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 2000 to 31 March 2001. 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
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 2000-2001

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Mr MJ Earwicker
(Office of Science and Technology) Representing the Secretary of State for Trade and Industry
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This has been a momentous year for science. The announcement earlier this year of the completion of the full sequence of the human genome brought home, even to many who had not thought in such terms before, the huge opportunities which genetics research offers for health care in this new century. This endeavour had its roots in MRC support for the very early days of sequencing under Fred Sanger at the MRC Laboratory of Molecular Biology in Cambridge in the late 1970s and 80s. Further groundwork was laid through MRC supported work on sequencing the nematode worm under John Sulston in the 1990s. The completion of the sequence was reported in last year’s Annual Report.

Another significant reminder during the year of the importance of long-term support for science from which society can reap the ultimate benefits, was the 25th anniversary of the discovery of monoclonal antibodies. Dr César Milstein (pictured right), also from the MRC Laboratory of Molecular Biology in Cambridge, was awarded the first MRC Millennium Medal in recognition of this Nobel prize-winning work and of its subsequent contribution to health and wealth. Over 200 companies are now marketing or developing research, diagnostic or therapeutic monoclonal antibody applications.

A key theme in this year’s Report is the range of MRC investments and initiatives which are being developed in partnership with others. Joint working with other research councils has been pursued with vigour as shown in chapter 3. Research Funders Fora in ageing, heart disease and cancer are bringing a range of interests together working for the common good on these major areas of public policy and interest.

Finally, we would like to express our thanks to the network of individuals who continue to give of their time to corporate strategy development and implementation, through our Boards and other committees. They have been joined this year by two new groups. These are the MRC Training Board which is developing a strategy for all our investment in training and careers both in MRC Units/Institutes and in the universities, and the MRC Consumer Liaison Group which advises Council on how best to involve consumers in the work of the MRC.
A small selection from last year’s many noteworthy MRC-funded scientific achievements:

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

Antisocial and aggressive behaviours are common in children and may lead to difficulties in adult life. Life-course studies have shown that a small proportion of antisocial children are particularly badly affected in adulthood. Recent MRC-funded work may help to identify such children early and contribute to improved intervention and treatment. Dr Barbara Maughan from the MRC Child Psychiatry Unit, London, together with UK and US colleagues, has used new statistical techniques to identify children with different patterns of aggressive and non-aggressive antisocial behaviours in childhood and adolescence. They found that high-risk children fell into two distinct but overlapping groups, which both had considerably disadvantaged family backgrounds and were highly vulnerable to other mental health problems in childhood.

Journal of Quantitative Criminology 16, 199-221

Dr Dilys Morgan of the MRC Programme on AIDS in Uganda has led a research team conducting detailed clinical studies of HIV-1 infection and AIDS in rural Uganda for over 10 years. Her group has found that the average survival time and disease progression rate are similar to those in industrialised countries before anti-HIV drugs were used. This research disproves the misconception that AIDS in Africa is a distinct disease from AIDS in developed countries and that little can be done to prevent or treat it. The work, which was part funded through the MRC/Department for International Development Concordat, also shows that there is a real opportunity to mitigate the effects of the African AIDS epidemic.

Nature Medicine 7, 143-144

A jointly funded MRC/World Health Organisation study by Professor Hilton Whittle and colleagues at the MRC Laboratories in The Gambia, has surveyed 30,000 pregnant women to compare mother-to-child transmission rates of HIV-1 and HIV-2 viruses, which are both common in West Africa. They found that women infected with HIV-1 had 37 times more virus in their blood than those with HIV-2 infection, and that this was reflected in the mother to child transmission rate, which was six times higher for HIV-1 infection. The findings firmly establish that HIV-1 replicates faster than HIV-2, explaining why HIV-1 infection spreads more easily and kills people more quickly. The knowledge will guide public health policies in The Gambia and other West African populations affected by both HIV-1 and HIV-2.

AIDS 2000, 14:411-448
Some scientists suggest that men’s risk of HIV infection may be reduced by circumcision. Professor Richard Hayes’ group at the London School of Hygiene and Tropical Medicine, have analysed all available data on possible links between HIV-1 infection and circumcision in sub-Saharan African men. The pooled results of seven such studies show that, taking everything into account, circumcised men are at about half the risk of HIV-1 infection as uncircumcised men. This protective effect was most evident among men in high-risk groups, but was also seen in the general population.

Current Opinion in Infectious Diseases 14, 71-75

Childhood obesity is an increasingly severe problem, but until now there has been no standard way to measure it; making it impossible to compare obesity rates from different studies. Professor Tim Cole from the Institute of Child Health, working with colleagues from the International Obesity Task Force (IOTF), has devised a new definition of child obesity, which is based on the body-mass index (BMI – weight (kg)/height (m)2) and applies world-wide. Children whose BMI is greater than the threshold calculated for their age are obese. Age thresholds are based on six large international surveys and are linked to those for adult obesity. The IOTF definition should clarify the scale and growth of the childhood obesity epidemic internationally.

British Medical Journal 320, 1240-43

The MRC General Practice Research Framework has studied asthmatic patients to address concerns that long-term regular use of drugs like salbutamol, a bronchodilator which relieves asthma symptoms by widening the lungs’ airways, may mask an underlying deterioration in the condition. After one year they found similar asthma control in patients taking intermittent bronchodilators and those taking salbutamol four times a day. The study provides reassurance that regular use of salbutamol should not make asthma worse, however, the need to use that much suggests that the ailment could be better controlled, and indicates that additional treatment should be considered.

Lancet 355, 1675-79

Young people in South Carolina, USA have unusually high rates of end-stage kidney disease, largely due to high blood pressure and diabetes. Researchers at the MRC Environmental Epidemiology Unit investigated whether poor kidney development before birth might account for this. They compared the birth weights of 1230 people with kidney failure to 2460 controls, and found that people who weighed less than 2.5 kilogrammes at birth were at increased risk of developing kidney failure. Since low birth weight is more common in South Carolina and the South East than in other areas of the USA, this work provides one explanation for the higher rates of chronic kidney failure seen in this region. It also indicates that improving babies’ health could help reduce the predicted increase in long-term kidney dialysis patients over the next 40 years.

Archives of Internal Medicine 160, 1472-76

Professor Julian Leff and colleagues from the Institute of Psychiatry, London, have compared different approaches to treating depression, and shown that couple therapy, a psychological treatment, is more effective in improving depression than antidepressant drugs. Couple therapy aims to help depressed people and their partners gain new outlooks on the depressed person’s problems, attach new and more positive meanings to the depressed person’s behaviour and to experiment with new ways of relating to each other. Over the course of a year, the team treated some depressed people with antidepressant drugs, and others through couple therapy sessions with their partners. They followed-up the patients for a further year after the treatment stopped. They found that couple therapy was the more effective treatment, both during and some time after the treatment period, and that fewer people
dropped out compared to the drug treatment group. The findings provide a strong argument for training primary care workers in the skills of couple therapy.

**British Journal of Psychiatry 177, 95-100**

**IMMUNITY AND INFECTION**

Most cancer treatments are not very specific and attack normal cells as well as tumour cells. Dr. Terry Rabbitts’ group, at the MRC Laboratory of Molecular Biology, has designed molecules that selectively kill cancer cells without harming normal ones. Their anti-cancer molecules have two parts, one that recognises and binds only to certain abnormal proteins specific to cancer cells, and another that triggers the body’s own cell-death mechanisms to kill those cells. This work could be translated into clinical treatment for many common cancers.

**Proceedings of the National Academy of Sciences 97, 12266-71**

Macrophages are large scavenger cells that help clear inflamed tissue and are involved in mediating the body’s immune response to infection. Professor Neil Barclay from Oxford and a team from the DNAX Research Institute, California, have shown that a molecule called CD200 is important in inhibiting macrophage activation. CD200 normally down-regulates macrophage cells in many tissues by interacting with an inhibitory receptor molecule called CD200R. They found that mice lacking CD200 have more active, and more numerous, macrophages than normal, and are more susceptible to certain auto-immune diseases, for example, a mouse-model of human Multiple Sclerosis (MS) in which macrophage over-activation results in nerve and tissue damage. These effects have important and broad implications for the treatment of neuro-degenerative diseases like MS and Alzheimer’s disease.

**Science 290, 1768-71**

The pneumococcus bacterium is the main cause of pneumonia and an important cause of meningitis in children in the developing world. It currently kills about one million children every year, but a new kind of vaccine called pneumococcal conjugate vaccine holds great promise for preventing this infection in the future. After many years of background epidemiological work and pilot vaccine trials, Professor Brian Greenwood from the London School of Hygiene and Tropical Medicine and his colleagues from the MRC Laboratories in The Gambia have started a large clinical trial of such a vaccine. The trial will last for 5-6 years and could lead to the introduction of a pneumococcal conjugate vaccine into the routine immunisation programme for children in developing countries.

**Lancet 356, 1210-11**

Leukaemia and other blood disorders can be cured with transplants of stem cells, or stem-cell containing bone marrow, which replenish healthy blood cells. Unfortunately, such transplants are contaminated with immune system cells called T cells, which attack the patient causing a serious illness called graft-versus-host disease. Professors Hale and Waldmann from the Therapeutic Antibody Centre in Oxford have worked for many years to perfect a method for removing T cells without damaging the stem cells; but have found that T cell removal makes patients more likely to reject the transplant. They have now developed an antibody which can be simply mixed with donor cells to prevent graft-versus-host disease and rejection. Many of the clinical trials were carried out in South Africa where the treatment has so reduced the cost of stem cell transplantation that it is made available to patients where otherwise it could not be afforded.

**Bone Marrow Transplantation 26, 69-79**
Immune responses to the Chlamydia bacterium are double edged; they help cure the infection but often lead to tissue damage. In designing new vaccines or treatments it is important to distinguish between beneficial and damaging immune responses. Professor Gaston and colleagues from Cambridge have searched recently completed Chlamidia gene sequence data to find previously unknown Chamydia proteins that are recognised by the immune system. They plan to determine whether immune responses to one of these proteins occur more frequently in patients with Chlamydia-induced tissue damage and inflammation.

European Journal of Immunology 31, 1513-1522

The Brain Inflammation and Immunity Group at the University of Wales College of Medicine, headed by MRC Senior Fellow Dr Philippe Gasque, is working to characterise the mechanisms involved in clearing disease causing organisms and toxic cell debris, such as dying cells, from the brain. They believe that nerve cells themselves can distinguish intruders and induce cell debris removal, while preserving normal brain cells. This local scavenger system is essential to prevent brain infections, such as meningitis, and ultimately to activate tissue repair following injury, for example, damage caused by a stroke. They are studying the role of a receptor protein family involved in the uptake and destruction of harmful material.

Journal of Biological Chemistry 275, 34382-92

Greater understanding of how immune system cells are stimulated and regulated is necessary to help develop efficient vaccines and disease treatments. Dr Rose Zamoyska and her group at the National Institute for Medical Research have developed a model system to investigate the role of a protein called lck, that it is involved in the proliferation and activation of immune system T cells. These studies will help to find out how these cells are regulated, and inform approaches to vaccine design and to tackling unwanted immune responses, such as autoimmune diseases.

Science 290, 127

Dendritic cells (DC) have been known to play a role in provoking and controlling immune responses for many years, but the molecular mechanisms involved remain obscure. Professor Herman Waldmann and colleagues from the Sir William Dunn School of Pathology, Oxford have begun to decipher the genetic code that defines a DC by directing the process that generates DC from embryonic stem cell precursors. This work provides a powerful new approach to identifying the function of individual genes, and suggests new ways of intervening in autoimmune disease and transplant rejection through taming DC activity.

Current Opinions in Immunology 12, 528-35

GENETICS, MOLECULAR STRUCTURE AND DYNAMICS

Professor Steve Brown and colleagues from the MRC Mammalian Genetics Unit, in collaboration with SmithKline Beecham, have used powerful genetic approaches to generate a large resource of mouse strains, many of which carry new genetic mutations. A comprehensive screen of the new strains, using a series of tests, has identified over 500 potential mouse models for a diverse range of human diseases including; osteoporosis, kidney failure, diabetes, abnormal cholesterol processing, spina-bifida, sight and hearing impairments. These models will help to identify gene defects causing human disease and further our understanding of how and why disease develops.

Nature Genetics 25, 440-43
Professor Robert Plomin from the Institute of Psychiatry has built on a surprising finding from human genetic research that the same genes affect many different cognitive processes, to develop a genetic mouse model of human learning and memory processes. The mice will be invaluable for identifying and understanding genes involved in cognitive disorders.

*Nature Reviews Neuroscience* 2, 136-41

The recent production of a first draft of the human genome is freely available on the internet. Dr Chris Ponting from the MRC Functional Genetics Unit in Oxford contributed to this collaboration by investigating how the set of human genes differs from those of worms, flies, plants and fungi. It is clear that although these organisms’ proteins are all assembled from a similar repertoire of ancient gene segments, human proteins are assembled in a much more complicated way.

*Nature* 409, 860-921

A team of international scientists, led by Professor Mike Owen from the University of Wales College of Medicine, has discovered new evidence of a gene involved in the common form of Alzheimer's disease. Their study of 429 Welsh and American sibling pairs over the age of 65 with Alzheimer's found that around two thirds of pairs shared the same genetic characteristic on chromosome 10, revealing that there is at least one major gene for the disease nearby. Identifying the responsible gene, or genes, could in the longer term lead to new and better treatments for Alzheimer's.

*Science* 290, 2304-05

Very large numbers of patients must be tested to find genes contributing to common diseases such as asthma. Professor Newton Morton and Dr Andrew Collins from Southampton University have set up an international consortium of 10 groups looking for asthma genes and have developed ways to combine the data that each group contributes to show where these genes might be. An initial analysis of chromosome 5 in a combined sample of 1037 families showed that a particular region may contain asthma genes. Chromosome 12 is the next target for analysis. Eventually, the consortium plans to review all asthma gene candidate regions, and to extend the analysis using techniques that enable them to home-in on asthma genes.

*Proceedings of the National Academy of Sciences* 97, 10942-47

TolC is a bacterial membrane protein that is central to disease causing capability and multidrug resistance in many infecting microbes. MRC programme grant holders Dr Vassilis Koronakis and Dr Colin Hughes from Cambridge University have made and analysed TolC crystals, to reveal a remarkable and as yet unique molecular structure, which they call the “channel tunnel”. This provides a large exit duct for a wide range of molecules, from large bacterial toxins to small antibacterial drugs. This is the culmination of many years’ work and has unveiled a previously unsuspected strategy used by infectious bacteria, which may provide a target for new drugs.

*Nature* 405, 914-19

DNA damage arises constantly from both normal cellular processes and environmental hazards such as radiation and chemicals. Accurate DNA repair is vital to survival, and all living organisms, including man, have specific mechanisms to do this. Professor John Thakker’s group at the MRC Radiation and Genome Stability Unit has recently isolated a gene called Xrcc2 and found that it belongs to a gene family which repairs broken DNA molecules. They created mice lacking the gene to assess its role in genetic stability and cancer, and found that Xrcc2-deficient mouse embryos show an increased level of...
chromosome defects compared to normal mouse embryos, have developmental abnormalities, and do not survive beyond birth. Surprisingly the embryos also have neurological defects, with certain particularly sensitive neurons in the developing brain dying prematurely. The researchers suggest that unrepaired DNA damage that persists in certain brain cells triggers cell-death, leading to poor neurological development and embryonic death.

**EMBO Journal 19, 6674-85**

Fibrillin molecules provide long-range elasticity to connective tissues through outer cell-surface assemblies that form extensive linear microfibrils and act as a template for elastin fibre formation. Mutations in fibrillin-1 cause the arterial weakness, and skeletal and eye defects of Marfan’s Syndrome. MRC Senior Fellow Professor Cay Kielty and colleagues from Manchester, have used state of the art electron microscopy to determine the 3D structure of fibrillin microfibril assemblies and have proposed a new model for their alignment. Additional work has established how cells synthesise and secrete fibrillin molecules and regulate their cell-surface assembly.

**Science Now 24 October 2000**

The primary human defence mechanism against microbial infection relies on cells that ingest invading micro-organisms and then kill them with highly reactive oxygen derivatives. The source of the protective oxygen-based cell-killing molecules is a large membrane-associated multi-protein complex called NADPH oxidase. However, inappropriate NADPH oxidase activation can also lead to inflammation and tissue damage. Dr Katrin Rittinger and colleagues at the National Institute for Medical Research have determined the structural details of the interaction between two NADPH oxidase components. Their work will help to reveal how the NADPH oxidase assembly is regulated and might provide the basis for the design of new anti-inflammatory drugs.

**Molecular Cell 6, 899-907**

Ribosomes are large molecular machines that cells use to make proteins. Ribosomes catalyse protein chain synthesis by binding and translating the genetic code of messenger RNA. A large number of natural antibiotics, including erythromycin, tetracycline, streptomycin and gentamycin work by binding to ribosomes and disrupting protein synthesis. Dr Ramakrishnan and colleagues from the MRC Laboratory of Molecular Biology, have solved the molecular structure of one of the two ribosome subunits, both alone and bound to antibiotics. This work makes important contributions to understanding how proteins are made and how many antibiotics work. The results could be used to help design new antibiotics.

**Science 291, 498-501**

The cone-shaped core of the human immunodeficiency virus (HIV) is built from about 1500 subunits of a protein called CA. Dr John Finch and colleagues from the MRC Laboratory of Molecular Biology, together with researchers from the University of Utah, have used a technique called cryo-electron microscopy to study tubular aggregates of CA protein. Computer analysis of the resulting images shows that the CA protein has a symmetrical hexagonal arrangement. The same CA arrangement on the surface of the conical viral particle gives the HIV core its particular shape.

**Nature 407, 409-13**
CELL BIOLOGY, DEVELOPMENT AND GROWTH

Professors Kondo and Raff from the MRC Laboratory of Molecular Cell Biology, have provided the first evidence that specialised precursor cells, destined to become a particular cell type, can be reprogrammed into stem cells, which are able to self-renew and generate a diverse range of other cells. If this proves to be true for other types of precursors, it could have implications for developing stem cell therapies, because precursor cells are easier to purify and expand than stem cells.

Science 289, 1754-57

The human body resists invasion by disease causing bacteria, for example tuberculosis, by attacking them with highly reactive free-radical molecules inside immune system macrophage cells. In turn, bacteria have developed powerful, but as yet poorly understood, systems to protect themselves within macrophages. Studies of the stress signalling mechanism in fission yeast by Dr Jonathan Millar from the MRC National Institute for Medical Research have uncovered an ancient mechanism that enables microbes to sense hydrogen peroxide radicals. These sensors appear to be conserved in disease-causing bacteria, but not in humans, and may represent a target for new drugs that compromise the intracellular bacterial protection mechanism without affecting the host.

Molecular Biology of the Cell 12, 407-19

Uncontrolled cell proliferation is a hallmark of cancer and certain other diseases. A family of enzymes called the cyclin-dependent kinases (CDKs) control the progress of cell division, and regulation of CDK activity is often lost in cancer cells. Professor David Newell and colleagues from the University of Newcastle, working with AstraZeneca, are developing potent and specific inhibitors of CDKs to study the role of these enzymes in more detail, with a view to generating new drugs for cancer treatment. In the first year of their LINK grant they have identified inhibitors as potent as the best compounds described in the literature so far.

Journal of Medicinal Chemistry 43, 2797-804

Nutrients, including amino acids, are known to regulate cellular processes involved in protein synthesis, but the mechanisms that enable amino acids to exert these effects within cells are poorly understood. Experiments in which Professor Proud and colleagues from Dundee microinjected amino acids directly into single cells have identified a putative intracellular amino acid sensor that is a key intermediary in protein synthesis control. It is important to identify and characterise this and other components in order to dissect the ways cells respond to changes in nutritional status, for example, through starvation or as a result of diseases such as diabetes.

Biochemical Journal 351, 677-682

Blood cells derive from stem cell precursors stored in the bone marrow. A better understanding of stem cell biology will make the treatment of blood diseases much easier. Stem cell activity is first detected during embryonic development at a site distinct from the yolk sac where embryonic blood is being made. However, there has been considerable debate about whether the stem cells originate in situ, or have migrated from the yolk sac. Work in the African toad Xenopus by Professor Roger Patient from Nottingham has shown that the site where the first stem cells are generated comes from a region of the early embryo that is distinct from those which give rise to embryonic blood. His observations indicate that different embryonic signals and nuclear factors programme stem cells and embryonic...
blood cells. Defining these signals and factors may make it possible to manipulate stem cells isolated from adult bone marrow or from umbilical-cord blood.

Cell 102, 787-96

Heparan sulphates are complex cell-surface molecules involved in binding and regulating the activities of many signalling proteins. Dr Jeremy Turnbull, MRC Senior Fellow at Birmingham, has collaborated with Dr Ram Saiseshkaran from MIT to apply a mass spectroscopy-based technique to accurately determine heparan sulphate structures. The method provides a tool for detailed analysis of the relationship between the structure and function of heparan sulphates, with the goal of identifying new therapeutic targets.

Proceedings of the National Academy of Sciences 97, 10359-64

Glucocorticoids are a family of hormones, including cortisone and hydrocortisone, that are widely used to suppress the inflammation which characterises conditions such as arthritis, asthma and transplant rejection. They inhibit the production of cell-to-cell signalling molecules called cytokines, and enzymes that drive inflammation. Genes expressing these inflammatory molecules are activated in response to cell-surface signals, such as the recognition of microbial products, that are transduced to the cell's nucleus by pathways of proteins called kinases. Professor Saklatvala’s group at the Kennedy Institute, Imperial College, has shown that the glucocorticoid, dexamethasone, inhibits activation of a key component of these pathways, called p38MAP kinase. Their work suggests that dexamethasone induces an anti-inflammatory regulator, whose identification should give new insights into the control of inflammation.

Molecular Cell Biology 21, 771-80

Professor John Gordon’s group at the MRC Centre for Immune Regulation at Birmingham is exploring new ways to kill lymphoma tumour cells. Lymphoma is often incurable because these cancer cells are loaded with survival genes. The researchers have found that minute amounts of a naturally produced toxin from the food poisoning bug E. coli O157 are able to kill cultured lymphoma cells, even when high levels of the survival genes are present. The work gives insight into ways of using the toxin to treat patients in the future.

Cell Death and Differentiation 7, 785-94

Professor Mark Marsh and colleagues at the MRC Laboratory for Molecular Cell Biology, London, in collaboration with Professor James Hoxie at the University of Philadelphia, are working on the simian immunodeficiency virus (SIV), the monkey equivalent of HIV. They have identified molecular signals that regulate SIV coat protein distribution in SIV infected cells and, together with Professor Fultz of the University of Alabama, have now shown that removing one of these signals significantly decreases the ability of SIV to cause disease. The research illuminates previously unknown viral mechanisms that may also apply to HIV and offer the potential for new therapies.

Journal of Virology 75, 27-91

A vital brain function is to “bind” together the visual features that make up complete objects, for example, a nib, a barrel and a cap, form a pen. Professor Mark Johnson and colleagues from the Centre for Brain and Cognitive Development, London, have used non-invasive brain-imaging to show that this ability develops during the first year of life. They saw characteristic high frequency electrical
oscillations associated with binding in adult brains in healthy eight month old babies, but not in six month olds. This work provides one of the first glimpses of how the pre-verbal infant’s brain works.

**Science 290, 1582-85**

Dr David Jane and colleagues from the MRC Centre for Synaptic Plasticity at Bristol University, have advanced understanding of glutamate receptor proteins, which mediate cell-to-cell signalling in the human brain. They have designed a compound which specifically activates a subtype of glutamate receptors called mGlu8 and shown that these play an important role in regulating communication between nerve cells in the spinal cord. Further work on this compound, together with Professor Brian Meldrum from the Institute of Psychiatry, has shown that it has anticonvulsant properties and that such compounds might therefore provide new epilepsy treatments.

**Neuropharmacology 40, 311-18**

**MEDICAL PHYSIOLOGY AND DISEASE PROCESSES**

Parathyroid hormone (PTH) controls the balance of calcium and phosphate in the body. John Potts from the Harvard Medical School, Boston, USA, characterised the structure of the active part of PTH and made pure PTH available in an MRC-Harvard collaboration. Although early reports that PTH increased bone density in young animals were widely disregarded, Dr Jonathan Reeve and colleagues from Cambridge decided to test PTH’s effectiveness in patients with severe osteoporosis, which was previously untreatable. They found that PTH increased bone formation much more than bone reabsorption, which was the opposite to what other people had expected, and that osteoporosis was often abolished. This was a much greater effect than that achieved with rival modern treatments.

**Journal of Bone and Mineral Metabolism 19, 102-114**

Macrophages are cells that engulf microbes and other invading materials and facilitate immune reactions against them. In certain immune diseases such as rheumatoid arthritis, there is an abnormal accumulation of macrophages in the inflamed joint, where these cells may have damaging effects. Professor Ten Feizi and colleagues from Imperial College have advanced understanding of a protein called the macrophage receptor which is important in the protective function of macrophages. Professor Feizi’s group has discovered that the macrophage receptor can bind to components of joint cartilage. This work could aid our understanding of prolonged joint inflammation and inform the development of new anti-inflammatory treatments for arthritis.

**Journal of Experimental Medicine 191, 1117-26**

Osteoarthritis is traditionally seen as a disease of the smooth, gristle-like cartilage that lines the surfaces of joints. MRC Senior Fellow Professor Richard Aspden and his group from the University of Aberdeen have already shown that significant changes also occur in the bone, even at some distance from joint surfaces, and that these changes cannot be explained as secondary consequences of cartilage disease. They are now looking for mechanisms that can explain why several joints are often involved and why there is such a strong link with obesity. They propose that generalised osteoarthritis is a systemic disorder related to lipid metabolism. This idea links metabolic factors with mechanisms that can regulate the whole skeleton, and suggests new explanations for joint degeneration.

**Lancet, 357 1118-1120**
To apply gene therapy to nervous system diseases it is necessary to be able to deliver genes to nerve cells, however the inaccessibility and specialised nature of these cells makes this a difficult challenge. Professor Charles Coutelle and colleagues from Imperial College, have developed a gene delivery system based on part of the tetanus bacterium toxin, called the He-fragment, which is non-toxic and is able to bind to and enter nerve cells. Although the He-fragment system was only effective in cultured cells, the team has achieved selective gene delivery to the brain stem by using the He-fragment to re-target a gene-bearing virus, which had been injected into muscle, to nerve cells. In the longer term this research may lead to the development of gene delivery systems that can be used to treat neurological diseases.

**Gene Therapy 7, 1584-92**

Structures known as plaques, which contain fats and the protein collagen, accumulate in our arteries as we age. Collagen is normally found in blood vessel walls, and only comes into contact with blood when the vessel is injured, at which time small blood cells called platelets stick to the collagen and clump to plug the leak. If a plaque splits, exposed collagen can cause a clump that blocks the vessel and leads to a heart attack. Professor Farndale and colleagues from Cambridge have analysed crystallised platelet and collagen proteins to understand the binding process at the atomic level. Their results will inform the design of new drugs to stop this process.

**Cell 101, 47-56**

Determination of the body's cell types depends on which genes are expressed and how gene expression patterns are maintained during cell division. Altered gene expression underpin cancer and many other disorders. Dr Niall Dillon and colleagues from the MRC Clinical Sciences Centre, have made a major contribution to our understanding of how specific intracellular proteins, called transcription factors, regulate gene expression by altering chromosome structure. The work has implications for achieving appropriate gene expression following gene therapy and also for accomplishing successful therapeutic cloning.

**Cell 103, 733-443**

Magnetic Resonance Imaging (MRI) is a powerful tool for examining the body's internal organs for medical diagnosis and research. A team at the MRC Clinical Sciences Centre, working with Marconi, has developed a new material, known as microstructured magnetic material, that may lead to dramatic improvements in the performance of MRI systems. Microstructured magnetic material helps to obtain images by guiding radio-frequency magnetic flux from the body to the receiver coils of an MRI scanner. To demonstrate its potential, the team placed the material between the object – a researcher's thumb – and a small receiver. They obtained a clear image of the thumb's internal structure. In control experiments where the material was replaced by a piece of inert plastic the thumb was not detected.

**Science 291, 849-51**

MRC Professor Ole Petersen and colleagues at the University of Liverpool have shown that changes in the pattern of calcium release within cells, leads to changes similar to those seen in patients with acute pancreatitis. An abnormal prolonged rise in the calcium concentration inside the pancreatic cells triggers an activation of digestive enzymes that start to digest the pancreas itself, rather than digesting food in the gut, often with fatal results. The inappropriate enzyme activation does not occur when calcium is prevented from entering the pancreatic cells. Drugs aimed specifically at blocking the excessive calcium entry could therefore be used to treat pancreatitis in the future.

**Proceedings of the National Academy of Sciences 97, 13126-13131**
Professor Lowry and his team from the University of Reading have made a breakthrough in the understanding of pre-eclampsia, which is a major, and potentially fatal, cause of fetal and maternal illness. It affects one in ten pregnancies world-wide. Currently the only treatment is to deliver the baby prematurely by caesarean section, which means that the baby often requires further intensive care. The team has discovered that a small protein called neurokinin B (NKB), which is secreted by the placenta, is raised significantly in mothers when pre-eclampsia develops. NKB can be detected as early as week 9 of pregnancy making it a potentially useful pre-eclampsia screening tool. Clinical studies are now being initiated to test whether a drug called neurokinin receptor antagonist, which is already available, could block the action of NKB and thereby alleviate this dangerous condition.

Nature 405, 797-800

Asthma is a disorder of the airways whose incidence world-wide is increasing due to factors linked to a Western life-style. Its symptoms of wheeze, shortness of breath and cough, result from a combination of inflammation and changes in airway structure known as remodelling. MRC Professor Stephen Holgate and his group from Southampton University have studied the disease in human volunteers to show that the airway-lining epithelial cells that form a barrier to the external environment are more susceptible to injury in asthma sufferers. Epithelial damage activates the underlying structural cells to promote remodelling and increased inflammation leading to excessive responsiveness, loss of lung function and reduced responses to treatment. This underlying epithelial sensitivity may explain why environmental and dietary changes have led to the rising trends in asthma.

FASEB Journal 14, 1362-74

NEUROSCIENCE AND MENTAL HEALTH

In order to identify new drug targets, Professor John Wood and colleagues from University College London have generated mice lacking the gene for a protein involved in electrical signalling in damage-sensing nerves. These mice have higher pain thresholds, but are otherwise completely normal. This suggests that a drug acting on the channel would be a good pain-killer, free from side effects.

Current Opinions in Pharmacology 1, 17-21

A disease called Dementia with Lewy bodies (DLB) is one of the major causes of dementia in old age. Changes seen in patients’ brains suggest that they might be particularly responsive to new Alzheimer’s disease drugs called cholinesterase inhibitors. Professor Perry and colleagues from the MRC/University Centre Development in Clinical Brain Ageing at Newcastle, with industrial support from Novartis, have conducted the first multicentre, placebo-controlled trial of the cholinesterase inhibitor rivastigmine. The drug produced significant improvements in the core clinical features of the disease, reducing hallucinations, delusions and agitation. This finding is leading to further trial studies and is already changing clinical practice as DLB patients are starting to receive the treatment.

Lancet 356, 2031-36

Most organisms possess a biological clock with a daily rhythm of about 24h, known as a circadian clock, which helps them to synchronise their activities to daily changes in the environment. Professor Tony Harmar’s team at Edinburgh University has discovered that a chemical messenger, vasoactive intestinal peptide, is an important regulator of the brain’s circadian clock. This discovery may lead to the development of drugs that can be used to alleviate the impaired physical and mental well-being that can occur through shift work, jet lag, dementia, and in normal ageing.

Proceedings of the National Academy of Sciences 97, 11575-580
Professor Richard Morris and colleagues from Edinburgh University working with Elan Pharmaceuticals of Dublin and San Francisco, have advanced understanding of Alzheimer’s disease through the development of a new diagnostic memory test for a mouse Alzheimer’s model. The loss of recent memory that characterises Alzheimer’s may or may not be related to the formation of extracellular nerve-cell debris deposits, called beta-amyloid plaques. The new test has been examined in transgenic mice that over express human mutant beta-amyloid and deposit plaques. As they get older, the mice lose their ability to remember recent information in proportion to plaque deposition. Versions of the test have already proved useful for examining a new anti-Alzheimer’s vaccine.

Nature 408, 975-79

The habitual behaviour of many opiate addicts means that they often experience the adverse effects of drug withdrawal in specific environments. Subsequent exposure to the same conditions can be enough to trigger a conditioned withdrawal response that often involves drug craving, drug seeking and relapse to addiction, even in people who have not used drugs for a long time. Professor Barry Everitt and colleagues from Cambridge, demonstrated that this phenomenon depends on part of the brain called the basolateral amygdala, since damage to this structure completely prevented conditioned withdrawal. This finding suggests that new drugs that are able to modify the changes in the amygdala which occur during re-exposure to environmental cues might disrupt the reaction they prompt and so help to treat opiate addiction.

Nature 405 1013-1014

It is well known that “intelligence tests” are useful in practice, but there has been a century-long debate about what these tests measure and why they are adept at predicting success in many important activities. Dr John Duncan and colleagues from the MRC Cognition and Brain Sciences Unit, with collaborators from Germany, used a technique called positron emission tomography (PET) to investigate what aspects of human brain activity intelligence tests actually measure. Their results show that particular frontal lobe regions are selectively employed during intelligence tests, suggesting that general intelligence reflects the function of a specific frontal lobe system important in organising diverse activities.

Science 289, 457-60

Although the origin of most forms of epilepsy is unknown, a genetic cause is suspected in many cases. MRC Senior Fellow Dimitri Kullman and colleagues from the Institute of Neurology, working as part of an MRC Co-operative Group, have examined families that carry mutations of a potassium channel gene. This has previously been associated with a rare disease called episodic ataxia type 1, that affects balance and movements. The team reported for the first time that episodic ataxia type 1 patients are affected in different ways, and that some have epilepsy as part of the disease. Test-tube studies of potassium channel function showed that mutations associated with a severe form of the disease cause greater disruption than those associated with a mild form. This provides a mechanistic link between the mutation and the disease, and sheds light on channel function.

Annals of Neurology 48, 647-56

Glial cells form the specialised supporting tissue that surrounds nerve cells. In the brain, a type of glial cell called oligodendrons provide insulating sheets for the branches of nerve cells, enabling them to conduct signals at high speed. Oligodendron damage results in the widespread neurological disorder multiple sclerosis. Glial cells were previously thought to communicate with each other and with nerve cells through much slower signals than used by nerve cells. Now, Professor Peter Somogyi’s group at the MRC Anatomical Neuropharmacology Unit, with collaborators from the USA, have discovered that cells called
oligodendrocyte precursor cells (OPCs), which generate new oligodendroglial cells, receive fast signals from nerve cells through synapses which use the same signalling molecules as used between nerve cells. For example, they found that OPCs in a brain area involved in learning and memory, receive signals mediated by the neurotransmitter glutamate. The discovery of fast signalling from nerve cells to OPCs opens up new avenues for regulating their function, which could lead to the treatment of multiple sclerosis.

_Nature 405, 187-91_

Our understanding of how general anaesthetics work has advanced greatly over the last few years. Recently, Professor Nick Franks and his colleagues at Imperial College, working as part of an MRC Co-operative Group in General Anaesthesia and Neuronal Excitability, have identified the likely target for xenon gas, whose anaesthetic and pain relieving properties have been known for over 50 years. Their work suggests that xenon acts on a protein called the NMDA receptor, which is a widespread neurotransmitter receptor that is believed to play an important role in memory, learning and the perception of pain. The possible clinical uses of xenon will be a future focus for the team.

_Anesthesiology 92, 1055-66_

Stroke occurs when a large blood vessel in the brain becomes blocked, causing prolonged biochemical changes that result in nerve cell death in the brain tissue which the vessel supplied. A study by Dr Jonathan Marshall and colleagues from the MRC Comparative Cognition Team in Cambridge, in collaboration with AstraZeneca, has demonstrated that a drug designed to minimise these biochemical changes, provides very effective brain tissue protection when given to a primate species following experimentally induced stroke. There are long-term benefits in skilled arm and hand use and more rapid recovery from spatial neglect, a debilitating mental stroke symptom in which the brain ignores events occurring in the side of space opposite the damaged area. The drug may therefore have valuable applications in a wide range of brain damage, including head injury and birth complications, and reduce long term disability following stroke. This would provide substantial cost savings to Health and Social Services.

_Stroke 32, 190-98_

A team of researchers led by Professor John Collinge at the MRC Prion Unit has found new evidence for the existence of a symptomless, “sub-clinical”, form of the prion disease BSE in mice. They tried to infect mice with hamster prions and although the mice showed no apparent signs of disease, closer examination revealed that they had high levels of mouse prions in their brains. The result was surprising since it had always been assumed that hamster prions could not cause the disease in mice, even when injected directly into the brain. The team also found that this previously unknown sub-clinical infection could be easily passed on when injected into healthy mice and hamsters. Their findings suggest that just because one species appears resistant to a strain of prions they have been exposed to, it should not be assumed that they are not silently carrying the infection. The data also lend weight to the view that apparently healthy cattle could harbour but never show signs of BSE.

_Proceedings of the National Academy of Sciences 97, 10248-53_
Progress is continuing in the two priority areas for MRC funded under the 1998 Comprehensive Spending Review (CSR). These are the Post Genome Challenge and Health of the Public. Recent developments include:

### POST GENOME CHALLENGE
- Distribution of human and mouse gene arrays to the academic community free-of-charge (p23)
- Collection of DNA samples from large disease focussed cohorts in order to establish the resources required to study the genetic basis of complex disease (p30)
- Call for expressions of interest as the first stage in establishing a UK network for DNA sample banking and genotyping (p31)
- MAD beamline at ESF funded jointly with BBSRC and EPSRC for UK crystallographers (p26)
- Discipline Hopping Awards launched to promote the application of chemistry and physics in the life sciences (p21)
- Workshop to examine the key priorities for future research in bioinformatics and to inform the community about Unit at University College, London (p27) as “the Grid” (p26)

### HEALTH OF THE PUBLIC
- Additional funding awarded following large scale calls for proposals
- Increased funding provided for primary care research
- Additional funding awarded with ESRC under the Innovative Health Technologies programme
- Funders’ Fora established in cancer, ageing and cardiovascular disease (p29, SO)
- Review commissioned by the DH on the incidence, causes and biomedical treatments for autism (p27)
- Resolution of the future location of the General Practice Research Framework Centre to the MRC Clinical Trials developing computing infrastructure in the UK, known

### SPENDING REVIEW 2000
The spending review to determine the levels of science funding for 2001/02 to 2003/04 (SR2000) began in the Autumn of 1999 and the allocations were announced by the Government in November 2000. MRC’s income has been boosted by £89m above the level established by the CSR. This increases the annual budget to £380m by 2003. £53m of this extra money has been earmarked for Genomics research, with an additional £12m capital funding for related infrastructure. £8m is reserved for E-Science (bioinformatics, health informatics and grid testbeds, part to be committed jointly with BBSRC) and the remainder will contribute to
Within the University sector, the MRC continues to provide support for a varied research portfolio through a range of grant schemes. Details of all grant schemes and of current awards are on the web site. In 2000 MRC made awards totalling £155m for research in universities and teaching hospitals.

CENTRE GRANTS

MRC Centre Grants aim to support multidisciplinary research-centred environments in partnership with universities. They involve significant investments by both the MRC and the host universities with full-time scientific leadership. MRC awarded two Centre Development Grants in 2000/01, on the important topics of Clinical Brain Ageing (Newcastle) and Genome Damage and Stability (Sussex). The Sussex Development is looking at the processes which can cause some cells in the body to become cancerous.

The Edinburgh Centre for Inflammation Research was formally opened in February 2001 by Sir George Radda and Professor Sir Stewart Sutherland, Principal of Edinburgh University.

CO-OPERATIVE GROUP GRANTS

These awards draw together researchers to improve the overall output of research and enhance individual research projects (supported by Component Grants where funded by MRC). In 2000 the MRC set up 39 new Co-operative Group Grants throughout the UK. Over a third of Co-operative Groups involved interests of other Research Councils. These new Co-operative Grants support the research projects of over 200 scientists funded through MRC Component Grants and by a wide range of other funders. New Co-operative Groups include a grant to Dundee University in partnership with the Cancer Research Campaign investigating the most commonly mutated gene in human cancer. Another Co-operative Group has been established in Oxford to improve our knowledge of the physiology of the heart so that new therapies for heart disease can be developed. This Co-operative is also supported by grants from the British Heart Foundation. Important awards in the field of mental health include groups at the Institute of Psychiatry exploring the developmental basis of schizophrenia, whilst groups at Imperial College and the Royal Free Hospital are developing improved interventions for mental health problems.

Many of the Co-operative Group Grants are linking basic and clinical research (e.g epilepsy), enabling scientists to use multidisciplinary approaches on major scientific problems of importance to human health. Core support is proving particularly valuable for the appointment of key scientific co-ordinator posts, which would be difficult to fund through other mechanisms.

SUPPORTING RESEARCH EXCELLENCE IN UNIVERSITIES

Within the University sector, the MRC continues to provide support for a varied research portfolio through a range of grant schemes. Details of all grant schemes and of current awards are on the web site. In 2000 MRC made awards totalling £155m for research in universities and teaching hospitals.

CAREER ESTABLISHMENT GRANTS

Career Establishment Grants are awarded for five years to recently appointed clinical and non-clinical university scientists. The scheme aims to facilitate their establishment as independent investigators capable of winning further support in open competition. Council was able to make 27 awards in 2000 (£1.43m), the third year of operation. Eight of the Career Establishment Grants awarded involved clinical research.
INNOVATION GRANTS

These grants provide 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 new awards (£0.57m) were made from the applications considered in 2000.

DISCIPLINE HOPPING AWARDS

MRC launched Discipline Hopping Awards during the year to encourage researchers already established in the physical sciences to spend time applying their expertise to problems in the life sciences. The awards, of up to £50,000 for a one year period, are aimed at pump priming new interdisciplinary collaborations. EPSRC provided supplementary funding to the programme thereby enabling 24 projects to be supported across physics, chemistry and engineering. Other Research Councils have recently expressed interest in the scheme; PPARC for example, contributed to one award in the area of detector development.

OTHER SCHEMES

33 awards were made under the Joint Research Equipment Initiative (JREI) in 1999/00 totalling £2.1m. In addition, thirty two awards were made under the Realising Our Potential Awards (ROPA) scheme amounting to £3.1m. £1.6m was awarded via LINK awards.

THE JOINT INFRASTRUCTURE FUND

The fourth round of the Joint (OST, HEFGE, Wellcome Trust) Infrastructure Fund (JIF) took place in 2000. A total of 28 projects in 16 universities have been funded, many in the biomedical field. Awards which complement major MRC investments include grants to Professor R Weiss (University College, London) on post genomic virology to advance research into ways of combating HIV. Funds have been provided for two 900MHz Nuclear Magnetic Resonance (NMR) facilities for the UK biomolecular NMR community.

SCIENCE RESEARCH INVESTMENT FUND

For the future, JIF will be replaced by a new scheme – the Science Research Investment Fund (SRIF). A total of £1bn has been made available for SRIF, including £225m from the Wellcome Trust. The Research Councils have each issued statements setting out their current strategic objectives so that the universities may take these into account when preparing applications to SRIF.

INTER BOARD INITIATIVE GROUP

In September 2000, Council established an Inter Board Initiatives Group (IBIG). It will take responsibility for peer reviewing research proposals that span the interests of more than one MRC Board, or that are collaborative with other funding agencies and may require fast track decisions. IBIG meets four times a year and its funding recommendations are assessed by Council in competition with all other applications. It is chaired by the Chief Executive and the membership comprises the four Board Chairmen and Deputy Chairmen. Additional members are co-opted to give specialist advice.

CLINICAL RESEARCH

A series of visits to University medical schools took place during 2000 to help improve the amount and quality of research proposals submitted to MRC. Council discussed issues arising from the visits. The next step is to look at the potential value of Career Establishment Grants in establishing clinical researchers, Cooperative Group Grants in developing basic research that can lead to clinical application, and the possible role of MRC units in supporting good clinical research.
MRC RESEARCH UNITS AND INSTITUTES

New Appointments

MRC MOLECULAR HAEMATOLOGY UNIT Professor Doug Higgs became the Director of the Unit in October 2000, following the retirement of Professor Sir David Weatherall. Professor Higgs has worked in the Unit since its establishment 20 years ago and is one of the leading figures researching the genetic basis for haematological diseases, and in particular thalassaemia.

New Units

MRC CELL BIOLOGY UNIT Following a review of the MRC Interdisciplinary Research Centre in Cell Biology (University College, London), Professor Alan Hall was appointed on 1 January 2001 to succeed Professor Colin Hopkins as Director of the MRC Laboratory of Molecular Cell Biology (LMCB). He will prepare proposals for a new MRC Cell Biology Unit to form the core of the LMCB.

Other Unit Developments

MRC CANCER CELL UNIT The new building for this Unit, which has been jointly funded by the MRC and Cambridge University, is now complete and is in the process of being fitted out. It is anticipated that the Unit, to be directed by Professor Ron Laskey, will open formally in the Summer of 2001.

MRC TOXICOLOGY UNIT Professor Pierluigi Nicotera took up his appointment as Director of the Unit on 1 October 2000. It is intended that the Unit’s focus will be redirected towards understanding the molecular and cellular mechanisms that regulate cell dysfunction and cell death.

MRC RESOURCE CENTRE FOR HUMAN NUTRITION RESEARCH The Resource Centre, which is directed by Dr Ann Prentice, moved into new purpose built facilities - the Elsie Widdowson Laboratory Cambridge - on 1 January 2000. The Laboratory provides state of the art facilities for human volunteer studies, genetic, biochemical and metabolic research aimed at providing scientific evidence of the relationship between nutrition and health to underpin public health policy.

MRC HUMAN MOVEMENT AND BALANCE UNIT In October 2000, we considered the future of this Unit following the death of its previous Director. It has been decided that the Unit should close on 31 March 2001. However, in recognition of the importance of the field and quality of the Unit’s research, Council agreed that the science should continue to be funded via programme grant support.

MRC HUMAN IMMUNOLOGY UNIT The Phase I trial of a novel DNA/MVA vaccine against HIV began in Oxford in August 2000. This is the culmination of many years of research led by Professor Andrew McMichael, the Unit Director. The Oxford trial is proceeding well and a complementary Phase I Nairobi trial has recently begun recruitment. Both are funded by the International AIDS Vaccine Initiative. Since there are many common mechanisms between AIDS and diseases such as malaria, tuberculosis, cancer and autoimmune diseases, the Unit’s research has broad implications for public health.

MRC INSTITUTE OF ENVIRONMENT AND HEALTH (IEH) MRC is considering, in conjunction with NERC, proposals from the University of Leicester for the future of IEH. The aim is to expand the Institute’s remit and establish an active research programme from existing strengths and research expertise within Leicester. Such research activities would complement the current and ongoing review function of IEH.

MARY LYON CENTRE Following a survey of research community needs, MRC is taking forward plans for a new state-of-the-art mouse facility. This will provide high quality housing and breeding space as well as laboratories where researchers can identify, develop and study new mouse models of human disease. The facility will offer leading edge expertise in mouse genetics/genomics to academics throughout the UK.
MRC HGMP RESOURCE CENTRE/MRC MAMMALIAN GENETICS UNIT The MRC microarray programme, provided by the MRC HGMP Resource Centre and MRC Mammalian Genetics Unit, has begun to distribute human and mouse gene arrays to the academic community free-of-charge. In addition the programme is developing the tools for, and training scientists to manage, interpret and share data accrued from microarrays. The investment required to fabricate arrays with several tens of thousands of genes represented is beyond the scope of most UK research groups and the centralised service provided by MRC is in many cases the only route for many researchers to obtain access to array technology.

The MRC mouse genome sequencing consortium, co-ordinated from the Mammalian Genetics Unit, is providing high-quality finished sequence in regions where there is focussed research effort in the UK; it will provide at least 50Mb of sequence into the public domain by 2002. The consortium additionally took on 12 small projects from the research community during 2000.

MRC HUMAN GENETICS UNIT (HGU) New research at HGU in Edinburgh includes a collaborative pilot project in complex human genetics, studying an isolated population in Sardinia. Insights gained from the Sardinian population are likely to be applicable to the UK population cohort planned by MRC, and the work aims to provide proof-of-principle that genetic factors can be identified for complex traits. The identification of such loci will provide insight into the mechanisms underlying disease progression, as well as the development of new therapies and diagnostics.

MRC LABORATORIES JAMAICA The MRC Laboratories (Jamaica) were transferred to the University of West Indies at the end of 1999. MRC has organised a workshop to be held in Jamaica in the summer of 2001 to review progress and help advise on the future development of the Sickle Cell Unit.

UNIT QUINQUENNIAL REVIEWS During the year, the following MRC Units/Groups were reviewed:MRC Muscle and Cell Motility Unit, MRC Human Genetics Unit, MRC Protein PhosphorylationUnit. Most work was judged to reach the highest standards in science.

SPEND BY SCIENTIFIC AREA (ESTIMATED GROSS SPEND IN 2000/01)
Working in partnership with other organisations continues to be an important component of MRC strategy, where it is clear that mutually beneficial outputs will be generated. Partnership working with industry is covered in Chapter 5. Other key examples from 2000/2001 follow.

Opportunities for working in partnership with other Research Councils have been pursued with vigour over the last year. For example:

**METROLOGY**

EPSRC, working with MRC and BBSRC, launched an initiative aimed at tackling important life science research questions through new approaches to the measurement and analysis of important parameters in biological and biomedical systems. This initiative will help meet the needs of the post genome era and Foresight. EPSRC made eight awards in April 2000. A second call was launched in the Autumn. MRC contributed to 50% of the funding of a project in Cambridge on mathematical modelling of disordered myocardial conduction in relation to arrhythmia.

**TISSUE ENGINEERING**

EPSRC, BBSRC and MRC funded a collaboration led by Professor T Hardingham and Professor M Ferguson (Manchester University) with Professor David Williams, (University of Liverpool). This Interdisciplinary Research Collaboration in tissue engineering will focus on cell behaviour relevant to clinical problems in skin and wound healing, cartilage/disc repair and the repair and modification of vascular tissue. It will have a strong commitment to the translation of basic research into clinical application.

**IMAGING**

A joint EPSRC/MRC Interdisciplinary Research Collaboration was established in 2000, directed by Professor of UCL, Manchester, M Brady (Oxford), for research on the generic problems involved with extracting clinically useful information from medical images and signals.

**NANOTECHNOLOGY**

In May 2000, MRC organised a workshop on “Nanotechnology in Biomedicine” to promote awareness of this new field (manipulation of materials and structures at the atomic and molecular level) and to discuss how and where developments might be applied more broadly in biomedical research. The workshop was attended by national and international scientists and representatives from interested Research Councils, charities and industry.

In July 2000, EPSRC, BBSRC, MRC, MoD and DTI issued a joint call for inter-disciplinary research collaborations (IRColls) in nanotechnology. Bids were expected to involve a broad range of disciplines such as materials science, chemistry, physics, biology, engineering and applied mathematics across several Universities. Sixteen outline bids were received. Five full proposals are being submitted and the outcome will be announced in 2001.
CHEMICAL BIOLOGY

MRC and EPSRC issued a joint highlight notice during the year encouraging applications in the area of chemical biology relevant to human health. Successful applications may be part funded by EPSRC if relevant to their scientific remit.

SYNCHROTRON RADIATION

The new synchrotron, “Diamond”, is to be constructed at the Rutherford Appleton Laboratories, Oxfordshire. MRC has been working with the other Research Councils to support OST in taking the project forward in partnership with the French Government and the Wellcome Trust. The Scientific Advisory Committee to Diamond, chaired by Dr Richard Henderson (MRC Laboratory of Molecular Biology) has agreed that the new synchrotron will be a 24 cell, 3.0 GeV machine, and that there will be 7 beamlines available from day one, half of which will be for the life sciences. The MRC is developing plans, in consultation with other Research Councils and funding agencies and the scientific community, for the research facilities associated with Diamond.

BIOINFORMATICS

Bioinformatics is playing an increasingly key role in facilitating life sciences research encompassing cellular to whole organism and population studies. In June 2000 the Research Councils held a workshop to examine the key priorities for future research in bioinformatics and to inform the community about developing computing infrastructure in the UK, known as “the Grid”. The workshop recognised that a small, high quality bioinformatics research community had been established in the UK, working at the interface between biology and computer science, which needed to be supported, expanded, and developed. MRC continues to strengthen training in bioinformatics by supporting 10 PhD studentships, 10 PhD + linked Masters studentships, 15 Masters studentships, 6 Special Training Fellowships (1 jointly with PPARC), 1 Research Fellowship, 1 Clinical Training Fellowship and 1 Career Development Award.

The Research Councils and Wellcome Trust now meet regularly to exchange information on bioinformatics via a “Funders Forum” which aims to provide a “one-stop-shop” for advice on funding opportunities in this field.

In November 2000 the MRC and BBSRC jointly funded “CCP11” a collaborative computational project focusing on DNA sequence and protein structure informatics, hosted by the MRC HGMP Resource Centre and aimed at supporting software developers.

The Research Councils issued a joint call for new Bioinformatics Groups last year and EPSRC reviewed full applications in July 2000. Four awards were made - to Oxford, Manchester, Imperial College and UCL.

NEUROINFORMATICS

The MRC and BBSRC recently held a workshop on neuroinformatics. Council agreed that this is an important area for further development, which will foster links between neuroscientists and computer scientists, and that the field should remain a training priority. In parallel, MRC is contributing to the work of the Organisation for Economic Co-operation and Development in neuroinformatics, which includes the establishment of a web-based resource site and the development of databases.

SMALL BUSINESS RESEARCH INITIATIVE

The Small Business Research Initiative (SBRI) was announced in the Science and Innovation White Paper in July 2000. It aims to increase demand for research and development from small and medium sized enterprises. The Research Councils are collaborating to develop this scheme, in consultation with the OST and published details on their respective Web sites and on a central SBRI Web site early in April 2001.
ENVIRONMENT AND HEALTH

MRC and NERC continue to welcome proposals under this joint initiative. It is aimed at encouraging research into the human health impacts of environmental exposures, specifically through collaboration between environmental and medical scientists. Three Co-operative Group grants have been awarded in the areas of global environmental change, air pollution and the role of environmental factors in Mycobacterium transmission in Crohn’s disease.

HEALTH OF THE PUBLIC

The MRC’s Health of the Public initiative aims to expand the UK’s capacity for research into the developmental, environmental and socio-economic factors affecting health and health inequalities and to strengthen research into interventions. A second tranche of 14 awards was made in 2000. To promote training in this area, the MRC and NHS R&D Directorate continue to fund research fellowships through the MRC Health Service Research Fellowship Scheme. Two new awards were funded in 2000 via the Health Department’s allocation to the Committee for Epidemiological Studies of Aids (CESA). A highlight notice for new CESA applications, in January 2001 is generating significant interest.

AUTISM

At the request of the Department of Health, the MRC has set up a Review Group to look into the key questions in understanding the incidence, causes and biomedical treatments for autism. The Review Group will include representative consumers, charities, practitioners and expert scientists and will meet over the Summer of 2001.

NICOTINE REPLACEMENT THERAPY (NRT)

The Department of Health will be working closely with the MRC to take forward research into smoking cessation through the use of NRT. There are a number of key areas where the efficacy of NRT is still to be evaluated and the MRC will provide expertise in carrying forward research in these areas.

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES (TSEs)

The MRC has developed a broad portfolio of research into TSEs, co-ordinated with other funders. TSE remains a priority area, a key objective being the expansion of the portfolio, in particular in the areas of diagnostics and therapeutics, by attracting young and new researchers to the field. MRC has taken the lead on two initiatives, a meeting between key academics and representatives from the

ENVIRONMENT AND HEALTH

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PARTNERSHIPS WITH THE NHS AND HEALTH DEPARTMENTS

MRC continues to work closely with the NHS and Health Departments at a number of levels across a range of shared interests. Devolution coupled with the Government’s appointment of Czars in key health areas has provided new opportunities. Developments in key priority areas included:

FUTURE OF THE MRC GENERAL PRACTICE RESEARCH FRAMEWORK (GPRF)

The GPRF is a network of over 1000 general practices throughout the UK providing access to over 10% of the population; it is a national resource that facilitates many different clinical and epidemiological studies. During the year, Council gave consideration to the future location of the GPRF Co-ordinating Centre, beyond closure of the MRC Epidemiology and Medical Care Unit, where it is current located. It has been agreed that the GPRF Centre should be relocated to the MRC Clinical Trials Unit at University College, London.

PRIMARY CARE RESEARCH

A total of ten strategic grants, including two programme grants and five trial grants, were supported under the first round of the joint MRC/DH initiative on Primary Care Research. A second call for proposals was issued in the Spring of 2000 with a view to making further awards in early 2001.
diagnostics industry, followed by a call for proposals on the development of diagnostic tools. The meeting, in February 2001, successfully highlighted the difficulties the field is facing and the problems that remain unsolved in an effort to try and encourage more industrial involvement. The joint TSE Research Funders Workshop took place at Keele University in April 2000 when grant holders presented their latest research findings. The Funders are working together to ensure efficient arrangements to provide researchers with clinical and animal material and other valuable TSE reagents.

An expert MRC/DH Steering Group is monitoring three DH funded studies aimed at determining the potential scale of vCJD infection in the UK population. These studies are examining around 20,000 samples of tonsil or appendix tissue, discarded after routine operations, for tell-tale signs of abnormal prion protein. During the year a preliminary analysis of 3,170 tonsil samples found no evidence of abnormal prion protein, however this encouraging result must be treated with caution. It is not possible to predict the level of vCJD infection in the population from these data, because the sample size is small, the incubation period of the disease is unknown and it is not known whether everyone with a positive test would necessarily go on to develop the disease. However, the results will inform the design of future surveys and the situation may become clearer when further samples have been analysed. The difficulties analysing the data highlight the need to develop a non-invasive, pre-clinical, vCJD test for widespread screening.

MOBILE TELECOMMUNICATIONS AND HEALTH RESEARCH PROGRAMMES

An Independent Expert Group on Mobile Phones (IEGMP), commissioned by the Government and led by Sir William Stewart, looked last year, at the potential effects of mobile phone technology on health; it scrutinised recent research, took evidence from scientists and listened to the views of the public at open meetings around the UK. The IEGMP report to Government recommended the establishment of a UK-based research programme. The report of the House of Commons Science and Technology Committee on mobile phones and health made a similar recommendation. Funds to support such an initiative were attracted from industry and matched by Government; MRC provided £600k towards the £7m raised. The programme has been set up as a LINK collaborative research programme. The first call for proposals was issued in February 2001 and a second call is planned for September; the outcome will be known later this year.

MENTAL HEALTH

The Council discussed future strategy in this area at its residential meeting in February 2000 – taking account of presentations from Professor Louis Appleby – the DH Mental Health National Service Framework (NFS) Director – and other experts. A number of areas were identified that will be carried forward by the MRC to potenti ate mental health research in close co-operation with both the Department of Health and the NHS, especially in providing the evidence for successful implementation of the National Service Framework for Mental Health. These plans will build on existing MRC expertise and infrastructures such as the General Practice Research Framework and the MRC Clinical Trials Unit.

CANCER

A new national Cancer Research Institute (NCRI) will be launched in April 2001; it is the first national research institute in the UK to focus on a specific disease and will oversee all aspects of cancer research including clinical trials of new treatments and genetics. Building on the work of the Cancer Research Funders Forum (p30) the NCRI will bring together all UK Health Departments, the MRC, the Cancer Research Campaign, the Imperial Cancer Research Fund, the Ludwig Institute for Cancer Research, the Marie Curie Research Institute and the pharmaceutical industry. The NCRI will be chaired initially by Sir George Radda and will be based at MRC Head Office; it will not fund initiatives directly, instead the constituent bodies will use their own budgets to fund initiatives either singly or collaboratively.
A consortium involving the MRC Clinical Trials Unit and groups at Leeds and York Universities will contribute to the National Cancer Research Network (NCRN) as one arm of the NCRN Coordinating Centre. These groups will operate a network for clinical trials and other research, such as promising new approaches to the diagnosis, treatment and care of cancer patients.

**ANTIBIOTIC RESISTANCE**

In December 1999 and March 2000, Council made the first awards resulting from a web Highlight Notice on Antibiotic Resistance. Seven strategic grants have been awarded and six further proposals are being reviewed.

**WORKING GROUP ON FLUORIDE AND HEALTH**

A review from the NHS Centre for Reviews and Dissemination noted that much of the evidence in the area of fluoride and health was of low quality, following this, the DH asked MRC to establish a working group to consider what further research might be required. The working group met for the first time in February 2001.

The Council has also been asked by the MoD to advise on the feasibility of a prospective epidemiological study of service personnel who participated in trials at Porton Down between 1939 and 1989.

**DEPARTMENT FOR INTERNATIONAL DEVELOPMENT**

The joint scoping study, commissioned by MRC and the Department for International Development to identify new areas where the Council’s portfolio of research relevant to developing societies might be expanded, has now been completed. A review of HIV vaccine strategies has also been carried out. Both reports will be discussed by the Strategy Development Group and Council later in 2001.

**MRC GUIDELINES ON VACCINE DEVELOPMENT FOR EARLY PHASE TRIALS**

MRC is taking the lead in developing guidelines for academics who wish to take bench research on vaccines through to early phase clinical trials. A working party was established last year, chaired by Professor Sir Leszek Borysiewicz (Cardiff; now Imperial College, London) that includes representatives from the DH, Medicines Control Agency, National Institute for Biological Standards and Control, Department for International Development, Centre for Applied Microbiology and Research, the Edward Jenner Institute for Vaccine Research, Industry, BBSRC and protagonists from the research community. The draft guidelines will be posted on the MRC Web page during 2001 with an invitation to comment.

**PARTNERSHIPS WITH OTHER GOVERNMENT DEPARTMENTS**

**MINISTRY OF DEFENCE**

The MRC continues to act as an independent adviser to the Ministry of Defence (MoD) on Gulf War Illness Research. During the year, the existing Steering Committee was succeeded by a Group charged with reviewing evidence for Gulf War Syndrome and developing strategic advice; it was further agreed that research proposals in this area should be reviewed by the relevant Research Board(s). In May 2000 the Physiological Medicine and Infections Board approved an award to Professor Simon Wessely and colleagues (King’s College, London) for a three year follow-up study of Gulf War veterans; this work was funded by the MoD.

**PARTNERSHIPS WITH MEDICAL RESEARCH CHARITIES**

**AGEING RESEARCH**

MRC, EPSRC, BBSRC, EPSRC and DH established last year a Funders Forum for Ageing Research that brings these agencies together with the major charities that fund research in this area:
Alzheimer’s Society, and British Heart Foundation, Stroke Association, Joseph Rowntree Foundation, Research into Ageing, Anchor Trust, Wellcome Trust, Nuffield Foundation, the other health departments and OST. The Forum, which is chaired in the first instance by Professor Sir John Pattison (Director of R&D at the Department of Health (England)), met for the first time in October 2000; it provides an opportunity for member organisations to discuss matters of mutual interest and to identify areas where joint working could make a greater impact and maximise value for money. MRC has commissioned, as part of the Forum’s workplan, a bibliometric analysis of ageing research. Professor Ian Philp, the Government’s newly appointed National Director for Older People’s Services has recently joined the Forum.

CARDIOVASCULAR DISEASE

The MRC recently helped establish the Cardiovascular Research Funder’s Forum, which will consider areas of mutual interest relating to cardiovascular disease that would benefit from a co-ordinated approach. It is envisaged that the Forum will help develop a concerted research strategy, foster future partnerships between researchers and their funders, and facilitate the exploitation of the research to develop new approaches to diagnosis and treatment. Membership of the Forum comprises senior representatives from the British Heart Foundation, Diabetes UK, the MRC, the Wellcome Trust, the Health Departments, and the National Director for Heart Disease; it is chaired by Sir Charles George (BHF). The first meeting took place in January 2001.

CANCER

During 2000, the MRC carried out a review of prostate cancer in the UK on behalf of the Cancer Research Funders Forum which was set up in 1999, under initial MRC chairmanship. The main recommendation from the review was that the UK should begin to generate critical mass in this area and to this end, the MRC, in partnership with DH, CRC and ICRF has recently established two CRFF Prostate Cancer Collaborative Groups. In addition to fulfilling a general research need, these Collaboratives have also been tasked with networking the wider UK prostate cancer community, pump priming developmental research and bridging the gap between basic and clinical research.

Other work being undertaken by the CRFF includes the development of a national strategy for tumour banking with a view to creating a national generic tumour bank.

HUMAN DNA COLLECTIONS

The risks of developing many common diseases such as cancer and cardiovascular disease are affected by a complex interplay between genetic predisposition and exposure to environment and lifestyle risk factors. The sequencing of the human genome and advances in technology for detecting variations between individuals opens up exciting possibilities for identifying the multiple genetic factors involved and understanding how they interact. Large collections of DNA samples associated with high quality clinical and environmental data are essential for such studies. In October 2000 we funded 14 large DNA collections from cohorts of patients and controls, selected from over 150 outlines. These will underpin genetic research in common conditions such as breast cancer, colorectal cancer, Parkinson’s disease and depression. They include a heart disease collection which builds on a project funded by the British Heart Foundation, a diabetes collection which extends work started by Diabetes UK, and a glomerulonephritis collection which is a funding partnership with the National Kidney Research Fund.

As part of this initiative MRC plans to set up a national network of banking facilities to store these collections, organise their distribution to researchers, and manage the databases of genetic information obtained from research using the samples. It is also intended that these centres will act as a foci for developing and evaluating new technologies for high throughput genotyping. In December 2000 a call was issued for outline expressions of interest from centres wishing to participate in this network. Full proposals will be invited later in 2001. In order to promote better collaboration between
scientists and more efficient use of resources. MRC and the Cancer Research Campaign have jointly developed a database of existing collections of human samples, which will be accessible via the internet. This will be published later this year.

Throughout the year MRC and the Wellcome Trust, together with the Department of Health, have continued to develop plans for a new large prospective UK population cohort involving around 500,000 adult volunteers. All three organisations have now agreed in principle to support this study. Consultation with a wide variety of potential stakeholders, including the public, NHS health and information technology professionals, government departments, the Human Genetics Commission, medical research charities, industry and the other research Councils, as well as the scientific community, is an important feature of the development of this complex project. The results of an initial phase of qualitative research on public attitudes, jointly commissioned by the MRC and the Wellcome Trust, and carried out by Cragg Ross Dawson, were published in September 2000 and are available on the Website.

**CLINICAL TRIALS**

MRC has continued to build on its links with the charities in the assessment and funding of clinical trials. Members of the Association of Medical Research Charities are now routinely consulted on new outline applications in their areas of interest to confirm whether they currently support or are planning to fund similar studies or contribute to the trial in question.

MRC is planning an informal meeting of Trial Steering Committee Chairmen and other interested parties to share experiences, problem solving and refining/developing policy.

**INTEGRATIVE BIOLOGY – A NEW APPROACH TO HEART DISEASE**

The MRC has continued to work with the British Heart Foundation to develop an initiative in integrative biology which will encourage new research to address the burden of heart disease in the UK. The aim, in the first instance, is to establish either a directly-supported Unit, or an indirectly-supported Centre within a University environment. An International Advisory Committee has been charged with identifying a Director of exceptional ability and international standing.

**INTERNATIONAL PARTNERSHIPS**

Science is global and the MRC attaches high priority to international collaborations, which are facilitated by joint working with international bodies and national agencies from other countries.

The MRC has a lead role, in partnership with the Department of Health and other Research Councils, in developing the UK policy in relation to the biomedical aspects of the 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) in Strasbourg. The UK subscription to these organisations is ~£5.5m p.a. and MRC is responsible for ensuring the maximum return to UK and international science from this investment.

**Framework V**

Four rounds of proposals have now been considered for funding under the “Quality of Life and Management of Living Resources” (QoL) life sciences programme of Framework V and the UK academic community is continuing to attract substantial funding. MRC Units, in particular, have been very successful and are now involved in more than 60 major European projects and training networks, funded under FPV, with about a quarter of these projects also being co-ordinated by MRC scientists.
MRC is represented on the Programme Management Committee (PMC) and MRC officers continue to act as national contact point and to advise UK scientists on proposals for QoL under FPV. Via the PMC, the MRC has had an influence this year on EC discussions in several areas, including EC support for the European Bioinformatics Institute, TSE research and a new initiative in ‘genomics and human health’.

**Framework VI**

The MRC, together with the other UK Research Councils and relevant Government Departments has been actively involved in the consultation exercise conducted by OST following publication of the EC policy paper “Towards a European Research Area” in January 2000. This provides the context in which the formal EC proposal for the next Framework programme was published in February this year. One of the thematic priority areas for this programme is “Genomes and Biotechnology for Health” and biomedical research is also included in several other thematic areas. Work has now begun on defining the specific content of these thematic programmes and MRC will continue to play a role in their development.

One area of particular interest to MRC in relation to the next Framework is the proposed new initiative on the major diseases of poverty – AIDS, TB and Malaria. This was launched at a High Level Round Table Meeting held in Brussels in September 2000, attended by Sir George Radda. In the light of MRC’s experience in research on these infectious diseases and substantial investments in Africa, we have been discussing with the EC and other potential partners development of a concerted European approach. This initiative is timely in light of the increased interest of the G8 countries in global poverty and the Cabinet Office review of this area initiated late in 2000.

**European Molecular Biology Laboratory (EMBL)**
The UK is one of 16 member states that contribute funding for the European Molecular Biology Laboratory (EMBL); MRC manages the UK contribution. To prepare for the Director General’s new research proposals and indicative budget for 2001-2005, MRC set up a multinational review of EMBL that reported to MRC Council in October 2000. The report informed the UK’s funding decisions which were transmitted to EMBL Council in November 2000; decisions taken by EMBL Council, which had to be unanimous, will mean that the UK contribution will increase by £1m per annum to £5m per annum. A significant proportion of this overall increase will be directed towards the European Bioinformatics Institute in Hinxton. EMBL Council also agreed to start planning for the appointment of the Director General’s successor when Professor Kafatos retires in 2005, and the future shape of the EMBL portfolio.

**European Molecular Biology Conference**
The MRC is also responsible for the UK contribution to the European Molecular Biology Conference (EMBC) in Heidelberg and is represented on a newly constituted EMBC Strategy Group. Council has agreed to contribute additional funding to a new EMBO Young Investigator Award Scheme, which will afford key networking opportunities to established groups in member states.

**The Human Frontier Science Program (HFSP)**

HFSP is an inter-governmental organisation whose mission is to promote inter-continental collaboration in interdisciplinary, basic research in life sciences. It provides funding for collaborative research projects and a range of prestigious Fellowships. MRC, and to a lesser extent BBSRC, are responsible for the UK contribution to HFSP. During last year we carried out consultation with UK researchers to assess the value of this contribution. Negotiations over the future level of funding by the UK and other member states will be ongoing during 2001/2. This review will provide the basis for budget discussions with the HFSP Board of Trustees during the coming year.
STRENGTHENING INTERNATIONAL PARTNERSHIPS

Clinical Trials

MRC has developed a programme of collaboration with the US Veterans Administration and the Canadian Institutes of Health Research to encourage proposals that address health care questions of common concern. Through access to a much larger pool of potential participants than is available nationally, the initiative allows studies to be completed more quickly than would otherwise be the case; it also promotes best practice in trial design, execution and management and maximises the effectiveness of the investment of the three funding bodies. The first study to be funded under the collaboration, a trial of new clinical management strategies for HIV patients (OPTIMA), will be launched in March.

Much needs to be done to facilitate the conduct of multi-national trials. To this end, the MRC Clinical Trials Unit hosted an ESF workshop on “Challenges in Developing pan-European Clinical Trials” in September 2000. Several very positive recommendations came out of this workshop and discussions are taking place with ESF as to how these might be taken forward. One of the major problems identified was the restrictive conditions for conducting publicly funded European Trials that would be imposed by the new EC Directive on the conduct of clinical trials on medicinal products. This Directive will potentially also make trials far more expensive. MRC and DoH are working closely with the Medicines Control Agency to ensure that views of public funders and the academic community are represented in the transposition of the Directive into UK law.

MRC is committed to the development of an international meta-register of randomised controlled trials. We are working with the company Current Controlled Trials (CCT) to develop the register and implement a system of unique identification numbers for tracking trials. The register will not only assist in the planning of new studies, but will also help avoid unnecessary duplication, encourage collaboration, facilitate patient access to information and help reduce the problem of publication bias. To this end, a unique International Standard Randomised Controlled Trial Number (ISRCTN) has now been assigned to the majority of MRC trials. Henceforth this number will be used in all aspects of trial management and documentation, including any publications that arise from the study. With advice from MRC, CCT are preparing a proposal to the EC FPV programme to extend their register and the ISRCTN concept to other European countries; discussions have also taken place with ESF.

GOOD CLINICAL PRACTICE

MRC and DH have been working with the Medicines Control Agency to ensure that the perspectives of public funders and the academic community are represented in the framing of the new European Directive on the implementation of good clinical practice in the conduct of clinical trials on medicinal products. Now that the Directive has been adopted, MRC’s involvement will continue in helping to draft the accompanying guidelines for the Directive and advise on its transposition into UK law.

The Max-Planck-Gesellschaft (MPG)

During the year, there have been several reciprocal visits between senior Officers of the MRC and the MPG. This ‘exchange of practice’ has been very informative at an operational level. At a scientific level we are optimistic that these contacts will also lead to closer collaborations and we are now organising a bi-lateral young investigators workshop in Developmental Neurobiology, which will take place later this year. We hope that this will be the first of a series of such topic-based workshops that might expand to encompass other funding agencies.

Institut Pasteur

In January 2001, a meeting took place between MRC and the Institut Pasteur, Paris to discuss opportunities for bi-lateral collaboration. The Institut Pasteur is potentially a key partner in the proposed EC initiative on the diseases of
poverty (see Framework VI above). Several other scientific areas, including technology development were identified where further bi-lateral exploratory workshops might be productive. These will be taken forward during the course of the next year.

CNRS

Following an MRC/CNRS meeting on mouse genomics in Paris in 1999, there was agreement to co-ordinate, at a bi-lateral level, the development of and access to mouse gene microarrays. The first meeting of a co-ordinating committee took place in Paris in May 2000, and a further meeting was held in early March 2001 at MRC in London. The meetings are co-chaired by Professor Radda and Professor Godet, Director of Life Sciences at CNRS, and the co-ordinating committee consists of senior scientists and administrators from both countries. A key development has been the sharing of knowledge and resources, particularly with respect to cDNA libraries.

National Institutes of Health (NIH)

There have been several meetings between senior MRC Officers and NIH Institute Directors. This has included two visits by Professor Radda to NIH in Washington. We are exchanging ideas and co-ordinating our activities with NIH in a number of important areas including cardiovascular disease, cancer and tropical medicine.

In recognition of the ever increasing power of computers and the potential impact of computational modelling on biomedical research, MRC and the US National Institute for General Medical Sciences have been working together to co-sponsor a workshop on Computational Cell Biology which will take place in June 2001. The aim of the workshop is to bring together key figures in the field, to promote awareness of new developments and discuss where such developments might be applied more broadly in biology and medicine.

Number and Value of formal international collaborative projects:

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<tbody>
<tr>
<td><strong>EC</strong></td>
<td>114 2.7</td>
<td>136 3.2</td>
<td>143 3.7</td>
<td>127 4.1</td>
</tr>
<tr>
<td>UN (including WHO, IARC)</td>
<td>11 0.3</td>
<td>17 0.4</td>
<td>11 0.6</td>
<td>4 0.2</td>
</tr>
<tr>
<td>Others (including HFSP, ESF, NATO, EMBO)</td>
<td>26 0.3</td>
<td>36 0.5</td>
<td>37 0.5</td>
<td>40 0.7</td>
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<tr>
<td>Other international agreements (including governments, charities and industries)</td>
<td>78 2.3</td>
<td>85 1.9</td>
<td>82 2.8</td>
<td>71 3.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>229 5.6</td>
<td>274 6.0</td>
<td>260 7.6</td>
<td>242 8.2</td>
</tr>
</tbody>
</table>
Imaging Research Solutions Ltd

In February 2001, Nycomed Amersham Imaging (NAI) and MRC announced a strategic joint venture to form Imaging Research Solutions Ltd (IRSL), a leading molecular level imaging centre at Hammersmith. This unique partnership between the public and private sector has been formed to leverage the opportunities presented by the increasingly important applications of Positron Emission Tomography (PET) to the pharmaceutical industry and in clinical diagnosis.

Higher Education Funding Council

Over the last year, MRC contributed views to the evidence-based review of the Research Assessment Exercise (RAE); topics debated in the review included research funding and policy. MRC is also participating, with observer status, in the current RAE review of the Universities.

Human Genetics Commission

As reported last year, MRC has established a new Advisory Committee on Scientific Advances in Genetics (ACSAG) chaired by Lord Patel. The Committee has regular contact, and cross-membership with the Government’s advisory body in this area, the Human Genetics Commission. Major areas of discussion for the Committee so far include pharmacogenomics, stem cell biology, and risk perception.

Office of Science and Technology - Foresight Programmes

MRC contributed to the priority setting of six of the thirteen Foresight Panels established for the current Foresight cycle starting in April 1999. The following MRC inputs warrant particular mention:

- The MRC/BBSRC Foresight Associate Programme in Human Nutrition Research - this comprised a joint Council review charged with identifying key goals in the field for the next 5-15 years; the report informed the work of the Foresight Food and Crop Panel and has been posted on the MRC web site and the Foresight Knowledge Pool web site. MRC and BBSRC have invited high quality applications in those areas where opportunities/niches were identified.

Joint Council’s Foresight Associate Programme on Technology for the Future – this comprised a joint review of the technology needs of the science and engineering base over the next 10-20 years; it informed the Foresight exercise and also fed into Spending Review 2000 submissions.

The Foresight Panel Reports were published in December 2000 and considered by Council in February 2001.

Office of Science and Technology - Foresight Fund Healthcare 2020

MRC submitted candidate priorities for the Dti-managed Foresight Fund, which will operate through LINK mechanisms for supporting industry-academia collaborations. Three of the four research areas chosen for this scheme (nanotechnology, biomaterials, sustainable technology, and mobile wireless communication) reflect MRC strategic priorities.

Food Standards Agency

MRC met with senior executives from the Agency in October 2000 to discuss areas of common interest. MRC representatives are also involved in the Agency’s review of its research portfolio. Further interaction is expected once the Agency has completed its research review and published its future strategy later in 2001.
The MRC directly employs over 3,800 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. We remain committed to best practice in health and safety of our employees.

<table>
<thead>
<tr>
<th>STAFF IN UNITS</th>
<th>Full-time</th>
<th></th>
<th>Part-time</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Science</td>
<td>1115</td>
<td>1117</td>
<td>37</td>
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<td>Research Project Support</td>
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<td>895</td>
<td>107</td>
<td>105</td>
</tr>
<tr>
<td>Management Admin and Policy</td>
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<td>421</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>Policy</td>
<td>342</td>
<td>344</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Technical Services</td>
<td>105</td>
<td>102</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Infrastructure</td>
<td>569</td>
<td>670</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Locally employed staff (overseas)</td>
<td>569</td>
<td>670</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>3448</td>
<td>3549</td>
<td>334</td>
<td>330</td>
</tr>
</tbody>
</table>

The MRC has completed the fourth pay review cycle under its delegated pay and grading structure. The aims of the 2000 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
- introduce a supplement for non clinical scientific staff to enable the MRC to continue to attract and retain for our research, the highest calibre scientists at the forefront of their fields

In addition we have developed our pay and reward strategy for 2001 to reflect current business needs and public sector pay policy.

The MRC has worked in partnership with the Trade Unions to address issues of mutual interest such as health management, family friendly policies and harassment in the workplace.

**EQUAL OPPORTUNITIES**

The MRC values the diverse skills and experience of its employees and is committed to achieving equality of treatment for all.

The MRC Equal Opportunities subcommittee undertook an audit of MRC employee data to ensure that the aims of its equal opportunities
policies and employment practices are being achieved and to identify any imbalances which may need to be addressed. This survey will now be conducted on an annual basis. In addition, measures have been introduced to raise awareness of MRC equal opportunities.

**SENIOR WOMEN SCIENTISTS IN THE MRC**

We will continue to investigate and address impediments to women rising to senior scientific posts.

In partnership with the Wellcome Trust and other Research Councils, the MRC carried out a survey of university research staff to identify reasons why fewer women than men apply for grants. The study shows that there is no evidence to suggest gender discrimination – men and women have similar award rates and this observation is consistent across the range of Council funding. The study suggests that many factors influence grant application behaviour, some of which may disproportionately deter women.

**TRAINING IN TRANSFERABLE SKILLS**

We implemented the first phase of structured, high quality training programmes for each staff group in core transferable skills to complement specialist and research skills. This year we established the Research Associates (postdoctoral scientists) and Administrative Staff Development Programmes. We also conducted a pilot programme to prepare new MRC career track scientists for their role as leaders of research teams and managers of staff.

**TRAINING AND CAREER DEVELOPMENT BOARD**

In July 2000 Council agreed to establish a Training and Career Development Board, a subcommittee of Council to advise Council on training policies. Key aims are to ensure coherence of policies across the various forms of support for people (direct support for staff in MRC establishments, fellows and contract research staff on grants), to provide accountability for the management of MRC’s scientific career opportunities, and to help make sure MRC policies are widely known and understood.

The Board has met twice. Its first action has been to recommend increased investment in postgraduate research training through higher maintenance grants for the students and a greater level of investment in masters studentships.

**DEVELOPING THE RESEARCH WORKFORCE CAPACITY**

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 fellowships in bioinformatics and neuroinformatics are in their third year. Six new fellowship awards were made in the 2000/01 award year, bringing the total to 18. Council has decided to extend the scheme in line with new strategic priorities agreed as part of the 2000 Spending Review.

The other main strategic, ring-fenced scheme is the joint MRC/NHS Region Special Training Fellowships in health services research jointly funded with the Health Department. This was expanded in 1999 as part of initiatives to build up the research base in health of the public. A target of 19 awards are available each year.
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.

**RESEARCH FELLOWSHIP FUNDING PARTNERSHIPS**

**MRC/PPARC Research Fellowships**

As part of a broad initiative to promote interdisciplinary research at the physical science/life sciences interface, the MRC/PPARC Research Fellowship scheme was established in 1999. A small number of applications have been received, with the first two fellows taking up their appointments in October 2000.

MRC participated in a joint Research Council workshop at Aston in March 2001 designed to inspire postgraduates with physical sciences expertise to apply their skills in the life sciences.

**Joint Clinical Training Fellowships with Royal Colleges**

Joint Clinical Training Fellowships schemes are now established for Surgeons, Obstetricians and Gynaecologists and Clinical Infections and Medical Microbiology specialists. All these schemes encourage take up of research training in medical specialties where the academic research base needs to be strengthened. There is an ongoing dialogue with the Royal Colleges about scope for extending this set of schemes.

**Postgraduate Research Training**

Postgraduate research training has been the first focus of the new Training and Career Development Board. Following consultation with MRC’s PhD supervisors and masters course convenors in summer 2000, the maintenance grant was increased to £10k p.a. (outside London) and £12.5k p.a. (in London) from October 2001. The Council has also endorsed a policy of support for flexible provision of four year programmes of training, in the form of one year masters
studentships with the option of going on to a three year PhD/DPhil studentship. The number of masters studentships will be increased from 2003, to create a ratio of one masters studentship for every two PhD/DPhil studentships currently provided. The Board will continue to review MRC policies to ensure that the Council can sustain its reputation for high quality training that provides the foundations of the UK research capacity.

A new scheme of salaried predoctoral fellowships was launched in October 2000. 15 new fellows will train towards a PhD in MRC establishments, taking up their posts in October 2001. This scheme aims to address the need for enhanced opportunities to attract outstanding graduates to a career in biomedical research. The scheme has been introduced with only 15 fellowships per year at first, but will be kept under review with the possibility that the established career path for MRC scientific staff will be extended to start at the postgraduate, rather than post-doctoral stage.

Tenure-Track Clinician Scientist Fellowships

The Royal College of Physicians and the Academy of Medical Sciences published reports highlighting concerns about academic clinical research careers. MRC has a strong track record of contribution in developing clinical research scientists. These reports provided the impetus for revision of the MRC Clinician Scientist Fellowship scheme to encourage tenure track agreements with host institutions. Two fellows were appointed as joint MRC tenure track fellows.

The Department of Health has responded to these reports by funding up to eight new clinician scientist fellowships per year from 2001/02. The MRC has agreed to act as managing agents for the selection and post-award administration of these fellows. This partnership will be included in plans for a new national monitoring group designed to foster this vital group of clinical researchers.

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. This year, the MRC attracted seven research scientists of international standing to senior positions in the UK through its International Appointments Scheme.

Five were recruited from the USA, one from Germany and one from France. Their research interests encompass bioinformatics, molecular and cell developmental biology and immunobiology, neurobiology and clinical neuroscience.

Health and Safety

The MRC remains committed to best practice in health and safety management and recognises the leading role it is expected to play under the Government's initiative 'Revitalising Health and Safety'. All directors and senior managers are attending training seminars to ensure that they are fully aware of the health and safety responsibilities Council places upon them.

The prosecution case against the MRC for the death of a member of support staff at the Human Genetics Unit was heard at Edinburgh Sheriff's Court on 20 June 2000. The cause of death was asphyxiation whilst handling liquid nitrogen. MRC pleaded guilty under the Health and Safety at Work Act 1974, and was fined.

Council acted quickly to review its use of liquid nitrogen and complete risk assessments of all its cryogenic liquid installations across the country. Staff handling bulk quantities of cryogenic liquids received refresher training. An independent review of the Council's health and safety risk assessments was commissioned and completed.

Each of Council's research establishments has an appointed Unit Safety Co-ordinator. The majority of these posts are held on a part-time basis by senior scientists or laboratory managers.
A structured training programme has been devised for these co-ordinators with a compulsory foundation course supplemented by further specialist courses to match the particular needs of each establishment.

A full health and safety audit of all research units is planned for this year. The audit will look specifically at two areas: risk management and health and safety management structure. Units will use the audit reports to formulate their own objectives.

Communication between units to enable them to share best practice is seen by Council to be critical to establishing a benchmark for good health and safety management. The Corporate Health & Safety website and discussion mailbase in conjunction with regional support groups have all been initiated to enable and encourage information sharing and problem solving.

HONOURS AWARDED TO MRC SCIENTISTS

BIRTHDAY HONOURS LIST - JUNE 2000

Knights Bachelor

● Professor George Karoly Radda CBE, FRS, Chief Executive, Medical Research Council, for services to biomedical Science.

● Dr Iain Geoffrey Chalmers, Director, UK Cochrane Centre (Oxford) - Strategic Project Grant Holder

CBE

● Professor Janet Thornton, FRS, for services to structural biology - Standard project grant holder and member of MRC’s former MCMB B-Grants Committee.

OBE - Diplomatic and Overseas

● Dr Hilton Carter Whittle, Director, MRC Laboratories The Gambia, for services to medical research and public health in the Gambia and across West Africa.

MBE

● James Michael Fordham, Head of the Technical Instrumentation Workshop at LMB, for services to the MRC Laboratory of Molecular Biology and to instrument design and engineering.

NEW YEARS HONOURS - JANUARY 2001

Knights Bachelor

● Professor Les Borysiewicz, former Council member and former Chair of MCMB, for service to medical research and education

● Professor John Sulston, MRC grant holder and former director of the Sanger Centre, for service to genome research

CBE

● Professor Nick Day, MRC Professor for service to statistics and epidemiology underpinning cancer biology

OBE

● Professor Bryn Bridges, Director of MRC Cell Mutation Unit for service to the effects of cellular radiation

● Professor John L Reid, Glasgow, for services to Biomedical Science - former MRC Grant Holder and past Systems A Board member 84-88
The MRC works with industry to exploit the commercial potential of its technology.

**WORKING WITH INDUSTRY**

Exploitation of research findings within MRC Institutes and Units has continued apace during 2000/1, with a mix of new initiatives coupled with consolidation of past activities.

During the year, 34 new patent applications were filed, and 36 licensing agreements completed, including licences both to existing companies and to permit the creation of new companies:

- Diversys Ltd. (further peptide and monoclonal antibody technology)
- Ardana Biosciences Ltd. (technology from the MRC Human Reproductive Sciences Unit, and focused on female health)
- Avidis S.A. (protein-folding technology; based in France but future UK research component to the company envisaged.)
- Zarpex Ltd (anti-infective technologies; in partnership with a number of Scottish HEIs)
- Matrix Therapeutics Ltd. (cancer diagnostics);
- D-Gen Ltd (led by Imperial College, Prion Disease diagnostics)

**MRC objectives for exploitation**

Objectives for exploitation reflect the MRC’s mission, and focus on the contribution of research to the health and wealth of the nation. The objectives are (in order of priority):

- to work through the mechanisms, and with the partner(s), judged most likely to develop MRC technology into services and products useful to society
- to maximise the contribution to national wealth creation and UK industrial competitiveness
- to maximise income to the MRC in the medium- to long-term

**Achievements assessed against objectives**

**Licensing and spin-out companies**

The conversion of research into therapeutic products is an extended activity within industry. Licensing agreements completed by the MRC, in some cases as early as the late 1980s/early 1990s, have underpinned successful drug development, and recently led to the introduction to the market place of important new drugs, especially “humanised monoclonal antibodies”. Commercial reality requires companies to focus on the registration of new drugs in the largest market, the USA, with introduction into the UK some months later.

Four humanised therapeutic antibodies have now been approved by the US FDA.

- prevention of transplant rejection,
- prevention of RSV infection in premature babies,
- treatment of breast cancer,
- treatment of acute myeloid leukaemia

Further therapeutic antibodies are in advanced
stages of development and/or registration especially for serious, chronic inflammatory diseases, e.g. arthritis, Crohn's disease, and asthma and for treatment of chronic lymphocytic leukaemia.

In addition to new MRC “spin-outs”, existing MRC-linked companies have grown significantly. Celltech plc, which originated from MRC is quoted on the FTSE 100, and Celltech introduced its first MRC technology-derived product, Mylotarg to treat acute myeloid leukaemia, to the US market during 2000. Cambridge Antibody Technology, which is also FTSE listed, continued to expand with its staff numbers increasing to 221. Other MRC “spin-out” companies continued to grow, with many raising new finance and completing significant corporate agreements. In a number of cases, further technology has been licensed from the MRC to these start-up” companies, boosting their competitiveness and increasing the financial return to the MRC.

The major contribution that MRC technology makes to national wealth creation follows from job creation in “spin-out” companies. Whilst successful growth follows from the qualities of the company management, it also reflects favourably on the nature of the founding MRC technology. MRC “spin-out” companies now employ more than 3,000 direct jobs. Although primarily within Celltech and Cambridge Antibody Technology, these are spread across 20 companies.

2000/1 saw a sharp increase in MRC exploitation income, from £7.6m in 1999/2000 to more than £17.9m in 2000/1. This increase derives from a continuing growth in royalty income, plus the sale of a part of the MRC’s share holding in Cambridge Antibody Technology Ltd.

MRC Technology (MRCT)

The year under review has been the first full year of the re-structured MRCT. This new structure has brought the collective expertise of the previous Technology Transfer Group and the two MRC Collaborative Centres together to increase effectiveness. The growth in MRC licensing income has also allowed MRC to provide increased financial support for exploitation, and additional staff have been recruited into MRCT.

During the year, Council approved a budget, from exploitation income, to be used by MRCT to support research work specifically to investigate and expand the commercial value of promising results emerging from “core” research.

MRCT staff are regularly invited to give lectures and address technology transfer conferences. and serve on Government Department committees.

UK Medical Ventures Fund/MVM Ltd.
MVM Ltd. continued to participate with MRC scientists and MRCT to create new companies and further develop existing MRC “spin-out” companies. During the year, Council formally reviewed the progress of UK Medical Ventures Fund/MVM in relation to Council exploitation objectives, and approved the proposal from MVM Ltd that a second fund should be raised with specific rights and obligations between the MRC and MVM.
The above list does not include Celltech which was originally, in 1980, a start-up company based on MRC technology.

*denotes companies where MRC is a shareholder

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**TOTAL**
The MRC’s communications strategy is designed to engage different publics in scientific issues, to develop a dialogue, and to learn from the public’s input.

**Science and Society**

Following the reputation audit commissioned by the MRC, the first in a series of local opinion former events took place in Bristol in September. The meeting, aimed to open a new dialogue with key influential figures in the local community. It was hosted by Council member Richard Denton, and Professors Tavaré, Dieppe and Collingridge all gave short presentations on their science, explaining its importance in terms of human health. Similar events are now planned in other localities with significant MRC investment.

Throughout the year the MRC has continued to equip its scientists with improved communication skills in order to develop new and better dialogue with key audiences. Training courses include presentation masterclasses, media training at intermediate and advanced level and BRET (Biomedical Research Education Trust) courses which equip scientists to discuss the use of animals in research with schools audiences.

The new MRC Consumer Liaison Group held its first meeting in May 2000 and has had three further meetings during the year. Members (details on the web-site) were appointed following public advertisement. The aim of the Group is to advise on ways of promoting effective and appropriate involvement in MRC activities, and to advise MRC on consumer interests and concerns about research.

The CLG has tackled major topical issues - for example the Council’s strategy in genetics research; ethical and communication issues in the use of animals in medical research. The Group’s advice has also been sought on presentational issues. Members are also starting to provide a more explicit consumer perspective in particular MRC initiatives – for example in relation to the review of Autism and on fluoride in water, and in developing proposals for the UK Population Biomedical Collection (see p31).

**Other Public Events**

**25 Years of Monoclonal Antibodies**

In July, the MRC celebrated the 25th anniversary of the discovery of monoclonal antibodies with an international audience in the QEII Conference Centre in Westminster. Lord Sainsbury gave the keynote address. Dr César Milstein who made the initial discovery was presented with the first MRC Millennium Medal in recognition of his outstanding research and contribution to human health and wealth.

**Science and Music**

The Festival of science, music and the arts took place in London during September. MRC exhibited its ‘Science in Focus’ collection as well as supporting ‘Soundings’, an exhibition developed by MRC scientist Dr Jemma Hine of the MRC Institute of Hearing Research.

‘Making Waves’ was a partnership project between the MRC and the Royal College of Music on 28 September. A piece of music was
commissioned by the MRC and was composed as a collaboration between Cameron Sinclair, an experienced composer, conductor and performer and Professor Mark Haggard of the MRC Institute of Hearing Research and Dr Mike Page of the MRC Cognition and Brain Sciences Unit. After a day long rehearsal, 45 MRC scientists performed the piece for guests, staff and families and friends in the concert hall of the Royal College of Music.

Edinburgh Science Festival

The MRC sponsored and hosted an interactive exhibition on the theme of DNA Science at the family section of the Edinburgh Science Festival in April. MRC PhD students manned a lab bench and children participated in extracting DNA from kiwi fruits, setting up sequencing gels and working on puzzles about DNA. More than 10,000 children and parents attended the festival.

Science and Schools

Together with BBSRC and NERC the MRC exhibited the science research councils’ stand at the Association for Science Education Centenary Annual Meeting in January. MRC was one of the sponsors of a session entitled ‘A Century of Genetics’. It was attended by 100 teachers and presented current and potential development techniques in genomics research.

The Genetics Interest Group (GIG) is partially funded by MRC. The aim of the organisation is to promote awareness and understanding of genetic disorders and to increase knowledge of advances in genetic medicine.

In October, GIG arranged a workshop in Nottingham with the Trent Focus GP Research Network to explore GP and primary care teams’ views on ethics and practicalities of the proposed large DNA cohort (see p31). The meeting raised a number of practical issues which will inform the development of the project protocols.

The Times Higher Education Supplement in May reported the results of the MRC commissioned MORI survey on attitudes of the general public on the use of animals in medical research. An MRC booklet ‘Mice and Medicine’, addressed many of the issues that the survey had identified as being of concern to the public such as health outcomes of the research,
regulation and standards of care. 3,000 copies were distributed to key opinion-formers and the press and made available to members of the public at events and exhibitions.

**Publications**

New publications issued during the year included a new series of briefing sheets. These summarise current topics of particular interest to MRC's wider audiences. To date editions on stem cell research, therapeutic cloning, the use of animals in research, research on TSEs and monoclonal antibodies have been produced. New briefings on cancer, heart disease and mental health will be available in 2001. Details of all these MRC publications are available on the website.

**Media**

The MRC has a busy professional press office receiving in the region of 2000 media enquiries a year and over 1600 enquiries from members of the general public. A total of 60 press releases were issued during the year, highlighting some of the major events, achievements and initiatives featured elsewhere in this Report. Some examples which received wide media coverage follow:

A joint MRC/DH press briefing announcing the first results from the retrospective tonsil studies which have tested some 3,000 samples for the presence of the rogue protein believed to cause variant Creutzfeld Jacob disease. Some 40 journalists attended and Professor Sir Leszek Borysiewicz, who chaired the MRC/DH Steering Group for the studies outlined the results and was interviewed by several broadcasters.

A Press release in August announcing the identification of new mouse models was used in several media outlets. Professor Steve Brown, Director of the MRC Mammalian Genetics Unit and the MRC Mouse Genome Centre was interviewed by BBC Radio 4’s PM programme, Radio 5 Live, BBC News and BBC Online.

In August Dr Evan Harris MP became the first person to be vaccinated against HIV in a new clinical trial run by the MRC Human Immunology Unit. The press call gained widespread coverage in the UK and international media.

The press release issued in October announcing the publication of new MRC guidelines on the use of Personal Information in Medical Research was used by journalists writing for the British Medical Journal, Times Higher Education Supplement and Research Fortnight.

During the year approximately 120 parliamentary questions were dealt with by Head Office.

**Evidence to Parliamentary Enquiries**

House of Lords Enquiry into Human Genetic Databases: oral evidence and memorandum submitted Jan 2001

House of Lords Science and Technology Select Committee Follow up to Therapeutic Uses of Cannabis (1998): Memoranda regarding MRC trials submitted January 2001

House of Lords Science and Technology Select Committee Complementary and Alternative Medicine: oral evidence given May 2000

House of Commons Science and Technology Committee Inquiry, Are we realising our potential? Memorandum of evidence submitted June 2000

House of Commons International Development Select Committee HIV/AIDS: the impact on social and economic development: Memorandum of evidence submitted July 2000

House of Commons Science and Technology Committee Inquiry Cancer Research a Fresh Look: oral evidence given April 2000
The Council has always expected high standards to be followed in the conduct of animal experimentation and has actively sponsored advanced research methods which allow more and better quality knowledge to be gained from reduced or more refined work with animals, in-vitro alternatives, and novel methods, such as non-invasive imaging or antibody production using phage-display. Council decided in 2000 that it was timely to provide an MRC focus for synthesising and disseminating advice on animal welfare and use in research, including on issues related to reduction, refinement and replacement and on both new and existing research techniques. In the first instance, the new Centre for Best Practice for Animals in Research will work with the scientific community, other organisations concerned with research funding and the welfare of laboratory animals, and with policy makers. The Head of the new Centre was recruited in open competition in January 2001 and is expected to take up the post in May 2001.

In parallel MRC also issued a call for proposals for research projects addressing ways of reducing, reforming or replacing animal use.

STEM CELLS AND THERAPEUTIC CLONING

The MRC – working with charities and other research organisations - took part in many Parliamentary, media and other briefings on stem cell issues in advance of the free votes in the House of Commons and the House of Lords on extending the provisions of the Human Fertilisation and Embryology Act to encompass the study of embryo development and understanding and treatment of serious disease. In light of the Government decision to extend the Act’s provisions, the MRC, with other Research Councils, is taking forward one of the recommendations made in the August 2000 report of the Chief Medical Officer’s expert group on stem cell research i.e. to explore the feasibility of establishing collections of stem cells for research use.

GUIDELINES FOR HUMAN SAMPLES USED IN MEDICAL RESEARCH

These new MRC guidelines cover issues such as the importance of valid consent, protecting the confidentiality of people who donate samples, use of samples in commercial research, and feedback of information to donors. Consultation on the interim version of these new guidelines, first published in November 1999, has now been completed. The guidelines have been revised to reflect the many comments received and a new section has been added on the use of post-mortem tissue, which takes into account the findings of the enquiries into retention
of children's organs at Alder Hey and Bristol Royal Infirmary. Publication is planned for May 2001.

GUIDELINES ON RESEARCH USING PERSONAL INFORMATION

Most of the UK’s publicly-funded clinical research into the nature of disease, into new treatments, into the effectiveness of health care, and into the social and economic factors affecting health, depends on using data from medical records. Because there was no clear consensus on how legal and ethical principles should be applied when personal information is held or used, with and without prior consent, MRC formed a working party to draw together scientific, clinical, ethical, legal, and consumer views and establish new guidelines.

The new guidance "Personal Information in Medical Research" was published in October 2000, and widely circulated to MRC-funded researchers and ethics committees. The guidance sets higher standards for the information that patients and members of the public should received, and tighter limits on the analysis of any information without prior consent.

SCIENTIFIC MISCONDUCT

MRC is required to record incidence of scientific misconduct. As with last year, no incidents of scientific misconduct among MRC researchers were reported.

RESEARCH IN DEVELOPING COUNTRIES

The Council is a sponsor of the Global Forum on Bioethics in Research and was represented at the second annual meeting of the Forum held in Bangkok in October 2000. The MRC is the main organiser of the third annual Forum, which will be held in November 2001 in The Gambia; in January 2000 the Council hosted the programme planning group for that meeting. The MRC’s own Group on the Ethics of Research in Developing Countries continues to meet three times a year to advise Council on relevant research proposals.

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.

CLUSTER RANDOMISED TRIALS

In February 2000, the MRC hosted a workshop to consider the methodological and ethical issues raised by cluster randomised trials, to lay the foundation of future MRC guidance in this area.

MONITORING AND EVALUATING MRC’S FUNDING SCHEMES

The Council discussed during the year mechanisms to address the issues highlighted in a survey of the operation of the MRC Advisory Board; the outcome will be posted on the MRC web site during 2000.

Council also hosted a workshop on “Open Peer Review” which was attended by scientists, members of MRC Boards and Committees and representatives from other Research Councils and Charities. This led to the conclusion that whilst open peer review might be acceptable for articles submitted to journals for publication, it was much less satisfactory for research applications submitted to funding bodies for peer review.

Work is currently underway to develop mechanisms for reviewing individual Co-operative Group Grants; proposals posted on the MRC web site have benefitted from the views of the research community. In due course systems will be put in place to evaluate the success of this funding scheme overall.
AUDIT

Pursuing its expanded remit to include issues of corporate governance, the Audit Committee has reviewed implications for the Council of the Turnbull Report and the new requirement for a Statement of internal Control to accompany the Accounts. In this connection the CAC has worked closely with senior management and the RCIAS in the development of a policy for the management of risk throughout the Council.

During the year, a further 16 audits took place within the rolling programme of Compliance Audits (audits of the management of resources within MRC Institutes and Units). There were also 10 audits of corporate systems.

EFFICIENCY

Highlights this year included:

- The transfer of the preponderant interest in the Cyclotron Unit's activities to Nycomed Amersham in return for capital investment in the unit and technical, marketing and commercial expertise.

- The MRC has implemented the first phase of a new training strategy to provide high quality training in core transferable skills to complement specialist and research skills. This will allow staff to contribute more fully to Council's objectives eg. getting better value for money from resources, exploitation of research findings.

- The MRC has begun work on the Fellowships payment profiling project. This project is expected to effect efficiency gains in both Fellowships and Accounts administration and will improve Council's control of Fellowships expenditure. Higher Education Institutes are also expected to benefit from this project, through greater control in planning for expected income.

MRC'S SERVICE FIRST STATEMENT

Service First is the Government's new charter programme which aims to focus attention on service delivery across the public sector and is an integral part of the Better Government initiative.

The Research Councils and the Office of Science and Technology have agreed a list of key performance areas and each Research Council has set its own challenging standards. We will report on our performance against these targets both in our Annual Report and on our web site.

The MRC undertakes to:

- abide by equal opportunities and anti-discrimination legislation
- ensure that procedures exist for consulting users proactively e.g. concordats with government departments, the work of the Consumers Liaison Group, EAA roadshows in Universities etc
- provide contact details on all external documents
- uphold high standards of integrity in all areas of our operations
- operate a complaints procedure including name of contacts to which complaints should be directed.
- maintain an up to date web site

AREA AND TARGET  ACHIEVEMENTS IN 2000/01

| Grant applications | 100% through the new Electronic Application and Assessment system |
| General correspondence | 92% |
| Payment of invoices | 80% |
As a result of the 2000 Spending Review (SR2000), Grant-in-aid income was £319.2 million in 2000-01, an increase of £14.6 million from 1999-00.

Additional funding totalled £45 million in the year; the main element of which was external funding for research programmes derived 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 2000-01 - a separate fund for income derived from the licensing of intellectual property - was £18m, £2.9 million of which was allocated to MRC staff and units under the scheme of incentive payments to inventor.

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 £342k; the Council is very grateful to 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 £23 million.

Expenditure on existing and new programmes in the MRC’s own institutes and units (MRC ‘direct support’) was £196.5 million of which £12.3 million was allocated to the costs of ongoing estates care and maintenance work. Expenditure on direct support was more than in previous years as Council invested £16.2 million capital in a number of new units and in initiatives to renew, modernise and restructure existing research infrastructure (essential buildings and plant/laboratory equipment and information technology). Significant capital projects include:

- Several initiatives in Cambridge were completed including: a major new research building on the New Addenbrookes Hospital site to house the new MRC Cancer Cell unit (the MRC contributed 50% of construction costs); a new building to house Nuclear Magnetic Resonance (NMR) equipment; a
major programme of refurbishment and extension for the MRC Cognitive Brain Sciences Unit and a new building on the Peterhouse Science Park to house the MRC Resource Centre for Human Nutrition Research.

- The commencement of a major refurbishment programme at the MRC Human Genetics Unit in Edinburgh;
- Detailed planning for an important new Biological Services Unit at Harwell. Contract work to start early in the 2001/02 financial year.
- Refurbishment work at the MRC’s Toxicology Unit in Leicester to accommodate the new Director’s scientific programme.

Expenditure on indirect support, for research in universities and other organisations, amounted to £158.1 million. The bulk of this is for grants, research training awards and personal awards to scientists, but it also includes special contributions to 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.

Overall expenditure was £15 million less than income largely due to money retained within the commercial fund and all of which will be used to supplement the Council’s future spending plans.
From 1999/2000, costings 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 Accounting Officers Section towards the end of the calendar year.

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[1] 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.

[2] Activities which make resources available to the whole community - e.g. the UK Population Biomedical Collection, the Human Genome Mapping Resource Centre and the Human Nutrition Resource Centre (separately identified from other activities from 2000/01 onwards)