectors and locations. MRC training schemes seek alignment with the skills needed in industry, for example, through increased provision of training positions in whole-organism science and toxicology. The aim of supporting scientists from early career stages to established research leaders is to facilitate the optimal flow of people between industry and academia, and between the UK and other countries, for a healthy UK science base.

- The MRC invested £67.9m in studentships and fellowships in 2008/09, 30 per cent more than in 2006/07. There were estimated to be 1,400 active MRC-supported studentships and 350 MRC fellowships last year.
- The MRC is a significant employer with over 5,700 research active staff employed in its units and institutes, and supported via grant and fellowship support.
- The MRC e-Val survey[8] indicated that MRC research projects are successful in delivering skilled people to the workforce. Researchers reported details of the next destinations of over 3,000 staff previously employed on MRC grants or unit programmes between 2006 and 2009: 62 per cent remained in the academic sector, and 10 per cent obtained their next position in the private sector.
- Collaborative Industrial CASE PhD studentships provide students with not only a challenging research project, but also first-rate training involving intellectual and technical collaboration between scientists in industry and academia. The value of working across academic and commercial cultures is highlighted repeatedly by our CASE students. Recognising the benefits of the scheme for students, companies and academics, the MRC has increased support for CASE awards by 40 per cent, committing £2.5m in 2009/10. Projects involve 20 UK-based companies including seven small and medium enterprises.
- In response to recent rapid changes in the UK and global economies, the MRC Skills Gap Award scheme was introduced to ensure that high quality scientific or research support skills within industry were retained in the UK through recruitment to UK academic research organisations. The scheme provided fast-track start-up funding for appointments relevant to biomedical or biotechnology research addressing important UK skills needs. Our £2.5m commitment through the scheme resulted in 10 new appointments in vital areas such as animal pathology, imaging, neurodegeneration and translational drug discovery.
- In 2010, the MRC launched a £3.5m flagship programme in clinical pharmacology and pathology, enhancing professional skills and driving collaboration with industry.

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2 In the 1940s the MRC pioneered the development of the randomised control trial – the 'gold standard' in trial design. http://www.mrc.ac.uk/Achievementsimpact/Clinicaltrials/TheMRCandclinicaltrials/index.htm

3 MRC-funded trials in childhood leukaemia have led to massive improvements in survival, so that four out of five children with leukaemia now recover from the disease, compared with only one in five 25 years ago. http://www.mrc.ac.uk/Achievementsimpact/Storiesofimpact/Leukaemia/index.htm

4 Decades of MRC research into the human genome has led to the development of technologies such as DNA sequencing, fingerprinting and chips that have had a huge impact on medical research and medicine. Today, the industry based on genomics, including gene-based services, diagnostics and potential new drugs, is worth around £3.5 billion per year. http://www.mrc.ac.uk/Achievementsimpact/Storiesofimpact/DNAresearch/index.htm

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Medical Research Council
20 Park Crescent
London W1B 1AL
Tel: 020 7636 5422
Fax: 020 7436 6179

www.mrc.ac.uk

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