In accordance with Schedule 1 to the Science and Technology Act 1965, the Medical Research Council (MRC) submits the following report on its activities from 1 April 1999 to 31 March 2000. In submitting this account the MRC wishes to pay tribute to the work done by its own staff and by all other staff it supports. It also wishes to express its gratitude for all the advice and assistance received from those parties consulted in an individual capacity and from members of boards, committees and working parties.

Sir Anthony Cleaver
Chairman

Professor Sir George Radda
Chief Executive

© Medical Research Council 2000
Published by The Medical Research Council

Head Office
20 Park Crescent, London, W1N 4AL
Tel: 020 7636 5422
Fax: 020 7436 6179
Web: www.mrc.ac.uk

£20.00 net
ISSN 0141 - 2256

Layout: Precise
Design: Justin Hegenbarth and Fatima de Abreu
Print and Reprographics: Warwick Printing Company Ltd. (Tel: 01926 491 666)
Photo credits: Strat Mastoris (page 5), Science Photo Library (Page 24), James King-Holmes (Page 36), Keith Brame (Page 54)
The Council’s mission is set out in our Royal Charter: in summary MRC’s purpose is:

- To encourage and support high quality research with the aim of maintaining and improving human health.

- To train skilled people, and to advance and disseminate knowledge and technology with the aim of meeting national needs in terms of health, quality of life and economic competitiveness.

- To promote public engagement with medical research.

The Council members 1999-2000

Sir Anthony Cleaver
Chairman
Professor GK Radda
Chief Executive
Professor JI Bell
University of Oxford
Professor LK Borysiewicz
University of Wales College of Medicine
Professor L Donaldson
Department of Health
Professor Sir David Carter
Scottish Office Home and Health Department
Professor RM Denton
University of Bristol
Professor R Fitzpatrick
University of Oxford
Professor R Mirsky
University College London

Mr D Flint
Director of Alliance and Leicester Insurance
Professor EJ Johns tone
Royal Edinburgh Hospital
Professor AM McGregor
King’s College School of Medicine, London
Rabbi J Neuberger
The King’s Fund
Professor Sir J ohn Pattison
Department of Health
Sir Ross Buckland
Unigate plc
Dr R Auty*
AstraZeneca Pharmaceuticals
Mr MJ Earwicker
(Office of Science and Technology) Representing the Secretary of State for Trade and Industry

*Dr Auty became Director of Salient Consulting Ltd from June 1999
*Professor G K Radda received a Knighthood in the Queen’s Birthday Honours 2000
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th></th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOREWORD</td>
<td>from the Chairman</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>and Chief Executive</td>
<td></td>
</tr>
<tr>
<td>ACHIEVEMENTS</td>
<td>scientific achievements</td>
<td>5</td>
</tr>
<tr>
<td>RESEARCH</td>
<td>other research</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>developments</td>
<td></td>
</tr>
<tr>
<td>PARTNERSHIPS</td>
<td>key partnerships</td>
<td>22</td>
</tr>
<tr>
<td>PEOPLE</td>
<td>developing first rate</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>people in medical research</td>
<td></td>
</tr>
<tr>
<td>KNOWLEDGE</td>
<td>knowledge transfer</td>
<td>40</td>
</tr>
<tr>
<td>PUBLIC</td>
<td>public engagement</td>
<td>45</td>
</tr>
<tr>
<td>PRINCIPLES</td>
<td>ethics and business</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>principles in the</td>
<td></td>
</tr>
<tr>
<td></td>
<td>management of research</td>
<td></td>
</tr>
<tr>
<td>FRAMEWORK</td>
<td>the financial framework</td>
<td>51</td>
</tr>
</tbody>
</table>
The first full year of spend under the funding programme agreed in the Government’s Comprehensive Spending Review in 1998 has witnessed increased research activity and expansion of important programmes, particularly in the key areas of genomics and the health of the public.

High points of the year have been new beginnings and welcoming new scientists to strengthen the Council’s portfolio of research.

MRC appointed two new unit Directors: Professor Simon Thompson as the head of the MRC Biostatistics Unit in Cambridge (p23) and Professor Pierluigi Nicotera who will direct the MRC Toxicology Unit in Leicester (p23). Two further units were established by Council; the MRC Functional Genetics Unit, which is directed by Professor Kay Davies within the University of Oxford (p22) and the MRC Cancer Cell Unit, to be directed by Professor Ron Laskey as part of the MRC/CRC collaboration at the MRC Hutchinson Centre, University of Cambridge (p22).

At the opening of the new MRC Human Immunology Unit in Oxford, the Secretary of State for International Development spoke of her confidence that the MRC Human Immunology Unit ‘marks a significant step forward in the continuing battle against AIDS and other diseases.’

The new MRC Resource Centre for Human Nutrition Research in Cambridge, which will provide scientific evidence of the relationship between nutrition and health to underpin public health policy, was established this year. Veteran researcher Elsie Widdowson, famous for her work on the nutritious ‘wartime diet’, cut the first turf for the new Centre.

MRC support for research in Universities continues to increase. This year saw some £145 million of new research funded. Some of the achievements from University and MRC Scientists are listed on pages 7 –15.

Commercialisation of MRC research remains a high priority. Six companies based on MRC technology have received investment capital through the MRC’s £40 million investment Fund, UK Medical Ventures, which is regulated by IMRO. Technology Transfer is now managed by a single not-for-profit company which brings together the expertise of the MRC Collaborative Centres and the Technology Transfer Group.

With the Wellcome Trust and Department of Health, the MRC have taken forward plans to develop a new National DNA Collection, which will help scientists and doctors to understand more about the interaction between genes, environment and lifestyle in the development of diseases.

This year also saw the funding by the MRC of the very first clinical trial to test cannabinoids for their efficacy in spasticity of Multiple Sclerosis patients.
A small selection from last year’s many noteworthy MRC-funded scientific achievements:

**PEOPLE AND POPULATION STUDIES: HEALTH SERVICES AND HEALTH OF THE PUBLIC**

Fluoride is added to drinking water to improve dental health, but higher than average levels in some areas were thought to be a possible cause of increased hip fracture rates. Professor David Coggon’s group at the MRC Environmental Epidemiology Unit showed that such concerns were unsubstantiated. According to the results of their study – which took other known causes of hip fracture, for example, poor nutrition and lack of exercise into account – there was no evidence that higher fluoride levels increased hip fracture risk.

*Lancet*: 355, 265-69

Professor Darbyshire and colleagues at the MRC Clinical Trials Unit combined the results from more than 30 studies comparing immediate and deferred treatment with anti-HIV drugs, revealing important new information that will benefit AIDS patients. Their work aimed to provide a more reliable evaluation of the different treatment strategies, and to enable comparison between different patient subgroups, for example, men and women. A key finding was that the beneficial effects of immediate treatment with the anti-AIDS drug zidovudine (AZT) are limited to the short term, and do not delay long-term disease progression or improve the chances of survival. However, disease progression and death can be delayed by combining AZT with the drugs didanoside and zalcitabine.


Professor Whitworth of the MRC Programme on AIDS in Uganda has thrown new light onto the poorly understood dynamics of how HIV infection spreads within populations. His long term study among married couples in Uganda found that husbands bring HIV to the marriage twice as often as their wives, and also that if one partner is infected, transmission is twice as fast from men to women as it is from women to men. The findings have important implications for the improvement and development of public health measures.

*Lancet*: 354, 1000-1

A new way to analyse breast-cancer X-rays can distinguish cancers that have an excellent chance of recovery, from those that are likely to kill. Although treatment of most breast cancers while they are small (less than 15mm) is usually successful, a few can reoccur and prove fatal. Researchers at the MRC Biostatistics Unit, in collaboration with Swedish colleagues, have now found a feature on X-rays that is associated with 15% of tumours which account for 70% of all breast cancer deaths, enabling identification of patients who might benefit from more aggressive therapy.

*Lancet*: 355, 249-33
Professor Copeland and colleagues at Liverpool, who are participants in the MRC funded Cognitive Function and Ageing Study, measured the incidence of different types of dementia in over 5,000 local people. They found that incidence rates increase with age, that the age profiles of Alzheimer’s disease and vascular dementia are similar, and that gender appears to be influential in Alzheimer’s disease. These incidence rates are equivalent to 155,200 new dementia cases a year in England and Wales, which raises profound implications for health service planning.

*British Journal of Psychiatry: 175, 433-38*

The NHS National Specialist Commissioning and Advisory Group has funded Professor Pepys’ research team at Royal Free and University College Medical School as the “National Amyloidosis Centre”, representing a notable success for MRC-funded research and development. Professor Pepys’ work on amyloidosis, a fatal metabolic disease, has been supported by an MRC programme grant since 1979. His work has contributed to increased understanding of this disease, and to the development of new diagnostic and monitoring procedures that have improved patient survival. The new centre will provide diagnostic and management advice for amyloidosis throughout the UK.

*NHS Centre*

**MEDICAL PHYSIOLOGY AND DISEASE PROCESSES**

Drs Michael Barnes and Richard Farndale, MRC scientists at the University of Cambridge, have focused on the cascade of events that can cause heart attacks through coronary thrombosis, blood clotting that blocks the arteries which supply the heart. Initial damage to the artery linings exposes a structural protein component of the cell wall, called collagen. Exposed collagen binds blood cells called platelets in a protective response that prevents bleeding by sealing leaks at the site of damage, but which can also cause internally damaged heart arteries to become blocked, leading to heart attack. Drs Barnes and Farndale have discovered how platelets and collagen interact, which will help to design drugs that will interrupt the process and prevent thrombosis in potential heart attack victims.

*Journal of Biological Chemistry: 275, 35-40*

Dr Soutar and colleagues at the MRC Clinical Sciences Centre have identified an additional genetic cause of the inherited disease Familial Hypercholesterolaemia (FH), a condition characterised by elevated blood cholesterol levels that increase FH sufferers’ risk of developing early heart disease. Treating FH patients with drugs that lower blood cholesterol concentration can reduce this risk, and once this new genetic defect has been characterised it should be possible to identify and treat more high-risk patients.

*Journal of Clinical Investigation: 104, 619-28*

MRC Senior Clinical Fellow Dr Vincenzo Cerundolo and his team at Oxford have developed a new test and potential therapeutic agents for melanoma, a severe form of skin cancer triggered by sun exposure. The test uses a custom made reagent that stains immune cells called tumor-specific cytotoxic-T-lymphocytes (CTL), which recognise and kill cancer cells, and has revealed high CTL numbers in patient lymph nodes infiltrated with melanoma. Melanoma cells often carry distinctive outer cell surface molecules that make them targets for CTL killing. The team has cloned CTL that recognise these surface molecules, and which may therefore be of potential use for cancer therapy.

*Journal of Immunology: 162, 6959-62*

MRC grant holder, Professor Collins of University College, London, has made progress towards developing a gene therapy treatment for melanoma that spreads to other tissues. Her team has found a way of selectively delivering genes to melanomas, so that they kill tumour cells but not surrounding normal cells. In addition, the team has completed its first gene therapy clinical trial using cells from the
patient's own tumour, genetically modified to produce a molecule called interleukin 2 which stimulates the immune system. Four of the first twelve of patients treated using the new procedure showed enhanced killing of tumour cells by their white blood cells.

**Human Gene Therapy: 10, 1261-68**

Dr Peter Rowe of Royal Free and University College has identified the genetic mutation causing an inherited form of rickets that results in a deformed skeleton, and defective processing of vitamin D and renal-phosphate. He has also identified and isolated a previously unknown hormone, secreted by certain tumours that cause similar abnormalities. His data suggest that the gene's normal product and the hormone may interact in the same regulatory pathway. This work may have direct applications in the treatment of this type of rickets, osteoporosis and other conditions.

**Genomics: 67, 54-68**

Professor Lechler's team at Imperial College and Hammersmith Hospital demonstrated that Leptin – a hormone involved in regulating appetite, energy expenditure and reproductive function – is necessary for the function of mouse and human immune cells called T-lymphocytes. In particular, they showed that Leptin is crucially involved in countering the effects of starvation that cause immune depression, and cell death in the thymus gland, where T-lymphocytes are made. The researchers were able to fully protect starved mice from these effects by giving them extra Leptin, confirming that Leptin is an important regulator of immune function and that Leptin deficiency provides a key link between malnutrition and reduced immune function.

**Journal of Clinical Investigation: 104, 1051-59**

Research by Dr Dominic Withers of Imperial College and Hammersmith Hospital has provided valuable insights into type 2 diabetes. This type of diabetes is caused by the eventual failure of insulin producing beta cells in the pancreas, due to an initial compensatory increase in insulin production in response to a loss of sensitivity to insulin. Dr Withers has demonstrated that two molecules, insulin-like growth-factor-1 and insulin-receptor substrate-2, are critically involved in these processes. His studies will contribute to the development of treatments for beta-cell failure and possibly type 2 diabetes.

**Nature Genetics: 23, 32-40**

---

**GENETICS, MOLECULAR STRUCTURE AND DYNAMICS**

An international consortium that includes the MRC Human Genome Mapping Project Resource Centre has determined the entire genetic code of a chromosomal region called the Major Histocompatibility Complex (MHC). The MHC is essential to the immune system's ability to fight infections, and MHC-gene mutations are associated with more diseases than any known region of the human genome. The data should make it easier to identify individuals who might be carrying defective MHC genes and offer them appropriate counselling or treatment.

**Nature: 401, 921-23**

Scientists from the Whitehead Institute for Biomedical Research and the MRC UK Mouse Genome Centre jointly reported the assembly of the first physical map of the mouse genome. The map is a major step towards precise characterisation of mice's genetic makeup, providing a framework that will enable more detailed genetic information to be assembled. Because mice and humans share many genes in common, the mouse is an ideal model system for studying the function of the thousands of genes identified by the human genome project and their role in genetic diseases.

**Nature Genetics: 22, 388-93**
The genetics of the fruit-fly, *Drosophila*, can also offer important insights into human genetics. MRC funded scientists in Cambridge have collaborated with colleagues in Berkeley, California, to precisely characterise a region of this fly’s genome that has been very extensively studied in Cambridge for the last 20 years. They have refined the genetic information from this region down to the DNA sequence level, reading-off and describing the details of three million base-pairs of DNA sequence.

*Genetics: 153, 179-219*

MRC programme grant holder Professor Ed Southern has made a seminal contribution towards the goal of understanding gene function. In his laboratory at Oxford, he has invented a technique for attaching ordered arrays of DNA molecules to the surface of a "DNA-chip". This pioneering DNA microarray technology has not only revolutionised genetic analysis, but will also lead to new methods of diagnosing inherited diseases and will help researchers to analyse drug effects.

*Nature Biotechnology: 17, 788-92*

Dr Ramakrishnan and his colleagues at the MRC Laboratory of Molecular Biology have used X-ray crystallography to determine the structure of the 30S ribosomal subunit, which together with its partner the 50S subunit, forms the ribosome. Ribosomes play a fundamental biological role, they translate the genetic code to construct proteins in all living organisms and are of great medical importance, because many natural antibiotics work by selectively targeting bacterial ribosomes. This work will provide insights into how ribosomes work and how antibiotics inhibit their function.

*Nature: 400, 833-40*

Daniela Stock at the MRC Laboratory of Molecular Biology and Sir John Walker of the MRC Dunn Human Nutrition Unit have extended the work for which Sir John won a Nobel Prize in 1997. They have determined further structural details of the molecular motor that makes Adenosine Triphosphate (ATP), a molecule crucial to cellular energy storage in all life-forms. They have described a ring of 10 molecules, called c-subunits, that spans the membrane of the mitochondrion, the part of the cell where ATP is made, and constitutes the "drive-shaft" end of the motor. They think that energy generated by a flow of hydrogen ions across the mitochondrial membrane drives rotation of the ring, powering ATP production at the other end of the molecule. Their work is a major step forward since it shows the working relationship between both ends of the structure.

*Science: 286, 1700-05*

Scientists at the National Institute for Medical Research, in collaboration with several other groups, have established a method for visualising the molecular changes in protein structure which underlie muscle contraction and movement. The approach is potentially applicable to many types of protein motion, such as occur in the heart-beat and in pumping blood through blood vessels.

*Nature: 400, 425-30*

**NEUROSCIENCE AND MENTAL HEALTH**

Professor Lumsden and colleagues at King’s College, London, have significantly contributed to knowledge of the early stages in brainstem development. The brainstem develops from a repeated series of similar cell-blocks, called rhombomeres, in the embryo and controls vital functions such as, eating, swallowing, breathing and heart rate. The group have shown that the expression of a single gene defines the eventual function of a given rhombomere, and also that the segmentation process plays a key role in establishing the nerve connections involved in the control of breathing.

*Science: 284, 2168-71*
Professor Collingridge of the MRC Centre for Synaptic Plasticity, at Bristol, has advanced the understanding of glutamate receptors, the protein molecules that mediate much of the communication between adjacent nerve cells in the human brain. These receptors are important in learning and memory and have been implicated in diseases such as epilepsy and Alzheimer’s. Professor Collingridge has discovered that a subtype of glutamate receptors, called kainate receptors, are involved in triggering changes in the efficiency of communication at certain junctions between neighbouring nerve cells. The work should give important insights into how learning and memory work and could lead to new treatments for brain diseases.

*Nature*: 402, 297-301

Dr Roeper and colleagues at the MRC Anatomical Neuropharmacology Unit have used a genetically-engineered-mouse model of Parkinson’s disease to gain a better understanding of the disease mechanisms. Parkinson’s key feature is the selective degeneration of the midbrain nerve cells which respond to the neurotransmitter dopamine. The team isolated individual cells that had escaped this process and showed that a cell’s survival depended on its ability to make a working version of a particular protein, called an ATP-sensitive potassium channel. The protein and its corresponding gene are potential targets for anti-Parkinson’s treatments.

*Journal of Neuroscience*: 19, 8839-48

Dementia with Lewy bodies (DLB) is the second most common cause of dementia after Alzheimer’s. In addition to mental dysfunction, DLB patients suffer from similar movement control problems to those seen in Parkinson’s disease. Professor Perry’s team at the MRC Neurochemical Pathology Unit have shown that DLB movement disorder is caused by reduced levels of the signalling molecule, dopamine, and that in contrast to Parkinson’s patients, DLB patients fail to respond to dopamine loss. This failure may explain DLB patient’s poor response to dopamine replacement therapy and their sensitivity to antipsychotic drugs. The pattern of dopamine loss in DLB may be helpful in diagnosing the condition and in differentiating DLB from Alzheimer’s and Parkinson’s using live brain-imaging methods.

*Brain*: 122, 1449-68

Professor Cowen has used brain imaging techniques at Oxford in collaboration with the MRC Cyclotron Unit, to show reduced binding of the chemical messenger serotonin to brain receptors in patients with major clinical depression, compared to healthy individuals. The observation is direct evidence that serotonin activity decreases during clinical depression and suggests that this might be because fewer serotonin receptors are available. The work may benefit the diagnosis of depression, the detection of people at risk of depression, and the design of treatments to stimulate serotonin receptors.

* Archives of Psychiatry*: 57, 174-180

A clinical trial conducted by Dr John Teasdale and colleagues at the MRC Cognition and Brain Sciences Unit has shown that the prospects of long-term recovery from depression can be improved. The study showed that cognitive therapy was more effective than continuing antidepressant medication in reducing the high frequency of relapse that contributes to poor long-term recovery rates at present.

*Archives of General Psychiatry*: 56, 829-35

Grant holder Professor Eve Johnstone at Edinburgh University, has found that young people from families prone to schizophrenia have alterations in brain structure and function that correlate with their risk of developing the disease. She examined 200 such youngsters and compared them to other young schizophrenics and to a control group in good mental health. She detected abnormalities present in the at risk group in the year before any illness developed, suggesting new ways to diagnose, and perhaps even prevent, inherited schizophrenia in susceptible individuals.

*Lancet*: 353, 30-33
The work of Professor Woolf and colleagues at University College, London, has provided a deeper understanding of the complex factors contributing to the sensation of pain, and may contribute to the development of new painkillers. They have characterised chemical changes, triggered by inflammation, that switch nerves that normally signal harmless sensations to signalling pain. They think that this mechanism is probably a major factor in generating hypersensitivity to pain. They have also identified a previously unknown molecule that keeps adult nerve cells alive. Neonatal nerve cell loss following nerve injury is due to the absence of this "survival factor".

Lancet: 353, 1959-64

Paul Matthews, an MRC Reader at Oxford, and his colleagues have used advanced functional magnetic resonance imaging methods to understand how brain function is disrupted by injury and how the brain reorganises itself in response to damage. They have shown how nerve cells and their supporting structures interact in animal tissue and demonstrated that the clinical effects of injuries are determined not only by their extent, but also by the specific location of the changes they cause. In particular, they have discovered that long distance changes can occur far from the damage site.

Brain 122 1933-9

Dr Ros Ridley of the MRC Comparative Cognition Team has tested a drug that may significantly reduce the ill effects of a stroke. During stroke the blood supply to part of the brain is restricted, resulting in progressive local brain damage that lasts for some hours. Administering drugs that protect the brain during this time could limit the degree of damage. Dr Ridley treated animals with surgically induced strokes using the drug Clomethiazole, and found that the brain damage and one-sided paralysis typical of stroke were both reduced. This is the first demonstration of a drug's therapeutic effect in a model of stroke relevant to humans.

Experimental Neurology: 156, 121-29

CELL BIOLOGY, DEVELOPMENT AND GROWTH

Studies of the nematode worm, C. elegans, by Drs Ahmed and Hodgkin at the MRC Laboratory of Molecular Biology have provided clues as to why egg and sperm cells live for ever as they are passed from one generation to the next, whereas other cells die after about 50 divisions. They identified worms with a genetic mutation that leads to sterility in subsequent generations and showed that this was due to the lack of a protein, first identified in yeast, that senses damage to DNA and stops cell division until it is repaired. Without this protein, the worms lose DNA from the ends of their chromosomes from generation to generation, which limits their cells' life-spans. Detection and repair of damage to chromosome ends therefore seems necessary for cell immortality.

Nature: 403, 159-64

David Wilkinson of the MRC National Institute for Medical Research has shown that interacting proteins at the surface of neighbouring cells both send and receive signals, and act as repellents that prevent cells from crossing between adjacent tissues. His discovery contributes to our understanding of how correct cell location is normally maintained, and how this process might go wrong in diseases such as cancer.

Nature: 400, 77-81

Cells can die either due to natural wear and tear or because they are programmed to self-destruct. Dr Gavin Screaton, an MRC Senior Fellow at Oxford, has determined the molecular structure of two cell surface molecules involved in triggering programmed cell death. These discoveries shed light onto how cell death is controlled, and may have therapeutic applications in the treatment of diseases including, HIV, cancer and autoimmune diseases.

Nature Structural Biology: 6, 1048-53
Dr Williams and his colleagues at the MRC Laboratory of Molecular Biology have advanced understanding of the events leading to inflammation. Unregulated and inappropriate inflammation can lead to disorders such as arthritis, tissue rejection and arterial disease. A key early event in the onset of inflammation is the activation of a protein called phosphoinositide 3-kinase in white blood cells. Dr William's group has determined structural details of phosphoinositide 3-kinase, which help to explain how inflammation is triggered and how anti-inflammatory drugs might be designed to work by specifically inhibiting the protein.

*Nature*: 402, 313-19

The lymphatic system is a network of tiny vessels that has medically important involvement in immune function and the spread of cancer. However, little is currently known about how the system works. David Jackson, an MRC Senior Fellow at Oxford, has discovered a molecule, called LYVE-1, that is unique to the surface of lymph-vessel lining cells and has made LYVE-1 antibodies that can be used to "light up" the lymphatics when examined by a microscope. This new research tool should help investigation of how the lymphatics work in normal tissues, and whether cancers spread by attracting new lymph vessels, or by invading existing ones.

*Journal of Cell Biology*: 144, 789-801

Work from the laboratory of Steve Ley at the MRC National Institute for Medical Research may contribute to the development of new drugs to treat rheumatoid arthritis and other inflammatory diseases, for example, septic shock. The group has been investigating a protein called TNF-α, which plays an important role in the development of rheumatoid arthritis. Overproduction of TNF-α in arthritic joints induces the intracellular activation of another protein, NF-κB, which then turns on multiple target genes. Ley's group has identified a previously unknown mechanism that regulates NF-κB's activation by TNF-α.

*Nature*: 397, 363-68

Programme grant holder Ermanno Gherardi at the Cambridge Centre for Protein Engineering is working on a protein called HGF/SF, which is essential for the development of the placenta, liver and certain types of muscle. HGF/SF and its receptor are also involved in the spread of cancer to adjacent tissues and distant sites in the body, and are therefore primary targets for new treatments designed to counter tumour migration. The design of new anti-cancer and tissue regeneration therapies that act on HGF/SF and its receptor will be greatly aided by structural characterisation of the HGF/SF receptor-binding fragment.

*Nature Structural Biology*: 6, 72-9

Professor Miles Houslay's team at Glasgow has made progress towards improving recently developed treatments for asthma and rheumatoid arthritis. The new drugs reduce the inflammation associated with these conditions by increasing the levels of a chemical messenger molecule, called cAMP, in immune cells. These compounds work by inhibiting cAMP degradation by a group of enzymes called PDE4 phosphodiesterases, but unfortunately they also cause nausea due to their actions on an unknown PDE4 'high affinity' state. The Glasgow group's discovery of how a specific PDE4 enzyme can be switched between low and high affinity states, will aid the development of drugs without side-effects.

*Journal of Biological Chemistry*: 274, 11796-810
Molecules called Ribonucleic Acids, or RNAs, play a major role in translating the genetic instructions encoded by genes, into proteins, which are the main structural and functional components of cells. String-like RNA molecules can form very complex twisted structures, and proteins called RNA helicases are required to unwind these structures to obtain the correct functional RNA conformation. Work at Dundee, by MRC Senior Fellow Frances Fuller-Pace, has shown that an RNA helicase, called DbpA, from the bacterium Escherichia coli, interacts specifically with bacterial RNA, but not with similar RNAs from higher organisms, including humans. This specificity makes DbpA a potentially useful target for the generation of new antibiotics.

*Journal of Molecular Biology*: 292, 771-78

Jeremy Turnbull, an MRC Senior Fellow in the School of Biosciences at the University of Birmingham, has developed the first method for determining the precise molecular structure of heparan sulphates, which are complex cell-surface molecules involved in binding and regulating the activities of many signalling proteins. This new technique provides an opportunity to examine the structure and function of these important regulatory molecules, with the goal of identifying new therapeutic targets.

*Proceedings of the National Academy of Sciences USA*: 96, 2698-703

The vital life processes of all organisms are mediated by proteins called enzymes, which significantly speed up biochemical reactions. Naturally occurring enzymes are used by the pharmaceutical industry to make new drugs, and are administered therapeutically to speed reactions in the body. Professor Alan Fersht, Director of the MRC Centre for Protein Engineering has devised a test-tube method for making new enzymes. His synthetic enzymes will be of particular use where naturally occurring enzymes are not available.

*Nature*: 403, 617-22

**IMMUNITY AND INFECTION**

Geoff Hale and Herman Waldmann at Oxford have found a way to improve the success rate of kidney transplant operations. They treated thirty one transplant patients with two small doses of a monoclonal antibody called CAMPATH-1H, to deplete white blood cells called lymphocytes at the time of surgery, together with half the normal dose of only one of three standard immunosuppressive drugs. The new regime decreased the rate of transplant rejection, reduced side-effects and improved the patients’ prospects of recovery. A larger, multi-centre, trial is planned.

*Transplantation*: 68, 1613-16

Professor Michael Curtis of Barts and Royal London Hospitals has discovered how the bacterium Porphyromonas gingivalis, which is a leading cause of gum disease, combats the mouth’s immune defences. Professor Curtis has examined the chemical composition of bacterial enzymes called proteases, which are able to degrade human immune system proteins. He found that proteases contain high quantities of sugars which may make them more stable and also shield them from antibodies produced by patients with disease.

*Infection and Immunity*: 67, 3816-23

MRC Professor Dominic Kwiatkowski, of the Molecular Infectious Diseases Group at the Institute of Molecular Medicine, Oxford, has made progress towards understanding the genetics of malaria susceptibility in African children. One of the genes that determine a child’s risk of dying from malaria produces a potent immune protein called Tumor Necrosis Factor (TNF). Professor K Kwiatkowski has identified several different TNF gene variants that independently appear to affect malaria susceptibility. These studies have revealed a specific molecular mechanism by which one of these variant genes may
alter the amount of TNF that immune cells produce, thereby determining the effectiveness of the immune response to infection.

*Nature Genetics: 22, 145-50*

Malaria is caused by the multiplication of malaria parasites inside host red blood cells which they have invaded. The parasite’s ability to evade the host’s immune system is one of the main problems facing the development of an effective malaria vaccine. Dr Peter Preiser, at the MRC National Institute for Medical Research has demonstrated that a gene family, thought to be involved in red blood cell invasion, also allows the parasite to adapt to changes in the host environment as well as to evade the immune system.

*Nature: 398, 618-22*

Allergic diseases, like asthma, affect about 30% of the population and may arise from the breakdown of regulatory control of the immune system. Professor Jonathan Lamb of the University of Edinburgh, has discovered that a protein called Notch, which is involved in the regulation of cell growth and differentiation, plays an important role in the inhibition of immune responses. These data aid understanding of how the immune system maintains the correct balance between suppressing and generating responses and may help with the design of new treatments for allergic disorders.

*International Immunology: 12, 177-85*

Dr Lever and colleagues at Cambridge are using Simian Immunodeficiency Virus (SIV), a monkey virus closely related to Human Immunodeficiency Virus (HIV), as a model system for studying and understanding how HIV causes AIDS in humans. They have examined the SIV assembly mechanism used to recognise and incorporate the correct genetic material into the viral particle, and identified the viral component responsible for this identification process. The work will hasten the design of new treatments for HIV and will inform the design of gene delivery vectors based on similar viruses.

*Journal of Virology: 73, 3023-31*

Collaborations between the research groups of Professor McMichael at the MRC Human Immunology Unit and Professor Borysiewicz at Cardiff University have described one of only two known examples where a virus has evolved to evade the killer cells of its host’s immune system. The researchers have identified a gene in human cytomegalovirus that changes the surface proteins of virus infected cells to inhibit immune attack.

*Science: 287, 1031*

A bacterium called Neisseria meningitidis causes the life-threatening infections meningococcal septicaemia and meningitis. Professor Richard Moxon and colleagues at Oxford have identified a bacterial cell-surface component that has great promise as a vaccine. They have shown that a part of a molecule, called lipopolysaccharide (LPS), is present on the surface of over 70% of virulent strains and that it can be a target for human immune responses. Additional LPS components that would enable all virulent strains of the bacterium to be covered by the potential vaccine have also been identified.

*Infection and Immunity: 67, 5417-26*

A bacterium called methicillin resistant Staphylococcus aureus (MRSA), which is resistant to virtually all clinically available antibiotics, poses a serious emerging health threat. Studies by Nottingham based MRC grant holder Professor Paul Williams are providing new opportunities to prevent or treat MRSA infections. He is investigating how S. aureus co-ordinates the control of tissue damaging toxins at the molecular level, with a view to designing new antibiotics that prevent the bacterium growing in human tissues. Professor Williams has determined the chemical structures of small signal molecules crucial to S. aureus toxin regulation and used the information to design antagonists which block toxin production.

*International patent filed*
During 1999, in order to inform strategy, the MRC decided to explore new bibliometric techniques which analyse patterns of research rather than simple measures of performance that had been used in the past. The first area to be examined in this way is likely to be ageing and the study should be complete by the autumn of 2000.

In addition, the MRC assessed the potential for routinely using bibliometric measures to inform peer review of major long term programmes. It found that bibliometric analysis offered a good measure of research group’s past performance which generally matched the assessment by the MRC Boards, but did not allow for strategic weighting as applied to MRC future proposals. The steering group set up to oversee the review therefore concluded that bibliometric analysis would not add sufficient value to peer review to be worthwhile routinely and should not be introduced into MRC procedures.

### MRC-SUPPORTED PUBLICATIONS (1988-97)

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of papers published with MRC grant or institute support (a)</th>
<th>Number of (a) published jointly with industry funding (%)</th>
<th>Number of (a) published jointly with UK charity and foundation funding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>3,764</td>
<td>333 (8.8)</td>
<td>1,165 31.0</td>
</tr>
<tr>
<td>1989</td>
<td>3,870</td>
<td>338 (8.7)</td>
<td>1,281 33.1</td>
</tr>
<tr>
<td>1990</td>
<td>3,910</td>
<td>440 (11.3)</td>
<td>1,369 35.0</td>
</tr>
<tr>
<td>1991</td>
<td>3,915</td>
<td>431 (11.0)</td>
<td>1,401 35.8</td>
</tr>
<tr>
<td>1992</td>
<td>3,889</td>
<td>415 (10.7)</td>
<td>1,385 35.0</td>
</tr>
<tr>
<td>1993</td>
<td>3,909</td>
<td>475 (12.2)</td>
<td>1,474 37.7</td>
</tr>
<tr>
<td>1994</td>
<td>3,912</td>
<td>439 (11.2)</td>
<td>1,558 39.8</td>
</tr>
<tr>
<td>1995</td>
<td>3,954</td>
<td>478 (12.1)</td>
<td>1,521 38.5</td>
</tr>
<tr>
<td>1996</td>
<td>3,945</td>
<td>526 (13.3)</td>
<td>1,544 39.1</td>
</tr>
<tr>
<td>1997</td>
<td>3,667</td>
<td>445 (12.1)</td>
<td>1,452 39.6</td>
</tr>
</tbody>
</table>
AWARDS AND PRIZES

Order of the British Empire

CBE

Professor Alan Baddeley, Professor of Psychology, Bristol University and former Director of the MRC Cognitive Development Unit (formerly the MRC Applied Psychology Unit) Cambridge, for services to the study of human memory.

Professor David Baird, Research Professor in Reproductive Endocrinology, for services to obstetrics and gynaecology, (MRC Clinical Research Professor 1985, former member of MRC Systems Board).

OBE

Dr Catherine Law, Senior Research Fellow at the MRC Environmental Epidemiology Unit, for services to public health

Leonard Stephen Levy, Head of Toxicology and Risk Assessment Group, MRC Institute for Environment and Health, for services to health and safety

MBE

Joyce Maxwell for services to the MRC Child Psychiatry Unit.

Robert John Moore, recently retired long serving member of staff at the MRC National Institute for Medical Research, for services to scientific librarianship.

ROYAL SOCIETY FELLOWS

Dr Cyrus Chothia, MRC Laboratory of Molecular Biology, Cambridge

Dr Michel Goedert, MRC Laboratory of Molecular Biology, Cambridge

Dr Kiyoshi Nagai, MRC Laboratory of Molecular Biology, Cambridge

Professor Peter Somogyi, Director of MRC Anatomical Neuropharmacology Unit, Oxford

Professor Ole Holger Peterson, MRC Research Professor, University of Liverpool
The spending review to determine levels of science funding for 2001/02 to 2003/04 began in Autumn 1999. As part of the review, MRC reported on progress since the 1998 Comprehensive Spending Review in the priority areas of Post Genome Challenge and Health of the Public. Highlights included:

**POST GENOME CHALLENGE**
- formation of a new Functional Genetics Unit (p22)
- expanded funding for genetic studies in *C.elegans* (worms), Fugu (fish) and mouse, as models of human gene function
- progress towards a large-scale national collection of human genetic samples to study links between genetics, lifestyle, environment and health (p29)
- expanded postgraduate training in bioinformatics (p27)
- capital investment in proteomics facilities in major research centres

**HEALTH OF THE PUBLIC**
- large-scale call for proposals (p31)
- new Social and Public Health Sciences Unit created in collaboration with Scottish Office (see annual report 98/99)
- expanded Clinical Trials Unit, with a broader remit (see annual report 98/99)
- increased funding for nutrition research (p33)
- call for proposals in antibiotic resistance (p31)

In the current spending review, MRC set out proposals for taking these initiatives further, and for building on opportunities to foster cross-disciplinary and cross-research council research.
Within the University sector, the MRC continues to provide support for a large and varied research portfolio through a range of grant schemes. In 1999 the MRC made awards totalling over £145m for research in universities and teaching hospitals. The schemes aim to help the MRC and higher education institutions to develop productive and mutually beneficial strategies and research programmes in partnership. The grants make funding available to investigators in response to their proposals (response-mode funding) after scrutiny of the applications by their scientific peers in order to ensure that the research will be of the highest quality.

**CENTRE GRANTS**

MRC Centre Grants aim to support multidisciplinary, research-centred environments in partnership with universities and involve significant investments by both the MRC and the host universities with full-time scientific leadership. MRC awarded three new centres in 1999/00 for work on a number of topics important to health; on Inflammation Research in Edinburgh under the Directorship of Professor John Savill, on Social, Genetic and Developmental Psychiatry under Professor Peter McGuffin at the Institute of Psychiatry and on developmental neurobiology directed by Professor Andrew Lumsden at King’s College London. The Council was also able to fund a Centre Development Grant, which will help set the scene for the evolution of a Centre, to University College London in Medical Molecular Virology headed by Professor Robin Weiss.

**CO-OPERATIVE GROUP GRANTS**

This scheme draws together researchers to improve the output of research environments and enhance individual research projects (supported by Component Grants where funded by the MRC). In 1999/00, the MRC set up 38 new Co-operative Group Grants throughout the UK. Over a third of Co-operative Groups involved interests of other research councils, for example the Group in St Andrew’s is using structural and chemical biology approaches to develop new ways of fighting infection. These new Co-operative Grants support the research projects of over 230 scientists funded through MRC Component Grants and by a wide range of other funders.

**PROPORTION OF CO-OPERATIVE GROUP GRANTS WITH KEY PARTNERS**

<table>
<thead>
<tr>
<th></th>
<th>With charities</th>
<th>With other research councils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>35 out of 38 awarded</td>
<td>13 out of 38 awarded</td>
</tr>
<tr>
<td>Percentage</td>
<td>92%</td>
<td>34%</td>
</tr>
</tbody>
</table>
CAREER ESTABLISHMENT GRANTS

Career Establishment Grants are awarded for five years to recently appointed clinical and non-clinical university scientists. The scheme aims to provide support to facilitate their establishment as independent investigators capable of winning further support in open competition. The scheme continues to be very popular with investigators; Council was able to make a further 15 awards in 1999, the second year of operation. The Council was able to increase the proportion of Career Establishment Grants involving clinical research to a third of the grants awarded.

INNOVATION GRANTS

This scheme provides small-scale, short-term funding for high-risk speculative or innovative research. Awards are made on the basis of the applicant’s track record of achievement from previous MRC funding. 12 awards were made from the applications considered in the 1999/00 competition.

OTHER SCHEMES

Forty four awards were made under the Joint Research Equipment Initiative in 1998/9 – value £2.07m. Thirty seven awards were made under the Realising Our Potential Award scheme – value £4.2m, and £1.2m was awarded under the LINK scheme.

The Joint Infrastructure Fund

The Joint Infrastructure Fund (JIF) was established in 1998 to improve infrastructure and provide major equipment in UK universities so that they can remain internationally competitive in research. The JIF has a total budget of £750m made up of £300m each from MRC’s parent Government Department – the DTI, and the Wellcome Trust plus £150m from HEFCE. The first three rounds of this competition have taken place and a total of 109 projects in 22 universities have been funded, many in the biomedical field. Awards which complement major MRC investments include grants to the Institute of Psychiatry for a Social, Genetic and Development Psychiatry Research Centre; University College London for work on Neurodegenerative Diseases; the University of Sussex for Research on Genome Damage and Stability and Cambridge University on Translational Cancer Research.

CLINICAL RESEARCH

As part of an effort to improve the quantity and quality of research proposals submitted to MRC in the area of clinical research a series of visits have been organised to selected University medical schools; these have highlighted a number of issues that will be considered by the Strategy Development Group and Council during 2000.

MRC WORKSHOPS

The Council hosted a number of workshops over the last year, attended by university and MRC scientists, both to inform the development of strategy and also to bring researchers into contact with other interested stakeholders. Such events were held, for example, to identify UK needs and priorities in proteomics (with BBSRC, EPSRC, academia and industry), microarray technology, synchrotron radiation (jointly with BBSRC on behalf of OST and the Wellcome Trust), neuroinformatics (with other research councils and the Wellcome Trust), the neurobiology of mental health and chemical biology. Other workshops were designed to inform trials design in sepsis and the critically ill and to consider the evaluation of complex packages of care.
RESEARCH UNITS AND INSTITUTES

A number of new MRC Units have been established and/or formally opened.

New Units

MRC Functional Genetics Unit  A new Functional Genetics Unit was established at the University of Oxford in October 1999 under the Honorary Directorship of Professor Kay Davies. The unit builds on Professor Davies’ long standing programme grant on the molecular genetics of muscular dystrophy and X-linked mental retardation; its mission is to determine the function of genes and their relevance to human disease using the most advanced technology available (e.g. genetics; proteomics; molecular physiology; structural studies; informatics) and a range of model systems (e.g. Drosophila melanogaster, Caenorhabditis elegans mouse).

MRC Cancer Cell Unit  In April 1999, some £15m was awarded to support cutting edge cancer research at the new MRC Cancer Cell Unit to be directed by Professor Ron Laskey (see 1999 Annual Report); the Unit will be integrated closely with the University of Cambridge Department of Clinical Oncology which is directed by Professor Bruce Ponder of the Cancer Research Campaign. Last year, the MRC contributed £5 million towards the construction of the new building; the University of Cambridge has contributed a matching amount.

MRC Human Immunology Unit  The Unit was established in October 1998 under the directorship of Professor Andrew McMichael. It was formally opened by the Secretary of State for International Development, the Rt Hon Clare Short, MP on 10 January 2000. The Unit will unite research groups and their projects across different disciplines in immunology, to create a single, dynamic entity. As well as a commitment to training clinical and non-clinical scientists, the initial focus of the Unit will be the human immune response and its role in disease processes notably HIV and AIDS.

MRC Resource Centre for Human Nutrition Research  On 8 December, Dr Elsie Widdowson cut the first turf in preparation for a new building which will be named in her honour and will house the MRC’s Resource Centre for Human Nutrition Research. The Resource Centre, directed by Dr Ann Prentice, will continue and expand the MRC’s commitment to nutrition research in Cambridge. It will contain purpose-built facilities for human volunteer studies, together with state-of-the-art laboratories for genetic, biochemical and metabolic research. The research will provide scientific evidence of the relationship between nutrition and health to underpin public health policy.

Other Unit Developments

MRC Human Reproductive Sciences Unit  In December 1999, Council approved research proposals for the MRC Human Reproductive Sciences Unit (formally the MRC Reproductive Biology Unit), Edinburgh submitted by the new Director, Professor Bob Millar. The Unit’s research will focus on reproductive health issues pertinent to a developed society with an ageing population. Key areas of research will be a) improving fertility and conception, b) lifestyle and environment effects on reproductive health, c) hormone dependent diseases and d) ageing and reproduction.

MRC Laboratories Jamaica: New Agreement with University of West Indies  In October 1999, the ownership of the MRC Laboratories (Jamaica) was transferred to the University of West Indies (UWI) on the retirement of the current Director, Professor Graham Serjeant. At that time, a renewable five-year tripartite agreement, (originally signed by MRC, UWI and the Jamaican Government in March 1997), came into force and this now provides the framework for the continuation of the on-going partnership between the MRC and UWI. The former MRC unit is now part of the newly established Tropical Medicine Research Institute (Director: Professor Terrance Forrester), which also encompasses the work of the Tropical Metabolism Research Unit.
(Jamaica) and the Chronic Disease Research Centre (Barbados), through the cross-cutting theme of clinical epidemiology. Some of the key areas being addressed are sickle cell disease, diabetes, hypertension and nutrition.

**MRC Mammalian Genetics Unit / MRC Human Genome Resource Centre** Studies of the mouse genome are being conducted in parallel with human genomics to generate comparative data and aid functional understanding of the human genome. The UK’s international lead in mouse genomics has been sustained over the last year by several new initiatives. In December 1999, the Council funded a mouse sequencing programme co-ordinated by Professor Steve Brown from the MRC Mammalian Genetics Unit (MGU) and involving a consortium of researchers from MRC units and UK universities. In addition, the Council recognised the need to make microarraying technology available to the scientific community and agreed to fund mouse and human arraying services via the MGU and the Human Genome Resource Centre respectively.

**MRC / University of Newcastle Development in Clinical Brain Ageing** The MRC has supported long-term research on dementia in Newcastle since 1979, via the MRC Neurochemical Pathology Unit. This year, MRC and University teams joined to establish a ‘Centre Development for Clinical Brain Ageing’ under the Directorship of Professor Jim Edwardson. Work is focused on dementia with Lewy bodies (the second most common cause of dementia after Alzheimer’s), how changes in the blood vessels and blood supply to the brain lead to dementia, the role of major genetic risk factors in dementia and a primary care research programme to address problems in management and treatment of these conditions in the community.

**New Appointments**

**MRC Social, Genetic and Developmental Psychiatry Centre** Professor Peter McGuffin was appointed to direct this Centre which seeks to bridge the gap between ‘nature’ (genetics) and ‘nurture’ (environment) as they interact in the development of complex behaviour patterns and disorders. The research spans epidemiology to family environment, twin and adoptee studies plus molecular genetics. In December 1999 Professor McGuffin was awarded a JIF grant of up to £14.4 million to fund infrastructure underpinning the work of the Centre.

**MRC Biostatistics Unit** Professor Simon Thompson took up the Directorship of the Biostatistics Unit in January 2000. His expertise includes the development of statistical methods and their direct application in areas of medical research such as psychiatry, primary care, surgery and cardiovascular medicine. The former Director, Professor Nick Day, retired during the year and was awarded an MRC Professorship to enable him to concentrate on his existing programme of work on the European Prospective Investigation into Cancer (EPIC).

**MRC Toxicology Unit** The search for a new Director for the MRC Toxicology Unit following the resignation of Professor Lewis Smith, was successfully completed with the appointment of Professor Pierluigi Nicotera, (currently at the University of Konstanz in Germany). Professor Nicotera will take up his post in the Autumn of 2000.
Unit Quinquennial Reviews

Quinquennial reviews continue to be an important part of strategy for long-term support of interdisciplinary research. During the year, the following six MRC units were reviewed. All work received high rankings.

- MRC Environmental Epidemiology Unit
- MRC Social and Public Health Sciences
- MRC Institute of Hearing Research
- MRC Toxicology
- MRC Human Reproductive Sciences Unit
- MRC Human Movement and Balance Unit

The five year strategic plan for the MRC Clinical Sciences Centre was endorsed by Council in July 1999
Working in partnership with other organisations is an important part of MRC strategy and increased energy has been devoted to promoting this where mutually beneficial. Prominent examples from 1999-2000 are as follows.

PARTNERSHIPS WITH OTHER RESEARCH COUNCILS

The Comprehensive Spending Review has provided the stimulus to set up a number of partnerships with other research councils to co-ordinate strategy and maximise the value of investment.

GENOMICS

A cross council working group was established during the year to co-ordinate genomics research and explore the scope for increased collaboration both on emerging technologies and on the ethical and social implications of genetics.

BIOINFORMATICS

To strengthen the UK research base in bioinformatics and facilitate modern research in areas such as biological function, treatment of disease, care of the environment and progress in manufacturing, a joint research council (BBSRC, EPSRC, MRC, NERC and PPARC) call for proposals was announced in July 1999 with the aim of establishing new bioinformatics research groups. Outline proposals were considered during December 1999 and full applications invited. The outcome will be known in 2000.

SYNCHROTRON RADIATION

The MRC co-ordinated a workshop in May 1999 on behalf of the research councils, the Wellcome Trust and OST to define UK needs for synchrotron radiation amongst those engaged in structural analysis of biological
macromolecules; the workshop was informed by a survey of almost 100 users of synchrotron radiation. Following consultations with the research community and the research councils and evidence to the House of Commons Science and Technology Committee, the UK Government in partnership with the Wellcome Trust, and the French Government announced in March 2000 that a new third generation synchrotron facility will be built at The Rutherford Appleton Laboratory, Oxford. This will be essential for taking forward UK strategy in the area, for enhancing industrial competitiveness through innovation by, for example, exploiting the fruits of the human genome project, and will be a key element in maintaining the excellence of the national research base.

MRC and BBSRC have submitted a joint bid to fund (over a five year period) one of the MAD beamlines, that was otherwise scheduled to close, at the European Synchrotron Radiation Source in Grenoble, France. If successful, this will maintain a high quality MAD beamline for the UK protein crystallography community until the new synchrotron is established.

THE LIFE SCIENCES, PHYSICAL SCIENCES AND ENGINEERING INTERFACE

MRC in collaboration with EPSRC and BBSRC, is participating in a series of workshops at 13 UK universities, aimed at promoting collaborations between researchers in the physical and biological sciences. These events, which encompass both presentations and discussion groups, focus on identifying opportunities and overcoming barriers to enable modern research to flourish.

ENVIRONMENT AND HEALTH

MRC and NERC issued a joint call for proposals in 1998 to stimulate research into the human health impacts of environmental exposures and to encourage collaborations between environmental and medical scientists. Under this initiative a Co-operative Group Grant was awarded to Professor A J McMichael (London School of Hygiene & Tropical Medicine) and colleagues, for work on human-induced climate change, ozone depletion and the impacts of such events on human health.

METROLOGY

A new EPSRC-led initiative was established during the year to increase the interaction of engineers and physicists in tackling important life science research areas involving measurement and analysis. MRC and BBSRC are working with EPSRC on this important new area. The first awards, funded by EPSRC, will be made in April 2000.

TISSUE ENGINEERING

EPSRC, BBSRC and MRC issued a joint call for proposals in August 1999 for the establishment of an interdisciplinary research centre in tissue engineering. Applications are expected to involve a broad range of relevant research groups and disciplines including molecular biology, developmental biology, cell biology, biochemistry, physiology, anatomy, material science, imaging, modelling, chemistry and engineering. The outcome will be known in 2000.

IMAGING

A call for proposals was issued by EPSRC in July 1999 for new Interdisciplinary Research Collaborations centring on information technology, but embracing a range of cognate disciplines. The proposal from Professor J M Brady (Oxford) for work on the generic problems involved in extracting clinically useful information from medical images and signals was particularly relevant to the MRC.
PARTNERSHIPS WITH THE MEDICAL RESEARCH CHARITIES

CANCER

Following a seminar at Downing Street in May 1999, a Cancer Research Funders Forum (CRFF) was established chaired by the MRC Chief Executive and comprising the senior representatives of major cancer charities (ICRF, CRC, LRF, Marie Curie, Ludwig), NHS R&D, Scottish, Welsh and Northern Ireland Health Departments. The MRC is carrying out (with CRC, ICRF and DH) a review of prostate cancer on behalf of the Forum.

CARDIOVASCULAR DISEASE

Over the past year, the Council has worked with the British Heart Foundation to develop an initiative in integrative biology. The aim of this initiative is to strengthen cardiovascular disease research in the UK by establishing a Cardiovascular Consortium which will bring together groups working within, and outside, the UK. A directly supported unit or centre within a University environment will form the core of the Consortium and the focus for other activities. Once established, the core will develop formal links with other groups (in the UK and abroad) drawing in areas of expertise which add strength to the overall network.

In December 1999, the MRC and the BHF agreed to continue support for the MRC/BHF Heart Protection Study. This trial, which began in 1993, is comparing cholesterol-lowering therapy over a five-year period versus placebo, (and separately, using a factorial design, antioxidants versus placebo), in 20,000 randomised patients at high-risk of coronary heart disease. The trial is expected to report at the end of 2001.

HUMAN DNA COLLECTIONS

Publication of the full human genome sequence will be an important milestone for medical research, but this is simply a starting point. Real health benefits will only come about from the greater understanding of gene function and regulation. The collection of very large numbers of human samples with associated clinical information, will allow the identification of genetic variation associated with greater disease risk and differences in how disease progresses in different people.

In January 2000, the MRC issued a call for proposals for DNA collections from large patient cohorts, to be developed as nationally available resources for studies of genetic factors influencing common multifactorial diseases. A new large prospective UK population cohort, currently under discussion by MRC, the Wellcome Trust and the NHS, will enable studies of the interaction between genetic, environmental and lifestyle risks for common diseases of adult life (for example, cardiovascular disease, breast and prostate cancer, arthritis) which may lead to:

- Identification of genetic variation that protects against disease
- Individualised risk assessment and preventative advice or treatment
- Developing and targeting of new interventions to prevent disease
- A major shift in emphasis from treatment towards prevention

The number of people needed for such a study (around 500,000 individuals) means that electronic access to diagnostic information from NHS records may be needed for efficient and cost effective follow-up. In March 2000 the MRC agreed to proceed to the next stage of developing this project. Recruitment is likely to be via those GP networks that are experienced in research.

This type of research raises important ethical issues, and for studies of this scale to be successful, it is crucial that they are done in a way that is publicly acceptable. MRC and the Wellcome Trust have jointly funded some qualitative research to gain a better understanding of public opinion on research that uses human biological samples. This study is the start of an ongoing public consultation process and will inform policy makers about how research in this area should be managed.
The Council continues to work closely with the NHS and the Health Departments at a number of levels across a range of shared interests. Developments in key priority areas agreed with Health Departments included:

**STRATEGIC REVIEW OF THE NHS R&D LEVY**

The Central Research and Development Committee of the Department of Health has undertaken a review of the NHS R&D Levy to revise the strategic framework for its use. The review was led by Professor Michael Clarke supported by a sub group of CRDC. The report concludes that the Levy remains the most appropriate way for the NHS to fund health related and health services research and the NHS costs of partners’ research. However, it also identifies the need for clearer focus on NHS needs and priorities, improved quality assurance systems for research programmes, involvement of wider communities and consumers in NHS R&D and the development of research capacity. Revisions to the arrangements for distributing the Levy are expected with a clear distinction between support for science undertaken in the health care system and funding for research on Central and Regional needs and priorities. The Boards and Council are currently considering the implications of this review.

The Clarke Group was additionally asked to examine opportunities and spending in five areas of national priority: ageing, cancer, cardiovascular disease and stroke, mental health, and primary care. Given that these are also areas of strategic importance to MRC, the Council is looking to ensure complementarity and synergy with the Clarke Group recommendations.

**CANCER**

Ovarian cancer is the fourth most common cancer amongst women in the UK and is potentially treatable if detected early enough. MRC, two major cancer charities and DH have collaborated in agreeing to invest £22m in a clinical trial of Ovarian Cancer Screening.

**SEXUAL ATTITUDES**

Sexual and reproductive health issues are not only central to UK Government health policy, but are also giving rise to global concern. The MRC Social and Public Health Sciences Unit has responded by developing a programme of research that will enhance understanding of the social, structural and environmental influences on sexual and reproductive health, and investigate the relationship of socio-economic status, gender and social context to particular health outcomes.

**NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE (NICE)**

NICE has two main objectives: firstly to improve the overall quality of health care delivered and secondly to reduce the unnecessary variations existing in clinical practice within the UK, both in terms of individual decisions and organisational policies. NICE will not commission research directly, but will depend on the quality of the research produced by industry, public sector funders and charities. The MRC will have an important role in strengthening evaluation methodology and broadening the application of cost effective measures.
TRANSMISSIBLE Spongiform Encephalopathies

The MRC has developed a broad portfolio of research into TSEs which is co-ordinated with other funders. Council has identified two areas – diagnostics and therapeutics – where the portfolio needs to be strengthened. The first of these areas is largely being addressed by the new MRC Prion Unit directed by Professor John Collinge, which aims to develop a blood-based test for vCJD. A workshop was held during the year, involving UK and overseas researchers, to identify opportunities for research into therapeutics, potential barriers to their development and how these barriers might be overcome.

Antibiotic Resistance

In December 1999 and March 2000, Council made the first tranche of awards resulting from a Web Highlight Notice on Antibiotic Resistance. Four proposals were funded out of 17 submitted; a further four grant proposals are currently being peer reviewed.

Future of the MRC General Practice Research Framework (GPRF)

The GPRF is a network of about 900 general practices throughout the UK providing access to over 10% of the population and is a national resource that facilitates many different clinical and epidemiological studies. It is currently embedded in the MRC Epidemiology and Medical Care Unit, which will close on the retirement of the Director Professor Tom Meade. In order to assure the future of the GPRF the Council has looked at a variety of options for relocating it elsewhere; a decision will be made later in 2000.

Primary Care

The first round of the joint MRC/DH initiative on Primary Health Care Research was initiated and completed during the 98/99 session; nine strategic grants including one programme grant and five trial grants were supported. A second call for proposals was issued in the Autumn of 1999 with a view to making further awards in 2000.

Health of the Public

The MRC’s Health of the Public initiative will expand the UK’s capacity for high quality research into the developmental, environmental and socio-economic factors affecting health and health inequalities and strengthen research into interventions. The first tranche of four awards was made in 1999 following a call for proposals; and evaluation of proposals submitted under the second round is currently underway. To promote training in this area, a pilot project was initiated with the NHS R&D Directorate to fund research fellowships; this was accommodated by expanding the MRC Health Services Research Fellowship Scheme.

MMR Vaccination, Autism and Inflammatory Bowel Disorders

The Council established at DH’s request an expert Strategy Development Subgroup to review research into inflammatory bowel disorders (IBD) and autism. The Subgroup found no evidence of a causal link between measles, mumps and rubella vaccine (MMR) and chronic gastrointestinal inflammation and autism, but recommended that the MRC and DH should continue to keep this area under review. The MRC is now seeking proposals in the areas specifically highlighted by the Subgroup, and particularly in the field of IBD.
CONTRACEPTIVE DEVELOPMENT NETWORK

The control of fertility is a prerequisite for human reproductive health. In December 1999, Council approved an award of £2.7m over five years to Professor Baird and colleagues (Edinburgh) to continue research conducted under the Contraceptive Development Network that was established in 1995 with funding from MRC and DFID. The research will focus on the development of new methods of contraception for men and women, utilising the network which links Edinburgh with Cape Town, Hong Kong, Shanghai and Nigeria.

DEPARTMENT FOR INTERNATIONAL DEVELOPMENT

MRC and Department for International Development are commissioning a joint scoping study to identify new areas where the Council’s portfolio of research relevant to developing societies might be expanded. The study will identify research priorities and opportunities or gaps taking into account global issues but focussing on the UK perspective. The London and Liverpool Schools of Tropical Medicine are working together to develop the proposals for the study, which will be considered by MRC and DFID in the coming year.

DEPARTMENT OF THE ENVIRONMENT, TRANSPORT AND THE REGIONS

The MRC Institute for Environment and Health published a report in November 1999 on Benzene in the Environment: An evaluation of exposure of the UK general population and possible adverse health which was commissioned by DETR. The report studied data on contemporary sources and population exposure to benzene in the UK, together with information on the known human health effects (in particular leukaemia) and assessed any likely risks. The report summarises and presents all the relevant data and provides an overall evaluation of the risks to public health of benzene in the environment.
HIGHER EDUCATION FUNDING COUNCIL

MRC was invited to contribute views, in November 1999, to an evidence-based review of the Research Assessment Exercise. Topics being debated in the review include the dual support system; selectivity in research funding and research training; the special nature of health-related disciplines; career development for young academic researchers and for researchers; interdisciplinarity and discipline boundaries; and comparisons with research funding models in other countries.

FOOD STANDARDS AGENCY

The Food Standards Agency came into existence in April 2000 under the Chairmanship of Sir John Krebs; the Council has taken steps to forge interactions with this new body.

OFFICE OF SCIENCE AND TECHNOLOGY – FORESIGHT PROGRAMMES

Technology needs across the science base - A joint research councils’ Foresight Associate Programme, coordinated by PPARC, was established in 1999 to explore what technologies are expected to be in UK laboratories and research facilities in the next ten to twenty years, to explore the major opportunities this presents for UK industry and to seek areas of common interest where technologies are needed in more than one sector. The final report will be published later in 2000.

Genomics - The MRC, in collaboration with BBSRC, EPSRC, NERC and the DTI under the aegis of ‘Foresight’ has produced ‘Demystifying Genomics’ a publication to explain the basis for and implications of genomics in the broadest context - its origins, implications and future directions, as well as the dilemmas it raises and how they might be tackled.

Human Nutrition Research - MRC and BBSRC jointly established in 1998 a Foresight Associate Programme in Human Nutrition Research to survey the field in the UK and identify, in an international context, the major current and emerging issues and opportunities. The report of the review will inform the work of the Foresight Panels and Networks, as well as research council strategy in this area.

WORLD HEALTH ORGANISATION

Pneumonia caused by Streptococcus pneumoniae leading cause of death in young children in West Africa. The currently licensed vaccine is poorly immunogenic in this age group. The MRC Laboratories, The Gambia will begin a Phase III efficacy trial of a new 9 valent pneumococcal polysaccharide/protein conjugate vaccine in the first half of 2000 in Central and Upper River Divisions, The Gambia, following successful completion of the Phase II safety and immunogenicity study. The trial will be co-funded by the MRC, the Bill and Melinda Gates Foundation, WHO and Wyeth-Lederle.

EUROPEAN MOLECULAR BIOLOGY LABORATORY

The UK is one of 16 member states that contribute funding for the European Molecular Biology Laboratory (EMBL); MRC manages that contribution on behalf of the Government. In light of the fact that the Director of EMBL is preparing new research proposals and an indicative budget for the quinquennial period 2001-2005, the Council set in train, during 1999, a multinational review of EMBL to inform funding decisions.
INTERNATIONAL COLLABORATIONS

Science is global, and the MRC attaches a high priority to international collaborations, joint working with international partners and links with organisations which can assist better international scientific networks.

The MRC has a lead role in partnership with Department of Health and other research councils in developing the UK policy in relation to the biomedical aspects of EC framework programmes.

The MRC is responsible for the UK contribution and input to a number of international biomedical organisations including the European Molecular Biology Laboratory (EMBL) and the European Molecular Biology Conference (EMBC) in Heidelberg, the International Agency for Research on Cancer (IARC), in Lyon and the Human Frontier Science Program (HFSP) and European Science Foundation (ESF) both based in Strasbourg.

Council will receive the MRC review of EMBL during 2000. A review of HFSP has now been initiated and should be completed over the next year.

STRENGTHENING INTERNATIONAL PARTNERSHIPS

During the year two joint workshops were held in Paris and Cambridge in partnership with CNRS, INSEMER and the British Council. These brought together leading UK and French scientists to exchange ideas and discuss potential collaborative opportunities in two key strategic areas: 1) mouse genomics and 2) genetic epidemiology. A multinational scientific coordinating committee will be meeting soon. The workshop on genetic epidemiology, also acted as an impetus for closer co-ordination of DNA collections. A follow-up workshop on statistical methodology has also been proposed.

EUROPEAN BIOINFORMATICS INSTITUTE

MRC, on behalf of the UK, has worked with other member states of EMBL over the last year to resolve an unexpected shortfall in funding for the European Bioinformatics Institute (the Cambridge Outstation of EMBL) that resulted from withdrawal of support by one of its original sponsors. The Council has additionally agreed to open up MRC funding schemes to EBI scientists in order to help strengthen research programmes there.

The European Mouse Mutant Archive is a pan-European facility for the storage and provision of valuable mouse models to the whole scientific community. This facility was initially developed with support from the EC, together with national investments in several European countries, including support from the MRC. The central site is Monterotondo in Italy with nodes in the UK, France, Sweden and Portugal. As EC funding is now coming to an end the MRC is actively exploring alternative options for more stable long-term funding.

The Human Frontiers Science Programme, a transcontinental grants and fellowship programme celebrated its 10th anniversary this year with scientific and political events being held in Japan, Europe and the USA.

The European Science Foundation (ESF) also celebrated its 25th anniversary in 1999.

EUROPEAN COMMISSION FRAMEWORK PROGRAMMES

Framework V

The call for proposals under the “Quality of Life and Management of Living Resources” programme of the Vth Framework was in March 1999. Two rounds of proposals have been considered, with the UK academic community doing extremely well. UK scientists participated in 71% of all successful proposals in
the first evaluation round. The percentage of UK co-ordinated successful proposals was exceptionally high, 21%. MRC units/institutes have a success rate nearly twice as high as the overall rate (34%, compared with 17.8%) and are partners in a number of important pan-European projects including:

- A European collaborative project on the development of a malaria vaccine
- A large scale project on tuberculosis vaccine development
- An international collaborative molecular genetic study of autism
- A “European Vaccine Effort Against HIV/AIDS”
- A European comparative genetics resource project whose aim is to achieve a better understanding of the molecular basis of inherited diseases. This infrastructure project will create a unique resource for the scientific community and the pharmaceutical industry.

MRC is represented on the Programme Management Committee and MRC Officers continue to play a key role as national contact points for this framework programme, in advising UK researchers.

Framework VI

In preparation for Framework VI, the MRC carried out a survey of unit/institute Directors and board members in Autumn 1999. This identified a number of key scientific areas where a European approach to research was either necessary or provided significant ‘added value’. Hence MRC was in a good position when the preliminary negotiations on FPVI (2003 onwards) began early this year.

The EC produced a policy paper “Towards a European Research Area” in January, which initiated the debate on the next Framework programme, FPVI, as well as providing a longer-term vision for European research. MRC has subsequently been actively involved in discussions with policy makers in Brussels and with its UK partners in the research councils and Government, to make sure that its views are put on the agenda at this critical early stage of negotiations. The formal negotiation process for FPVI will begin in earnest in Summer 2000 and MRC will continue to play a very active part in these discussions.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>International Collaborative Projects (number and income)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EC</td>
<td>137</td>
<td>114</td>
<td>136</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>£2.7</td>
<td>£2.7</td>
<td>£3.2</td>
<td>£3.7</td>
</tr>
<tr>
<td>UN (including WHO, IARC)</td>
<td>14</td>
<td>11</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>£0.3</td>
<td>£0.3</td>
<td>£0.4</td>
<td>£0.6</td>
</tr>
<tr>
<td>Others (including HFSP, ESF, NATO, EMBO)</td>
<td>22</td>
<td>26</td>
<td>36</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>£0.3</td>
<td>£0.3</td>
<td>£0.5</td>
<td>£0.5</td>
</tr>
<tr>
<td>Other international agreements (including governments, charities and industries)</td>
<td>87</td>
<td>78</td>
<td>85</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>£2.1</td>
<td>£2.3</td>
<td>£1.9</td>
<td>£2.8</td>
</tr>
<tr>
<td>Total</td>
<td>260</td>
<td>229</td>
<td>274</td>
<td>260</td>
</tr>
<tr>
<td></td>
<td>£5.4</td>
<td>£5.6</td>
<td>£6.0</td>
<td>£7.6</td>
</tr>
</tbody>
</table>
The MRC directly employs over 3,000 staff in its own units and institutes which are mainly based within medical schools and universities. Training and career opportunities are also provided for a similar number of researchers in universities - from graduate students through to the most senior appointments of MRC Research Professorships.

<table>
<thead>
<tr>
<th>Family</th>
<th>April 1999</th>
<th>Full-time</th>
<th>February 2000</th>
<th>Part-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Science</td>
<td>1,060</td>
<td>1,115</td>
<td></td>
<td>43</td>
</tr>
<tr>
<td>Research Project Support</td>
<td>849</td>
<td>897</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>Management Admin and Policy</td>
<td>420</td>
<td>420</td>
<td></td>
<td>53</td>
</tr>
<tr>
<td>Technical Services</td>
<td>317</td>
<td>342</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>Infrastructure</td>
<td>102</td>
<td>105</td>
<td></td>
<td>64</td>
</tr>
<tr>
<td>Locally employed staff (overseas)</td>
<td>466</td>
<td>569</td>
<td></td>
<td>128</td>
</tr>
<tr>
<td>Total</td>
<td>3,214</td>
<td>3,448</td>
<td>427</td>
<td>334</td>
</tr>
</tbody>
</table>
PAY AND GRADING

The MRC has completed the third pay review cycle under its delegated pay and grading structure. The aims of the 1999 settlement were to:

- maintain competitive salaries to attract and retain high quality research staff in the face of direct competition from other employers
- reward outstanding performance with additional payments
- address specific difficulties in recruiting and retaining staff at units in Inner London and clinicians throughout the country.

NEW AWARDS OF FELLOWSHIPS AND STUDENTSHIPS

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and collaborative studentships</td>
<td>362</td>
<td>358</td>
<td>361</td>
<td>369</td>
<td>369</td>
<td>372</td>
</tr>
<tr>
<td>Industrial collaborative studentships</td>
<td>19</td>
<td>17</td>
<td>26</td>
<td>27</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Master level studentships</td>
<td>75</td>
<td>70</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FELLOWSHIP AWARDS</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Training Fellowships</td>
<td>73</td>
<td>69</td>
<td>65</td>
<td>75</td>
<td>88</td>
<td>22*</td>
</tr>
<tr>
<td>Clinician Scientist Fellowships</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Career Development Awards</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>5</td>
<td>15</td>
<td>*</td>
</tr>
<tr>
<td>Senior Non-Clinical Fellowships</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>8</td>
<td>*</td>
</tr>
<tr>
<td>Senior Clinical Fellowships</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

*awaiting results of subsequent competitions

EMPLOYMENT POLICIES

The following employment policies have been designed or redesigned to facilitate the management of high quality research staff to maintain Council’s policy of supporting scientific excellence:

- a policy setting out standards of conduct for MRC staff in relation to the security and use of information systems and information technology
- a set of principles to facilitate timely consultation with MRC staff during reviews of the merit of scientific work undertaken and the use of resources in its establishments or strategic reviews of a scientific field.
HEALTH AND SAFETY

The MRC has made steady progress towards its aim of demonstrating best practice in health and safety management. A key factor of the Council’s continuous improvement process is the use of risk management as a tool to ensure the protection of our staff, assets and research programmes.

Each research establishment is required to produce a contingency plan to ensure the continuity of their research programmes in adverse circumstances eg: fire, flood, loss of services.

The Health and Safety Management Section has strengthened its links with host institutions’ safety advisors and has agreed formal arrangements on the provision of day to day health and safety support for MRC staff.

Training has been a particularly active area. Training Courses have been developed for Unit Safety Co-ordinators, workstation risk assessment and hazardous substances risk assessment. The Council also launched its training course for Biological Safety Officers which has been received enthusiastically by the University Sector as well as its own staff.

It is the MRC’s intention over the coming year to provide health and safety management seminars for senior managers and formal training programmes for all unit safety co-ordinators.

WOMEN IN SCIENCE

The MRC Equal Opportunities Subcommittee is conducting an audit of MRC employee data to ensure that MRC offers equal opportunities in its employment practices and addresses any perceived imbalances.

The MRC is supporting an in-depth in-house study of the career experiences of scientific researchers to investigate factors which might erode the career commitment of women in science.

A survey of university research staff to identify reasons why fewer women than men apply for grants has been ongoing in partnership with the Wellcome Trust and other research councils. Publication of the findings is anticipated in the autumn 2000. A application and awards trends are shown in the gender tables at the end of this chapter. These show no evidence of gender bias in awards made.

TRAINING IN TRANSFERABLE SKILLS

It is now four years since the publication of the Concordat on Contract Research Staff, and action to address the needs of this group of employees continues. MRC aims to set a leading example of best practice.

For MRC staff a Council-wide training needs analysis was conducted to identify the management and communication skills needed to complement specialist and research skills to ensure staff can contribute fully to Council’s objectives e.g. effective management of resources, exploitation of research findings. As a result a pro-active training strategy has been adopted to provide tailored development programmes for each group of staff covering a range of relevant skills.

It is vital that postgraduate research trainees have a good appreciation of the generic skills training that a research studentship offers. Development of these skills benefit students’ future careers whether or not they remain in academic research. The Research Councils jointly sponsor the Graduate School Programme, which provides an intensive one week course to raise awareness and development of personal skills. In 1999 MRC increased its subscription to this scheme, so that the majority of MRC students now have the opportunity to attend a GSP course.
DEVELOPING THE RESEARCH WORKFORCE CAPACITY TO ENABLE THE SCIENTIFIC STRATEGY

The Council’s mainstream Research Career Award schemes all offer opportunities for research training and career development across the entire spectrum of the MRC scientific remit. When the scientific strategy identifies a need to develop the research workforce in a certain area, a number of steps are taken to address that need, including the development of partnerships with other funders to appoint Fellows in selected areas, as described below. Other steps might include the establishment of a separate, ring-fenced competition, or alternatively ‘earmarking’ of awards in some schemes for applicants from a particular scientific area.

The ring-fenced competitions for studentships and fellowships in Bioinformatics and neuroinformatics are now in their second year. 20 new research studentship awards and six new Fellowship awards were made in the 1999/2000 award year, bringing the total cadre of Fellows to 12, currently, with a further round of appointments anticipated in 2000/01. This scheme is kept under review to ensure that it is effective in meeting the challenge of providing new multidisciplinary expertise to tackle the explosion of information generated by the Human Genome Project.

A new type of Fellowship was offered for the first time in 1999 – the Patient-oriented Clinician Scientist Fellowship. This recognised the need for some Clinician Scientist Fellows (usually in more craft-based medical specialties) to spend a greater proportion of time in clinical contact with patients than the 20% of time that standard Fellowships provide. The first round of applications for this award generated 11 applications and five new Patient-oriented Clinician Scientist Fellows.

RESEARCH FELLOWSHIPS FUNDING PARTNERSHIPS

Across the portfolio of research career award schemes there has been an increase in the number of joint Fellowships offered in partnership with other organisations. This has been achieved through extension and tailoring of schemes to accommodate shared interests of MRC and the co-funding partner.

MRC/PPARC RESEARCH FELLOWSHIPS

As part of a broad initiative to promote interdisciplinary research at the physical sciences/life sciences interface, the MRC/PPARC Research Fellowship scheme was established in 1999. A small number of applications have been received with awards to be announced in May and June 2000, for take up in October 2000. The outcome of this first round will be taken into account in discussions with other research councils with a view to extending Fellowships to other areas.

JOINT CLINICAL TRAINING FELLOWSHIPS WITH ROYAL COLLEGES

Following on from the successful establishment of Joint Clinical Training Fellowships with the Royal Colleges of Surgeons, and the Royal College of Obstetrics and Gynaecology, a new joint Fellowship in Clinical Infections & Medical Microbiology was launched for the first time in autumn 1999. All these schemes encourage take up of research training in medical specialities where the academic research needs to attract more researchers.
MRC/ GLAXO-WELLCOME CLINICIAN SCIENTISTS FELLOWSHIP PILOT

In response to the pharmaceutical industry’s need for academic clinical researchers with a high level of understanding of commercial research and development, the MRC are piloting a new Clinician Scientist Fellowship jointly funded by Glaxo-Wellcome. The Fellow will be appointed in Summer 2000, and will benefit from the appointment of a senior scientist from Glaxo-Wellcome as their personal mentor.

MRC/ REGION SPECIAL TRAINING FELLOWSHIPS IN HEALTH OF THE PUBLIC

A well established joint scheme is the joint MRC/ Region Special Training Fellowships in health services research jointly funded with the Health Departments. This was expanded in 1999 as part of wider initiatives to build up the research base in health of the public. From a total of 19 awards under this scheme, 4 new MRC/ Region Health of the Public Fellows were appointed in March 2000.

RECRUITMENT TO THE UK RESEARCH BASE

A major issue throughout the year has been the growing level of national debate about the attractiveness of research careers within the UK. MRC has actively participated in policy debates to make constructive contributions on national needs and priorities and provide available evidence about the strength and quality of the UK research workforce. Recruitment from abroad is part of our longer-term strategy for building critical mass and addressing the shortfall in research capacity. The International Appointments Initiative plays an important role in this.

POSTGRADUATE RESEARCH STUDENTSHP POLICY

Postgraduate research training continues to be under the spotlight, but with debate now beginning to crystallise in some areas. The UK Life Sciences Committee published a report in January 2000 summarising available evidence as well as opinions on the way forward. This signals a high level of support for a 1+3 postgraduate model, and widespread support for fewer more highly paid students. In the coming year MRC will be reviewing its policies to ensure that the Council can sustain its reputation for high quality training that provides the foundations of the UK research capacity.

TENURE-TRACK CLINICIAN SCIENTIST FELLOWSHIPS

Both the Royal College of Physicians and the Academy of Medical Sciences published reports highlighting concerns about academic clinical research careers. MRC’s strong contribution to the health of the clinical cadre of research scientists, was favourably regarded. Nonetheless, the reports provided the impetus for revision of the MRC Clinician Scientist Fellowship scheme to ensure that it meets current needs, notably in securing tenure track agreements with host institutions.

INTERNATIONAL APPOINTMENTS SCHEME

The MRC seeks to respond rapidly to opportunities for recruitment and also to take positive action in areas of scientific priority where lack of scientific capacity nationally is the issue. The MRC attracted research scientists of international standing to senior positions in the UK through its International Appointments Scheme.
## GENDER DATA

### RESEARCH STUDENTSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>% of total</th>
<th>Female</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>227</td>
<td>48</td>
<td>248</td>
<td>52</td>
</tr>
<tr>
<td>1995</td>
<td>203</td>
<td>46</td>
<td>240</td>
<td>54</td>
</tr>
<tr>
<td>1996</td>
<td>207</td>
<td>46</td>
<td>241</td>
<td>54</td>
</tr>
<tr>
<td>1997</td>
<td>157</td>
<td>43</td>
<td>211</td>
<td>57</td>
</tr>
<tr>
<td>1998</td>
<td>153</td>
<td>42</td>
<td>213</td>
<td>58</td>
</tr>
</tbody>
</table>

Research studentships including Collaborative and Industrial Studentships

## RESEARCH FELLOWSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Number of applications</th>
<th>Number of awards</th>
<th>Female</th>
<th>Number of applications</th>
<th>Number of awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993/94</td>
<td>16</td>
<td>6</td>
<td>20</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994/95</td>
<td>40</td>
<td>7</td>
<td>26</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995/96</td>
<td>41</td>
<td>2</td>
<td>49</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996/97</td>
<td>56</td>
<td>6</td>
<td>63</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997/98</td>
<td>53</td>
<td>12</td>
<td>40</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998/99</td>
<td>33</td>
<td>13</td>
<td>22</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999/00</td>
<td>26</td>
<td>7</td>
<td>21</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### CAREER DEVELOPMENT AWARDS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male Number of applications</th>
<th>Male Number of awards</th>
<th>Female Number of applications</th>
<th>Female Number of awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993/94</td>
<td>39</td>
<td>10</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>1994/95</td>
<td>43</td>
<td>9</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>1995/96</td>
<td>55</td>
<td>5</td>
<td>36</td>
<td>5</td>
</tr>
<tr>
<td>1996/97</td>
<td>48</td>
<td>6</td>
<td>41</td>
<td>4</td>
</tr>
<tr>
<td>1997/98</td>
<td>70</td>
<td>8</td>
<td>55</td>
<td>2</td>
</tr>
<tr>
<td>1998/99</td>
<td>44</td>
<td>5</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>1999/00</td>
<td>36</td>
<td>4</td>
<td>27</td>
<td>6</td>
</tr>
</tbody>
</table>

### SENIOR NON-CLINICAL FELLOWSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male Number of applications</th>
<th>Male Number of awards</th>
<th>Female Number of applications</th>
<th>Female Number of awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993/94</td>
<td>47</td>
<td>5</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>1994/95</td>
<td>52</td>
<td>6</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>1995/96</td>
<td>36</td>
<td>4</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>1996/97</td>
<td>25</td>
<td>4</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>1997/98</td>
<td>35</td>
<td>8</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>1998/99</td>
<td>27</td>
<td>7</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1999/00*</td>
<td>25</td>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>
## CLINICAL TRAINING FELLOWSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of applications</td>
<td>Number of awards</td>
</tr>
<tr>
<td>1993/94</td>
<td>164</td>
<td>38</td>
</tr>
<tr>
<td>1994/95</td>
<td>192</td>
<td>39</td>
</tr>
<tr>
<td>1995/96</td>
<td>192</td>
<td>33</td>
</tr>
<tr>
<td>1996/97</td>
<td>155</td>
<td>26</td>
</tr>
<tr>
<td>1997/98</td>
<td>158</td>
<td>31</td>
</tr>
<tr>
<td>1998/99</td>
<td>172</td>
<td>32</td>
</tr>
<tr>
<td>1999/00*</td>
<td>159</td>
<td>39</td>
</tr>
</tbody>
</table>

* Nos. of applications indicate both competitions for 1999/00 year.

## CLINICAL SCIENTIST FELLOWSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of applications</td>
<td>Number of awards</td>
</tr>
<tr>
<td>1993/94</td>
<td>26</td>
<td>8</td>
</tr>
<tr>
<td>1994/95</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>1995/96</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>1996/97</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>1997/98</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>1998/99</td>
<td>26</td>
<td>8</td>
</tr>
<tr>
<td>1999/00</td>
<td>32</td>
<td>11</td>
</tr>
</tbody>
</table>
### SENIOR CLINICAL FELLOWSHIPS

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993/94</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>1994/95</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>1995/96</td>
<td>23</td>
<td>3</td>
</tr>
<tr>
<td>1996/97</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>1997/98</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>1998/99</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>1999/00</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

### SPECIAL TRAINING FELLOWSHIPS IN HEALTH SERVICES RESEARCH

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993/94</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>1994/95</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>1995/96</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>1996/97</td>
<td>24</td>
<td>39</td>
</tr>
<tr>
<td>1997/98</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td>1998/99</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>1999/00</td>
<td>19</td>
<td>25</td>
</tr>
</tbody>
</table>

### SPECIAL TRAINING FELLOWSHIPS IN BIOINFORMATICS (SCHEME INTRODUCED IN 1998/99 SESSION)

<table>
<thead>
<tr>
<th>START DATE</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998/99</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>1999/00</td>
<td>16</td>
<td>6</td>
</tr>
</tbody>
</table>
MRC commercial exploitation activities have been managed through a variety of mechanisms including:

- Technology Transfer Group (TTG) at MRC Head Office: responsible for the development of MRC exploitation strategy, management of the MRC’s intellectual property portfolio, exploitation of inventions (including licensing and “start-up” company formation) and related agreements and administration.

- MRC Collaborative Centres (Mill Hill and Edinburgh): the Collaborative Centres have offered laboratory based project management of applied research funded by industrial partners and incubation of “start-up” companies.

MRC has combined the functions undertaken by TTG and the Collaborative Centres into a single vehicle – Medical Research Council Technology (MRCT), with increased flexibility to further enhance exploitation. Medical Research Council Technology is a company limited by guarantee, and holds charitable status. Management reports to a MRC Council appointed Board of Directors (Governing Body). The MRC will retain the ownership of its intellectual property and MRCT will act as its exclusive agent to manage that intellectual property. Medical Research Council Technology and Cancer Research Campaign Technology are working together to develop a commercial exploitation strategy for the CRC/MRC Cancer Unit which is being established in Cambridge.

In addition to maintaining its existing activities, MRCT will manage “development gap” studies to enhance the value of MRC intellectual property, including: strengthening patent claims, technology validation and technology packaging. There will be greater use of its laboratories as incubators for “start-up” companies.

The MRC promotes the take-up and exploitation of MRC knowledge and research - by the NHS, by Industry and by Government.
The MRC continues to play an active role in the establishment of new companies to commercialise MRC proprietary technologies. Starting from Cambridge Antibody Technology’s establishment in the early 1990s, the companies are at various stages of growth with most having successfully completed several rounds of fund-raising. The companies are primarily based in the UK, although they operate globally.

Highlights last year included:

**Cobra Therapeutics Ltd** was acquired by ML Laboratories PLC and is now a wholly owned subsidiary within the ML Group.

**Gendaq Ltd** continues to be “incubated” in the MRCT centre at Mill Hill. In April 2000, the Company announced the completion of a £5.75 million private equity financing to develop further its proprietary platform of gene regulation technology.

**AERES Biomedica Ltd** and **Viogen Ltd**

Two new companies have been established as “spin-outs” from the former MRC Collaborative Centre, Mill Hill to incorporate the Centre’s antibody engineering business and virology business, respectively. Each company is being “incubated” within the MRCT centre, Mill Hill.

To facilitate the formation of spin out companies, MRC established its own investment Fund, UK Medical Ventures (regulated by IMRO). In April 1998, the Fund closed with £40 million from eight Limited Partners. The Fund is managed by a wholly-owned MRC subsidiary, MVM Ltd. To date UK Medical Ventures have invested in six companies, and are actively engaged in building further companies based on MRC technology.

**THERAPEUTIC ANTIBODIES**

The 1998/9 Annual Report noted the launch of new therapeutic products using licensed MRC patented technology in the field of ‘humanised’ monoclonal antibodies, developed at the MRC Laboratory of Molecular Biology. Increased royalty income from this source largely accounts for the rise in MRC’s income from exploitation of its intellectual property in 1999/2000 to £7.2 million (provisional figure).

MRC patented technology is also the basis of another approach (antibody phage display libraries) for the development of human therapeutic antibodies, undertaken by Cambridge Antibody Technology Ltd. As at 30 November 1999 four fully human monoclonal antibodies isolated and developed by Cambridge Antibody Technology were in clinical trials. The most advanced antibody derived from this route is being developed by BASF Pharma for the treatment of rheumatoid arthritis and is now in Phase 3 clinical trials. Yet another approach, based on patented collaborative research involving the MRC Laboratory of Molecular Biology and the (BBSRC) Babraham Institute, relates to the production of human antibodies in transgenic mice and has been licensed and developed by GenPharm (now part of Medarex Inc) and Abgenix Inc.

**LINK PROGRAMMES**

The Government’s LINK scheme promotes high-quality, pre-competitive research collaborations between academic and industrial researchers. The MRC currently takes the lead in two LINK Programmes: Integrated Approaches to Healthy Ageing and Genetic & Environmental Interactions in Health. The MRC is also a sponsoring partner in a number of other Programmes. The MRC, together with BBSRC and DTI, have decided to launch a new LINK Programme in Applied Genomics to assist UK companies in exploiting the wealth of information emerging from genome sequencing projects.
NUMBER OF STAFF EMPLOYED

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cambridge Antibody Technology*</td>
<td>47</td>
<td>66</td>
<td>108</td>
<td>150</td>
<td>154</td>
</tr>
<tr>
<td>COBRA (formerly Therexsys)*</td>
<td>32</td>
<td>52</td>
<td>55</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Prolifix*</td>
<td>6</td>
<td>10</td>
<td>23</td>
<td>25</td>
<td>31</td>
</tr>
<tr>
<td>Collaborative Centre, Mill Hill</td>
<td>50</td>
<td>39</td>
<td>46</td>
<td>44</td>
<td>22</td>
</tr>
<tr>
<td>Collaborative Centre, Scotland</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Ribotargets*</td>
<td>-</td>
<td>-</td>
<td>15</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>Cambridge Genetics*</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>Gendaq*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Aeres*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>Virogen*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>MVM*</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TOTAL

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Income (millions)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>1.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

(Celltech was founded to exploit MRC research. Celltech recently merged with Chirosciences and then with Medeva)

*denotes companies where MRC is a shareholder

The numbers of new patent filings and licensing agreements have shown steady growth. Annual income from licences has shown a greater increase.

Annual licensing income (1992 - 93 to 1999 - 00)
THE NHS

The MRC ensures its work addresses high priority health issues and continues to deploy a range of approaches to support and disseminate research directly applicable to policy and practice in health care, as well as working to exploit its more basic science.

HIP FRACTURE STUDIES

A study conducted by the MRC Environmental Epidemiology Unit showed that a lifetime exposure to flouridated water carries no increased risk of hip fractures. The findings, which were published in The Lancet show that concerns about possible risk of hip fracture should not be a reason for withholding flouridation of water supplies.

RELENZA NICE STUDY

The General Practice Research Framework undertook to co-ordinate a research study to provide data on influenza seen by doctors in general practice. The study, conducted during the winter “flu’ season”, was aimed at providing evidence on the accuracy of diagnosing influenza in general practice and on the number of patients whose influenza would be at the correct stage for treatment with a new drug, Relenza. The data will help the National Institute for Clinical Excellence (NICE) to determine whether prescribing Relenza would be clinically/ cost effective for the NHS. The results are expected during 2000.

CHILDREN’S DIET STUDY

A study by MRC scientists of 4,500 children’s diets in the 1950s, compared to a similar number of children of the same age in 1992 showed that today’s diets are less healthy. In the 1950s children ate considerably more bread and vegetables and less sugar and soft drinks, providing a higher carbohydrate and fibre content and more in line with current recommendations for healthy eating. Tea was the most common drink consumed by four year olds in 1950, while soft drinks, scarce in 1950, were consumed by 90% of the children in the 1990s. Consequently, sugar intake was higher in the modern children, and the proportion of energy they derived from total sugars was much higher. Although vitamin C intakes were similar, the 1992 children got most of their vitamin C from juices and drinks, whereas the 1950s children got most of theirs from vegetables. Intake of iron was less in the 1992 children mainly because the children in 1950 ate red meat rather than poultry. Although the 1950s children had more fat in their diet, the diet consumed in 1950 was of greater value in terms of vitamins, minerals and fibre.

MORE EFFECTIVE TREATMENT OF DEPRESSION

The clinical trial carried out by John Teasdale and colleagues at the MRC Cognition and Brain Sciences Unit showed that psychotherapy was more effective than continuing antidepressant medication in reducing the high frequency of relapse and recurrence that contributes to poor long-term recovery rates of patients suffering from depression.
MRC contributes to the national scientific advisory system and to scientific policy in a number of ways.

At an informal level the MRC provides briefing for parliamentarians on developments in medical research. For example, this year the MRC have provided scientific briefing/updates for the Parliamentary All-Party Group on Cancer.

The MRC provides evidence to parliamentary and other formal enquiries on health or medical science:

- House of Lords S&T Select Committee inquiry on Malaria
- House of Lords S&T Select Committee inquiry on Complementary Medicine
- House of Lords S&T Select Committee inquiry into Science and Society
- House of Commons S&T Select Committee into Industry and Health Risks of Smoking
- House of Commons S&T Select Committee on Mobile Phones
- House of Commons S&T Select Committee on EQUAL (Extend Quality of Life)
- House of Commons S&T Select Committee on “Cancer Research – a Fresh Look”

The MRC also provide briefing for ‘official enquiries’ ie Parliamentary Questions, enquiries from other Government Departments or letters received directly. 228 such responses were provided this year.

Many of the new units opened or established this year provide scientific expertise which is available to policy makers. For example, Professor Janet Darbyshire and Dr Max Parmar (MRC Clinical Trials Unit) provided evidence to the House of Commons S&T Select Committee on Cancer – a Fresh Look. Dr Max Parmar also provided the Commons All Party Group on Cancer with information at a presentation in December 1999.

The MRC has established an Advisory Committee on Scientific Advances in Genetics, chaired by Lord Patel, to address issues relating to the translation of discoveries into improved healthcare. This might involve examining how the potential benefits of research are perceived by the public and identifying any ethical issues raised. The Committee will work closely with other advisory bodies, particularly the newly established Human Genetics Commission and the Department of Health Laboratory Services Group, to help ensure that outputs from research are implemented effectively and appropriately by the Health Service. The Committee will also have an important role in assisting Council with the development of its research portfolio and alerting Council to future research needs. A major role for the Committee is to provide horizon scanning (public perceptions) for Council in the area of genetics and genomics.

MRC’s Concordats with Government Departments provide a framework for regular briefing of senior scientific advisers. Initiatives this year included the Chief Medical Officer’s review of therapeutic cloning (page 59) and the establishment of a Cancer Research Funders Forum (see page 29).
Part of the MRC’s mission is to promote the public’s understanding of science. Council’s communications activities are designed to engage the public in scientific issues, establish a dialogue and to learn from their input.

**PERCEPTIONS AUDIT**

The MRC commissioned Opinion Leader Research to carry out a reputation audit in 1999 to obtain some data on the level of awareness and perceived value of the role of the MRC amongst key audiences. The research, which used a mixture of qualitative and quantitative methods, measured familiarity with and favourability towards the MRC. It assessed perceptions of reputation, identified key issues likely to influence reputation, identified emerging issues and identified shifts in perceptions over time. As a result of considering the findings of the report, the MRC has taken a number of new initiatives to improve the visibility of the work of MRC units at local and national levels.

**PARLIAMENTARIANS AND OPINION FORMERS**

As a key audience for the MRC, several initiatives were taken during the year to improve and maintain links with groups who take a specific interest in the work of the Council.

In April 1999 Professor George Radda MRC Chief Executive and Dr Mike Dexter, Director of the Wellcome Trust gave a joint presentation to the Parliamentary and Scientific Committee of the Houses of Parliament entitled ‘The Future Direction of Medical Research’. An article comprising extracts of both speeches was subsequently published in the Committee’s Science in Parliament.

**MEDIA**

The MRC has a busy press office receiving in the region of 2000 calls a year. A total of 39 press releases were issued during the year. Highlights of media coverage this year are reported elsewhere in the report.

Regular features about recent work of the MRC have been placed in publications of interest to particular sections of our audiences such as NHS Managers and health professionals (The Health Summary), patients (Feelgood)opinion formers (SPA Magazine) and politicians (Science in Parliament).
Many MRC units have very well developed schools programmes, with scientists undertaking talks, units organising open days and visits and in some cases sixth form conferences, twilight sessions for teachers and summer schools.

Corporately the MRC supports the Researchers in Residence Scheme, which enables its PhD students to spend time in a school working alongside the science teachers. The students benefit from developing good communication skills, teachers benefit from hearing about the latest research and making contact with young scientists working at the bench and the youngsters gain from the relationships they build with the ‘Researcher in Residence’ as mentor, friend and role model. Often good links are formed between the unit/university department at which the researcher is based, and visits, other talks and even projects have been known to evolve as a result. In 1999-2000 40 MRC PhD students took part in the scheme.

MRC also supports the Nuffield Science Bursaries enabling Sixth Formers to carry out research projects at Universities and Institutes. In 1999, 14 placements were made in MRC units.

MRC’s current school curriculum resources are displayed at the Schoolscience website, and the increased take up of web technology in schools will enable the expansion of the availability of new materials in electronic form.

The MRC, in partnership with the other research councils, took exhibition space at the Science and Technology Regional Officers (SATRO) Conference in November 1999, at the Association for Science Education Annual Meeting in Leeds in January 2000 and at the Education Show at the NEC in Birmingham in March 2000.

Max Perutz Essay Competition seeks to encourage young scientists to develop the skills to write about their area of science in an interesting and informative way for lay audiences. A prize of £1000 is given to the winner, with £500 for the second prize and £250 for the third prize. This year’s winners were: Dr Paul Dark of the University of Manchester, first prize, Dr Allister Grant of the University of Birmingham, second prize, and Dr Marion Cuddy, of the Institute of Psychiatry at King’s College, London, third prize. There were five runners up.

During the year approximately 800 public inquiries were dealt with by the MRC Information Officer.

Science communication is a two way process and establishing and maintaining a dialogue is a very important area of public engagement with science. The MRC recognises the importance of providing its scientists with the skills to communicate effectively with lay audiences.

Media training courses are offered at two levels – high level training for Unit Directors and Institute Division Leaders, and an intermediate course for mid career/senior scientists. Additionally a series of presentation masterclasses are provided for senior scientists who might be required to speak to influential and opinion former audiences. At PhD level, the MRC believes that such transferable skills are very important as careers progress. The annual
PUBLIC ENGAGEMENT

Thirteen people have been selected following public advertisement and interview to form a Consumer Liaison Group which will advise the MRC on ways to promote consumer involvement in its activities. The group will set its own agenda but the MRC hopes that it will advise the Council on consumer perspectives on areas such as genetic research and research involving collections of human biological samples.

The group may also suggest other activities that would benefit from consumer involvement and advise on the dissemination of information.

The MRC is a funder of the Genetics Interest Group, a national alliance of organisations of over 100 charities which support children, families and individuals affected by genetic disorders. The aim of the organisation is to promote awareness and understanding of such genetic disorders and to increase knowledge of advances in genetic medicine.

PUBLIC EVENTS

From time to time the MRC runs events aimed at particular sections of the general public to encourage wider engagement.

In April 1999 the joint MRC/Wellcome Trust exhibition Nature Nurture received its final airing at the Gyle Shopping Centre as part of the Edinburgh International Science Festival.

The MRC in partnership with BBSRC, NERC and the Wellcome Trust, commissioned a major new exhibition on the theme of DNA Science. It was first used at the Tomorrow’s World Live exhibition in July 1999, which attracted some 90,000 visitors. At the lab section of the stand, visitors have a chance to extract DNA from vegetables, practice pipetting and observe DNA sequencing with the benefit of research council and Trust PhD student ‘instructors’ to answer questions and advise on technique. A stand on careers in biomedical sciences was resourced and staffed in the ‘Tomorrow’s Work’ section of the exhibition. A series of lectures took place in the lecture theatre sponsored by NESTA. The MRC contribution was from Dr Wendy Bickmore of the MRC Human Genetics Unit, who talked about her work on chromosome mapping.

In 1999 Professor George Radda, Chief Executive was President of the Medical Sciences Section of British Association Advancement of Science and put together a high level programme of speakers, largely MRC funded – or MRC staff scientists.

The theme of the Medical Sciences Section within the overall Festival theme of ‘Prospering Through Science’ was ‘Prospering Through a Healthy Society’.

MRC Professor Nancy Rothwell gave the 1998 Royal Institution Christmas Lectures and subsequently has repeated selected lectures for young audiences (through British Association Youth Section (BAYS) at the MRC’s invitation, in Sheffield in September at the British Association Festival of Science. She and her team created a new demonstration lecture ‘Exploring Inner Space’ which was presented to 1200 children during Science Week 2000 at Imperial College, London.

The MRC actively supports an increase and improvement in the amount and quality of science used as themes for TV drama. The council has sponsored a series of events through PAWS (Public Awareness of Science and Technology) where drama writers have the opportunity to meet MRC scientists and to hear about what interests them. These have taken place in Manchester, Glasgow and London and more such events are planned.

In February 2000 the MRC sponsored a public debate: ‘DNA Databases: Threat or Promise’ run by the Science and Public Affairs Forum of the BA which was featured in an article in the May 2000 SPA Magazine.
COMMUNICATIONS

During 1999, MRC, in partnership with OST and BBSRC, commissioned a major study of public knowledge, assumptions, and attitudes to animal research, to provide an evidence base for communications work and policy. The work was conducted by MORI, using both discussion groups and a quantitative survey.

The study showed that people without specialist knowledge could readily engage in sophisticated discussion of animal experiments. Almost all accepted that animal experiments could be justified, but the proportion considering animal experiments acceptable in practice ranged from 32% to 84% depending on the assumed context and conditions. Forty-four percent of people described themselves as “not supporting” animal research, but half of these would accept research if they thought the right conditions were met.

People often distrusted media coverage of the issue and campaign material, and were unsure where to turn for reliable information. Most did not know how animal use was regulated, and assumed that even if there were strict safeguards to protect animal welfare, they would not be enforced. But when people were asked what safeguard they would like to see in place, it was clear that the 1986 Animals (Scientific Procedures) Act already provides what most people want.

In parallel, MRC has taken steps to strengthen its work on communications. A new booklet “Mice and Medicine” describing the value of animal experiments in current MRC research has been produced, and a series of training seminars have been organised for MRC researchers who are interested in explaining their work in schools. MRC continues to highlight the role of animal research when publicising achievements, and when briefing MPs, the media, and opinion formers.

MEDICAL RESEARCH USING ANIMALS

COMMUNICATIONS

The MRC aims to set and disseminate the highest standards in all areas of research management. The following areas have been notable this year.

The MRC aims to set and disseminate the highest standards in all areas of research management. The following areas have been notable this year.

PRINCIPLES

ethics and business principles in the management of research

The MRC aims to set and disseminate the highest standards in all areas of research management. The following areas have been notable this year.

The MRC aims to set and disseminate the highest standards in all areas of research management. The following areas have been notable this year.
ANIMAL WELFARE AND RESEARCH QUALITY

In November, MRC’s new Expert Group on Research Animal Use met for the first time. The Group is drawn from scientists, managers and support staff in MRC establishments, and has a broad remit to advise Council on raising standards and skills in animal research, and strengthening MRC’s role in refining, reducing, or replacing animal use.

A survey showed numerous research programmes in MRC establishments already contribute – directly or indirectly – to refining use or improving welfare. Examples include research into small animal imaging to reduce the need for invasive studies, using embryo and sperm freezing and IVF to reduce the need for large breeding populations of mice, work on more sophisticated experimental design and monitoring, and development of new cell and tissue culture techniques. The MRC invests well over £1 million p.a. in projects contributing to animal welfare.

The Expert Group’s report to Council recommends building on this work by forming a new team to accelerate the exchange of information and training, and to establish and promote new methods and standards, especially in fast-moving areas such as mouse genetics. The report also recommended making extra funds available to allow individual researchers to consolidate and validate their work on new methods. These developments will be implemented during the year 2000.

PERSONAL INFORMATION IN MEDICAL RESEARCH

Council formed a Working Group in early 1999 to look into the ethical and legal issues around the use of personal information in research. Council took this step partly to ensure MRC’s advice to researchers reflected revisions to data protection law and the introduction of the Human Rights Act, and partly because there appeared to be growing divergence of opinion over when information from medical records could be used in research. The Group is chaired by Professor Andy Haines (Royal Free Hospital, London) and includes representatives from the Department of Health. After taking initial legal advice, and discussions with the Department of Health, General Medical Council and the Office of the Data Protection Registrar, the group prepared draft guidelines which were circulated for consultation in September. Over 70 individuals and organisations responded.

During the Summer of 1999 a court ruled that the Department of Health had legal grounds for blocking access to anonymised prescription information by a company, Source Informatics. The ruling suggested that anonymous information might be seen as personal and confidential in law, and led some organisations to suggest that consent might be needed even for research based only on anonymous data. The court of Appeal overturned the ruling. Some of the legal argument touched on the use of identifiable information and the Department of Health, MRC GMC ABPI and NPA all...
submitted evidence on the importance of anonymised data and insofar as was relevant identifiable data for research in the public interest.

GOOD PRACTICE IN MEDICAL RESEARCH

During the year the MRC issued detailed guidance to its own staff on the principles of good research practice, outlining the key organisational processes under which studies should be planned, performed, monitored, recorded and reported. This internal guide will be followed by a booklet for publication that distils the key elements of the process. In addition, the Chief Executive was a member of the General Medical Council’s working group on good practice in medical research, and the MRC submitted comments on the circulated draft document from that group.

RESEARCH IN DEVELOPING COUNTRIES

MRC has agreed to be a sponsor of the Global Forum on Bioethics in Research which aims to bring together those involved in research in resource-poor countries to discuss common issues and to stimulate research ethics capacity building in those countries. The Council was represented at the first annual Global Forum meeting, held in Bethesda in November 1999. The MRC’s own group on ethics of research in developing countries meets three times a year to advise Council on relevant research proposals.

GUIDELINES FOR HUMAN SAMPLES USED IN MEDICAL RESEARCH

Interim guidelines for the use of human blood and other samples used in medical research were published in November 1999. The MRC asked for views on the guidelines from members of the public, health professionals, consumer and patient groups, Research Ethics Committees as well as medical researchers. The operational and ethical guidelines cover issues such as the confidentiality of people who donate samples, the importance of gaining valid consent from donors and guidance on the specific issues related to genetic research. (The group is chaired by Professor Eve Johnstone, Professor of Psychiatry at the University of Edinburgh, who is an MRC Council Member).

STEM CELLS AND THERAPEUTIC CLONING

The MRC submitted comments on Therapeutic Cloning in Humans to the Chief Medical Officer’s Expert Advisory Group. The Council reaffirmed its view that therapeutic cloning is an important area for research and also highlighted the potential of stem cell research, much of which does not require cloning techniques.

MONITORING AND EVALUATING MRC’S FUNDING SCHEMES

During 1999, MRC commissioned a survey of the operation of the MRC Advisory Board, which reviews proposals for short-term funding, and also assessed the potential for routinely using bibliometric measures to inform peer review of major, long-term programmes.

The study on MRC’s Advisory Board confirmed that the peer review changes made in 1997 had reduced demands on researchers’ time, and that overall, the time spent on peer review for MRC was a relatively small, and acceptable, part of members’ non-research work. However, the study highlighted the need for better arrangements for supporting communications among members reviewing applications, and a need for better training and feedback, and opportunities for members to meet to exchange experiences.

The study on bibliometrics found that careful bibliometric analysis offered a good measure of research groups’ past performance, which generally matched the assessment by MRC’s Boards. Given the complexity of the analysis needed, and the many other factors that contribute to the final funding decision, the steering group concluded that bibliometric analysis would not add sufficient value to peer review to be worthwhile routinely.
The MRC’s income and expenditure for the year is summarised in the table on p64. Full, audited, Accounts will be available from the Council’s Accounts Section towards the end of 2000.

**INCOME**

Grant-in-aid income was increased by £10.6 million in the financial year 1999-00 as a result of the first allocation made under the three year period of the Government’s Comprehensive Spending Review (CSR).

Additional income totalled £46.3 million in the year. The main elements were external funding for research programmes and Commercial Fund income.

External funding derives mainly from the following:

- Government Departments sponsoring work in selected fields (major contributors are Department of Health for work in AIDS and nutrition and the Department for International Development, for work relevant to the health of developing countries).
- Income from industry, charities, and international organisations collaborating on specific research projects.

Income to the Commercial Fund in 1999-00 – a separate fund for income derived from the licensing of intellectual property – was £7.5m. £811,000 was allocated from this to MRC staff and units under the scheme of incentive payments to inventors.

**PRIVATE FUNDS**

The MRC frequently receives bequests and donations which are paid into the MRC’s Private Endowment Funds, a registered charity. This year new donations totalled £670k; the Council is very grateful to the benefactors concerned. The Council’s Private Funds investment policy and performance is kept under review by the Council Audit Committee. At the end of the year the total value of the Funds stood at £25 million.
EXPENDITURE

Expenditure on existing and new programmes in MRC’s own institutes and units (MRC “direct support”) was £180.7 million of which £12.4 million was allocated to the costs of ongoing estates care and maintenance work, and building projects. Expenditure on direct support was more than in previous years as Council investment in a number of new units started and capital investment was increased to meet initiatives to renew, modernise and restructure research infrastructure (essential buildings and plant/laboratory equipment and information technology). Significant new capital projects included:

- a number of initiatives in Cambridge: completion of the research building on the New Addenbrooke’s Hospital site, to be shared with Cambridge University, for the MRC Dunn Human Nutrition Unit (the MRC provided a 40% contribution to the construction costs of the building); start of a second new major research building to house the new MRC Cancer Cell Unit - also to be shared with Cambridge University (the MRC will contribute 50% of construction costs); the start of a new building to house Nuclear Magnetic Resonance (NMR) equipment; and commencement of a major programme of refurbishment and extension for the MRC Cognitive Brain Sciences Unit. Work has also begun on the new building on the Peterhouse Science Park in Cambridge to house the MRC Resource Centre for Human Nutrition Research.
- completion of the refurbishment of two buildings in central London to house the new MRC Clinical Trials Unit
- refurbishment work at the MRC Human Reproductive Sciences Unit in Edinburgh to house the new Director’s research programme
- provision of new stores and seminar facilities for the MRC units at Harwell
- provision of new meeting and support facilities at the MRC Clinical Sciences Centre at Hammersmith

Expenditure on indirect support, for research in universities and other organisations, amounted to £145.6 million. The bulk of this is for grants, research training awards and personal awards to scientists, but it also includes special contributions to the work of other research institutions such as the Sanger Centre and Edward Jenner Vaccine Research Institute. In addition, the MRC pays UK contributions to a number of international research organisations* on behalf of the Government.

Expenditure on new forms of support grew by more than £10 million to reach a total of £11.9 million for the year. This growth is off-set by a decline in expenditure caused by the phasing out of project grants. However, over the year, total expenditure in universities was £5.3 million more than in the previous year.

Overall, expenditure was £5.8 million less than income. This is broadly in line with the planned underspend and, together with the £9.9 million that the Council retained from a previous period, will be used to supplement the Council’s future spending plans.

* European Molecular Laboratory; European Molecular Biology Conference; Human Frontiers Science Program; and International Agency for Research on Cancer.
AUDITS

Internal Audit is provided by the research council's Internal Audit Service and external audit by the Comptroller and Auditor General. The Council's Audit Committee sets the priorities for internal audit, considers the outcome of all audit reviews, and the consequential action taken by MRC management, and advises the Accounting Officer on the effectiveness of internal financial controls.

The work of the Audit Committee has expanded to cover the wider issues of corporate governance which was introduced into the audit programme in 1998/99 and whose importance within corporate activity in organisations generally was highlighted by the Turnbull Report in 1999.

EFFICIENCY

During the year a further 14 audits took place within the rolling programme of Compliance Audits (audits of the management of resources within MRC institutes and units). There were also seven audits of corporate systems.

Highlights this year included

- Central administrative running costs were contained within the £12.6m target set by the Office of Science and Technology. This was an increase of £200,000 in cash terms compared to 1998/99, which was required to meet the increasing volume of activity needed to take forward CSR priorities. However, in real terms, it was a reduction in resources of about 1%, and represents a fall in the proportion of MRC expenditure spent on central administration from 3.9% to 3.7%.

- Increased efficiency and effectiveness will be achieved by the merger of the Headquarters Technology Transfer Group and the two Collaborative Centres into one organisational structure – Medical Research Council Technology (MRCT).

- Over the next few months, the MRC will launch a major initiative, which will improve efficiency by reducing the administrative burden on the peer review process. The launch of the Electronic Application and Assessment web-based system (EAA) will enable all new applications to be received electronically and facilitate the electronic peer review of applications.

THE MILLENNIUM BUG

The arrangements made as part of the Council’s Year 2000 compliance programme were successful and no significant problems were encountered.
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PARLIAMENTARY GRANT-IN-AID</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parliamentary Grant-in-Aid</td>
<td>£m</td>
<td>£m</td>
<td>£m</td>
<td>£m</td>
<td>£m</td>
</tr>
<tr>
<td>National Institute for Medical Research</td>
<td>23.8</td>
<td>25.0</td>
<td>25.2</td>
<td>25.4</td>
<td>27.6</td>
</tr>
<tr>
<td>Laboratory of Molecular Biology</td>
<td>13.8</td>
<td>13.9</td>
<td>14.3</td>
<td>15.0</td>
<td>16.7</td>
</tr>
<tr>
<td>Clinical Sciences Centre</td>
<td>14.2</td>
<td>11.7</td>
<td>9.3</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Research units and external staff</td>
<td>81.1</td>
<td>85.6</td>
<td>91.6</td>
<td>97.6</td>
<td>116.4</td>
</tr>
<tr>
<td>Capital building</td>
<td>51</td>
<td>6.3</td>
<td>6.8</td>
<td>5.2</td>
<td>8.4</td>
</tr>
<tr>
<td>Estates care and maintenance</td>
<td>6.4</td>
<td>5.4</td>
<td>5.0</td>
<td>5.0</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>TOTAL EXPENDITURE ON INSTITUTES &amp; STAFF</strong></td>
<td>144.4</td>
<td>147.9</td>
<td>152.2</td>
<td>155.8</td>
<td>180.7</td>
</tr>
<tr>
<td><strong>EXPERIMENTAL AND CAPITALEXPENDITURE ON INSTITUTES AND UNITS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Institute for Medical Research</td>
<td>23.8</td>
<td>25.0</td>
<td>25.2</td>
<td>25.4</td>
<td>27.6</td>
</tr>
<tr>
<td>Laboratory of Molecular Biology</td>
<td>13.8</td>
<td>13.9</td>
<td>14.3</td>
<td>15.0</td>
<td>16.7</td>
</tr>
<tr>
<td>Clinical Sciences Centre</td>
<td>14.2</td>
<td>11.7</td>
<td>9.3</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Research units and external staff</td>
<td>81.1</td>
<td>85.6</td>
<td>91.6</td>
<td>97.6</td>
<td>116.4</td>
</tr>
<tr>
<td>Capital building</td>
<td>51</td>
<td>6.3</td>
<td>6.8</td>
<td>5.2</td>
<td>8.4</td>
</tr>
<tr>
<td>Estates care and maintenance</td>
<td>6.4</td>
<td>5.4</td>
<td>5.0</td>
<td>5.0</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>TOTAL EXPENDITURE IN UNIVERSITIES &amp; OTHER INSTITUTES</strong></td>
<td>146.5</td>
<td>149.4</td>
<td>155.8</td>
<td>147.8</td>
<td>151.7</td>
</tr>
<tr>
<td><strong>TOTAL EXPENDITURE ON ADMINISTRATIVE RUNNING COSTS</strong></td>
<td>14.0</td>
<td>13.4</td>
<td>12.8</td>
<td>12.3</td>
<td>12.7</td>
</tr>
<tr>
<td><strong>TOTAL EXPENDITURE</strong></td>
<td>304.9</td>
<td>310.7</td>
<td>320.8</td>
<td>315.9</td>
<td>345.1</td>
</tr>
</tbody>
</table>

*From 1997/98 costs relating to the Cyclotron Unit, Magnetic Resonance Unit and the CSC Administrative & Technical Support Group were separately identified in the Accounts. Previously, these costs had been a direct charge to the CSC.*

NB. This statement has not been audited by the Comptroller and Auditor General. Full accounts, audited by the National Audit Office, will be available from the MRC accounts section towards the end of the calendar year.