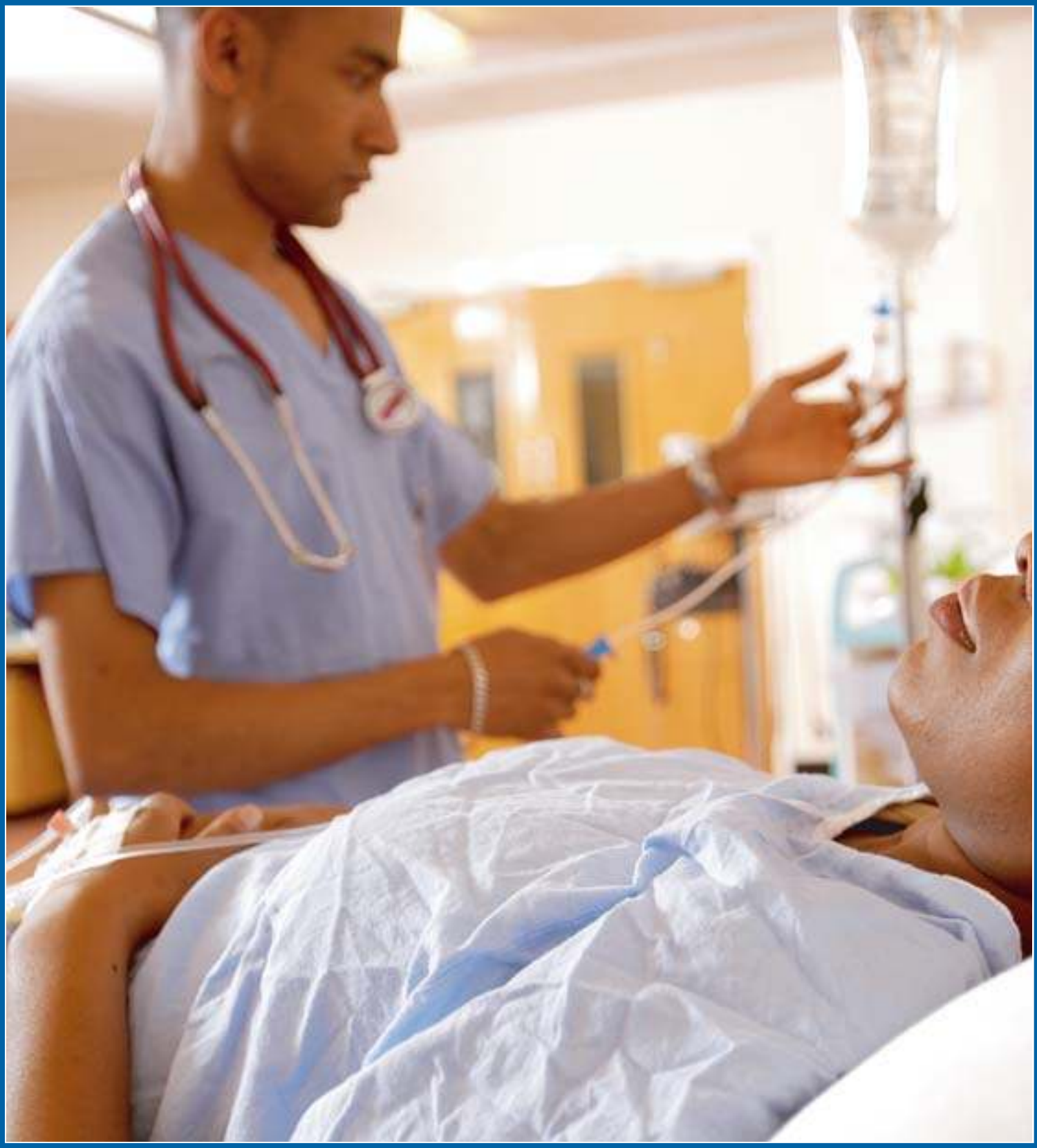
Annual Report and Accounts 2003 04



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MHRA

Medicines and Healthcare products Regulatory Agency

Safeguarding public health

Annual Report and Accounts 2003 04

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Accounts, prepared pursuant to section 4(6) of the Government Trading Funds Act 1973 as amended by the Government Trading Act 1990, of the MHRA Trading Fund as at 31 March 2004 together with the Report of the Comptroller and Auditor General thereon

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Contents

From the Chairman and Chief Executive

This is the first Annual Report of the Medicines and Healthcare products Regulatory Agency (MHRA), which brings together the work of the former Medicines Control Agency (MCA) and Medical Devices Agency (MDA). In 2003/04, the MHRA focused on two main priorities: continuing to deliver our key objectives; and managing the internal and external changes involved in creating a new agency. This is why we have chosen 'continuity and change' as the theme of this report.

Making an effective contribution to public health

The breadth of the Agency's activities is wide, complex and challenging but they all contribute to its most important task, protecting public health by effectively regulating medicines and devices. This year, the Agency addressed a number of key safety issues.

It continued to support an ongoing review of the safety of selective serotonin reuptake inhibitors (SSRIs) which has led, amongst other things, to new safety warnings governing their use by children. The Agency also monitored the sale of prescription only medicines via the Internet, along with other infringements of the Medicines Act, and has successfully prosecuted a number of offenders. The 40th anniversary of the Yellow Card Scheme was marked with a comprehensive review designed to ensure that the scheme continues to benefit the public and to prevent abuse of this important data set.

Supporting industry and scientific innovation

Protecting the public is vital, but the Agency also has a responsibility to ensure that regulatory burdens do not hamper innovation or delay patients' access to innovative medicines and devices. This year, the Agency maintained excellent service levels in terms both of the speed with which it processed licensing applications, and the quality of the decision-making process. Support by the regulator during the development phase for medicines is becoming more important and the Agency has devoted more time than ever to that process. The Agency also launched a review of the device evaluation service, a tool for both industry and the NHS, to ensure it continues to meet stakeholder needs.

The Agency worked with stakeholders to streamline the introduction of a range of new legislation, including the Clinical Trials Directive and the In Vitro Diagnostic Medical Devices Directive, and to ensure that these do not harm academic or non-commercial clinical trials or delivery of diagnostic services within the NHS. The Agency also played a key role in the Health Industry Task Force, which was set up to improve patient outcomes and enhance the performance of the devices industry in the UK and overseas. This work has strengthened links with industry, and will help influence the way medical devices are regulated in future.

Providing authoritative and accessible information

Patients and healthcare professionals are key stakeholders, and the Agency has a duty to provide them with the information they need to make decisions about their own care and the care of others. In November, the Agency began a review of its internal and external communications with two aims in mind: to raise awareness of medicines and devices safety issues; and to ensure that all our communications succeed in getting their message across to the people who need to hear them. The new information

management strategy underpins this work, by helping to develop effective information management systems and channels for delivering information to, and communicating with, all stakeholders.

Influencing European and international regulation

Both former agencies had strong European and international profiles, a legacy inherited by the MHRA. It is certainly something we wish to build on. In December, the UK adopted the EU's review of pharmaceutical legislation, which will ensure that the existing regulatory system continues to protect public health in an enlarged EU. It will, however, mean significant changes for the Agency and industry. Legislation was adopted to create a European system for the regulation of herbal medicinal products, introducing high standards of public health without adding undue burdens on this sector.

The Agency made a significant contribution to a Review of Medical Devices Legislation and to the negotiation of a Resolution on Medical Devices, which calls for better co-ordination and more information sharing between national competent authorities, and paves the way for future legislative changes. We also continued to play significant roles in the Global Harmonisation Task Force for devices and the International Conference on Harmonisation for medicines.

Operating a successful and fully integrated business

The Agency's achievements this year must be viewed in the context of the merger and all the changes this has brought with it.

We want to say thank you to our people – our most important asset – for their professionalism and expertise during a time of some upheaval. The Agency remains committed to helping all staff realise their potential and develop their skills: in January, it was awarded Investors in People status in recognition of the emphasis put on providing learning and development opportunities. Success also depends on the solid financial and administrative structures that underpin the work, and we are pleased to report that the Agency met all its financial objectives this year. The MHRA's launch in the Barbican Centre, London, in December was a celebration of these aspects of work, as much as of its scientific and technical excellence.

One year on from the merger there is still much work to be done, but solid foundations are in place. The new Agency must be greater than the sum of its two constituent parts in order to maximise its role in protecting public health. Looking forward, the next year looks likely to be one of further change, but also of consolidation. There is a great deal still to learn from each other, and this is an exciting time for us all.

Left/Above: Sir Alasdair Breckenridge and Kent Woods

About the MHRA

THE KEY AIMS, OBJECTIVES AND ACTIVITIES OF THE MHRA ARE OUTLINED BELOW.

Aims

Our aims are to safeguard public health by:

- ensuring that medicines for human use, sold or supplied in the UK, are of an acceptable standard of safety, quality and efficacy;
- ensuring that medical devices meet appropriate standards of safety, quality and performance; and
- promoting the safe use of medicines and devices.

Objectives

Our key objectives are to:

- make an effective contribution to public health;
- provide authoritative and accessible information;
- influence international regulation;
- support industry and scientific innovation;
- operate a successful and fully integrated business; and
- minimise the cost of regulation.

Activities

Our main activities are:

- assessing safety, quality and efficacy and authorising medicines sold or supplied in the UK for human use;
- overseeing the Notified Bodies that audit device manufacturers;
- operating post-marketing surveillance and other systems for reporting, investigating and monitoring adverse reactions to medicines and adverse incidents involving medical devices and taking any necessary action to safeguard public health, for example through safety warnings, removing or restricting the availability of products or improving designs;
- operating a quality surveillance system to sample and test medicines and to address quality defects, monitoring the safety and quality of imported unlicensed medicines and investigating Internet sales and potential counterfeiting of medicines;
- regulating clinical trials of medicines and medical devices;
- monitoring and ensuring compliance with statutory obligations relating to medicines and devices through inspection, taking enforcement action where necessary;
- promoting good practice in the safe use of medicines and devices; and
- managing the General Practice Research Database (GPRD), the *British Pharmacopoeia* (BP) and the Device Evaluation Service, and contributing to the development of performance standards for medical devices.

These activities are supported by our ten divisions which are also responsible for information management, providing executive support services, human resources, and finance.

Above: John Watkins, Sam Delahay, Ade Orhiere and Debbie Sargeant



Corporate governance

These structures and processes are designed to ensure accountability and give the Agency a framework for risk management:

- The Agency Board is made up of a non-executive Chairman, six non-executive members and the Agency's Chief Executive Officer (in place from June 2003).
- The Agency's Chief Executive is responsible for service, delivery and resources. Between 1 April and 31 December 2003, our Chairman acted as temporary Chief Executive and Accounting Officer. The Agency's permanent Chief Executive, Professor Kent Woods, took up his post on 1 January 2004.
- The Executive Board, consisting of the Agency's directors, takes overall responsibility for day to day management, strategic decision-making, line management, and all financial, policy, operational and resource management issues.
- The Risk and Audit Committee provides independent feedback to the Chief Executive – who is also the Accounting Officer – and the Management Board on the effectiveness of our risk management processes. The Committee is supported by the Agency's Risk Management Team.

Above from left: Geoff LeFevre, Doreen Hepburn, Gordon Munro, June Raine and Clive Bray;
Louise Loughlin, Kent Woods, Graham Savage and Susanne Ludgate;
Roy Alder, Louise Wood and Ian Hudson

Above from left: Damien Bishop, Kent Woods, Charles Kernahan, Garry Watts, Michael Fox, Angus Mackay
Lisa Arnold, Sir Alasdair Breckenridge and Shelley Dolan


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A year of achievement

IN ADDITION TO THE SUCCESSFUL LAUNCH OF THE MHRA, THE FOLLOWING SIGNIFICANT ACHIEVEMENTS WERE MADE IN 2003/04.

Highlights and successes

Working for Ministers

- successfully completed negotiations of the Traditional Herbal Medicines Directive, achieving key UK objectives
- revised reclassification procedures to increase the availability of medicines
- evaluated over 400 device products, supporting government priorities
- extended prescribing to allow supplementary prescribing by nurses and pharmacists
- launched consultation on proposal to streamline UK medicines advisory structure
- gained approval for merged Agency to co-locate on a single site in London

Public health

- launched website to provide rapid and direct access to the electronic Yellow Card (www.yellowcard.gov.uk)
- issued advice to doctors warning them not to use improvised medical devices
- communicated advice to health professionals and patients following a review of the safety and efficacy of selective serotonin reuptake inhibitors (SSRIs) in children and adolescents with depressive illness
- restricted the indication for hormone replacement therapy (HRT) products to second line in the prevention of osteoporosis
- collaborated with the National Patient Safety Agency (NPSA) on the reporting of adverse incidents
- GPRD conducted studies on drug safety, health outcomes and descriptive epidemiology
- organised a successful national conference for medical device liaison officers
- successfully prosecuted a supplier of an unsubstantiated cancer cure device
- introduced statutory warnings for all aspirin products on the risk of Reye's Syndrome in children and adolescents
- introduced legislation aimed at tackling the longstanding problem of accidental iron overdose, often fatal, in small children

Communications

- launched a full communications programme to highlight changes in medicines from BANs to rINNs
- designed a leaflet aimed at patients buying over-the-counter devices from pharmacies
- supported an extensive communications programme on the implementation of the Clinical Trials Directive
- helped develop the Chief Medical Officer's Safety Alert Broadcast System (SABS): an electronic system for the dissemination of important safety related information
- produced a manual aimed at patients undergoing hip replacement, heart valve replacement or implantable cardioverter defibrillator (ICD) insertion
- launched a national joint implant registry for hip and knee implants
- organised training days for health professionals covering infusion pumps and other devices used in practice
- forged close collaborative links with the US Food and Drug Administration (FDA), sharing experience on device issues
- set up a Committee on Safety of Medicines (CSM) working group to improve the quality of patient information provided with medicines

Industry

- introduced on-line reporting of adverse incidents for medical device manufacturers (MORE)
- worked successfully with various stakeholders to address concerns with the Clinical Trials Directive
- new drug assessment times remained very fast with a mean of 40 working days
- achieved 25 per cent increase in the number of abridged applications assessed
- developed guidelines on the use of umbrella segments of product names
- exceeded government targets for speed of invoice payments

Quality

- started statutory inspection programmes in pharmacovigilance
- implemented a strategic review of device adverse incident processing
- developed a screening method to detect illegal prescription only medicines in herbal medicines
- achieved approval of the Inspection and Enforcement Division to the 2000 revision of ISO 9001 Quality System
- British Pharmacopoeia incorporated into the Agency

Europe

- successfully completed negotiations in the 2001 Review of medicines licensing, with key UK objectives met
- made significant progress on the device reform agenda, addressing all the UK issues
- remained one of the top countries for assessment of community medicines
- reclassified breast implants and continued to promote the reclassification of certain orthopaedic implants
- continued to provide more scientific advice to the Committee on Proprietary Medicinal Products (CPMP) than any other Member State
- contributed to the Commission's Clinical Evaluation Task Force for manufacturers and Notified Bodies

Launching the MHRA

The MHRA was officially launched on 5 December at the Barbican Centre in London. Over 500 MHRA staff and 80 external guests attended, including representatives from trade associations, patient groups, other regulatory agencies and the press. Professor Sir Alasdair Breckenridge hosted the event, which included a keynote speech from Lord Warner, Parliamentary Under Secretary of State (Lords). Presentations were also given by:

- Sir Nigel Crisp, Permanent Secretary and NHS Chief Executive, who outlined the Department of Health's expectations of the new Agency;
- Mr Cliff Prior, Rethink, who covered the expectations of patients and the public; and
- Dr Murray (Mac) Lumpkin, FDA, who covered the expectations of the FDA.

Professor Kent Woods concluded the proceedings, giving his perspective on the MHRA and its future. Staff and guests then had the opportunity to look at an exhibition, including posters and demonstrations highlighting the varied work of the Agency.

Freedom of Information (FOI)

The Freedom of Information Act will be fully implemented in January 2005, replacing the non-statutory code on disclosure of information that currently covers the Agency's work. The Agency has set up a cross-Agency working group to:

- ensure effective record-keeping systems are in place;
- raise staff awareness;
- identify ways of tracking requests and monitoring performance;
- review our existing guidance on the disclosure of information; and
- establish a Code of Practice for external stakeholders, explaining how we will carry out our new legal responsibilities.

The Agency is also developing an action and training plan to ensure that it is ready to comply with the new Act by January 2005. The medicines sector and the pharmaceutical industry are working on a Memorandum of Understanding covering policies and practices on disclosure of information, and work is also under way on a single unified FOI publication scheme for devices and medicines.

Extending the prescribing, supply and administration of medicines

A number of initiatives arising from the NHS Plan have implications for the prescribing, supply and administration of medicines. Since 2000, the Agency and the CSM have been involved in major changes to legislation to implement independent prescribing by nurses, and 2003 saw further work to significantly expand the scope of the Nurse Prescribers' Extended Formulary. However, the extension of prescribing responsibilities is not restricted to nurses. Supplementary Prescribing was introduced in 2003 by which appropriately trained nurses and pharmacists prescribe medicines within parameters set by a doctor or dentist in accordance with a clinical management plan for an individual patient.

Also in 2003, the supply and administration of medicines under Patient Group Directions was extended to the healthcare services provided by the police and prison services, the Defence Medical Services and certain independent healthcare organisations. The Agency also expanded the range of medicines that paramedics and midwives are able to administer on their own initiative as part of their professional practice. The Agency has already started work on proposals to extend responsibilities for prescribing to a wider range of health professionals and that work will continue in the coming year.

Left: Sir Alasdair Breckenridge Above: Paras Shah and Paul Johnson

Review of medicines advisory committees

The current medicines advisory bodies' arrangements have remained essentially unchanged since their introduction under the Medicines Act of 1968. However, over time there have been significant changes to the environment in which the committees operate. The recent merger and forthcoming changes to the European regulatory framework provide an opportunity to consider the Agency's advisory structure for the future.

The Agency therefore launched a public consultation on proposals to amend the committee structure in February 2004. The consultation period ended on 17 May 2004. The results will be independently analysed and Ministers will make a final decision on the future committee structure.

Review of access to Yellow Card data

On 21 July 2003, Ministers announced an independent review, led by former Deputy Chief Medical Officer Dr Jeremy Metters, into the access to and use of data collected by the Yellow Card Scheme. The Review looked at whether – and if so, under what conditions and for what purposes – the data should be made more widely available. It was stimulated in part by increasing numbers of requests for access to Yellow Card data above and beyond the established policy on access, primarily for research purposes, but also including the interests of wider healthcare policy and delivery.

The public and key stakeholders were invited to contribute their views, and the report of the Review was formally delivered to the MHRA on 4 May 2004 – the Scheme's 40th anniversary. There will now be a public consultation on the recommendations.

Communications review

The Agency started a major programme by reviewing its communications with stakeholders. The National Audit Office and others highlighted that the role of the former MCA was not well understood by the public and by many health professionals. They recommended that the MHRA should communicate more widely about medicines and develop a stronger relationship with the public and other stakeholders.

There is a perception that the Agency is unduly uncommunicative and this impacts on the tone in which the MHRA's work is reported. Even more importantly, practitioners, patients and other users need greater openness in communications about the safe use of medicines and devices.

To tackle this issue, the Agency asked a specialist communications consultancy to develop a strategy and action plan, in consultation with a wide range of stakeholders. Their report was delivered in April 2004. A key priority for the Agency will be to agree an action plan to take forward this programme as a matter of priority.

Working with the Food and Drug Administration (FDA)

The Agency has had a number of video conferences with device colleagues at the FDA Centre for Devices and Radiological Health (CDRH), and a face-to-face meeting with a team from Health Canada. The aim was to share information, compare regulatory issues and update each other on current initiatives. Discussion topics included:

- the proposed European legislation for tissue-engineered products;
- single-use devices and the control of third-party re-processors;
- the reclassification of joint replacement in Europe;
- the accuracy of digital blood pressure monitors in patients with pre-eclampsia; and
- the use of needleless connectors.

A two-day visit to the CDRH site in Rockville identified a number of possible developments that could benefit both agencies. These include providing laboratory support for the CDRH's work programme and looking at whether the Office of Science and Technology could develop or handle joint projects.

The General Practice Research Database (GPRD)

The GPRD is the world's largest computerised database of anonymised longitudinal records from general practice. Information on three million patients throughout the UK (approximately five per cent of the population) is currently being collected. The GPRD is used internationally by academia, contract research organisations, government departments, medicines regulatory authorities and the pharmaceutical industry for studies on clinical epidemiology, health outcomes, drug safety, drug utilisation, pharmacoeconomics, clinical research and NHS planning. The Annual Report of the GPRD Scientific and Ethical Advisory Group, which reviews protocols for studies, and a bibliography are available at www.gprd.com.

The Agency has launched customised on-line services for researchers working in clinical research, portfolio management, pharmacovigilance and marketing. Users also get additional support via a user group and the development of tools (for example, case control matching, person-time calculation, random

Left: Jim Lefever Above: Rod Lawes, Susan Soanes and Tim Williams

sampling, daily dose conversion) to support epidemiological research.

The Research Team has conducted studies on drug safety issues, health outcomes and descriptive epidemiology during the year and continues to work with new stakeholders to expand the use of the database for the benefit of public health. Also planned is a pilot for assessing the usefulness of the data to support the medical device and appliance industries.

Manufacturers' On-Line Reporting Environment (MORE)

The Agency introduced a new on-line reporting system for medical device manufacturers to report adverse incidents and device recalls. The Manufacturers' On-Line Reporting Environment – known as MORE – is a secure, Internet-based system which transfers information into the incident-tracking database.

Improving information management (Sentinel)

The Agency has continued to implement the information management strategy (IMS), which was launched in January 2003. The programme that will deliver the IMS, Sentinel, has five main objectives:

- to enhance and accelerate decision-making at all levels;
- to improve the quality of our work;
- to improve operational efficiency;
- to establish an information infrastructure that can evolve to meet our changing needs; and
- to build towards the efficient provision of data or knowledge to external bodies.

In 2003/04, Sentinel's human resources component was rolled out to all medicines sector staff. Four applications, including document management and the finance component, were implemented; and business support applications for clinical trial applications and export certificates were designed and mostly built. Product licensing design also began. The finance component will be used from April 2004. The Agency has rolled out the document management system to all staff, enabling electronic records management to be achieved in line with government targets.

In implementing the IMS, the Agency will assist stakeholders by providing effective and efficient electronic means of communication which will enable the Agency to serve their needs better and to become an increasingly flexible and dynamic organisation. It will enable improved access to information to assist in the protection of public health and provide a better service to all its stakeholders.

The *British Pharmacopoeia*

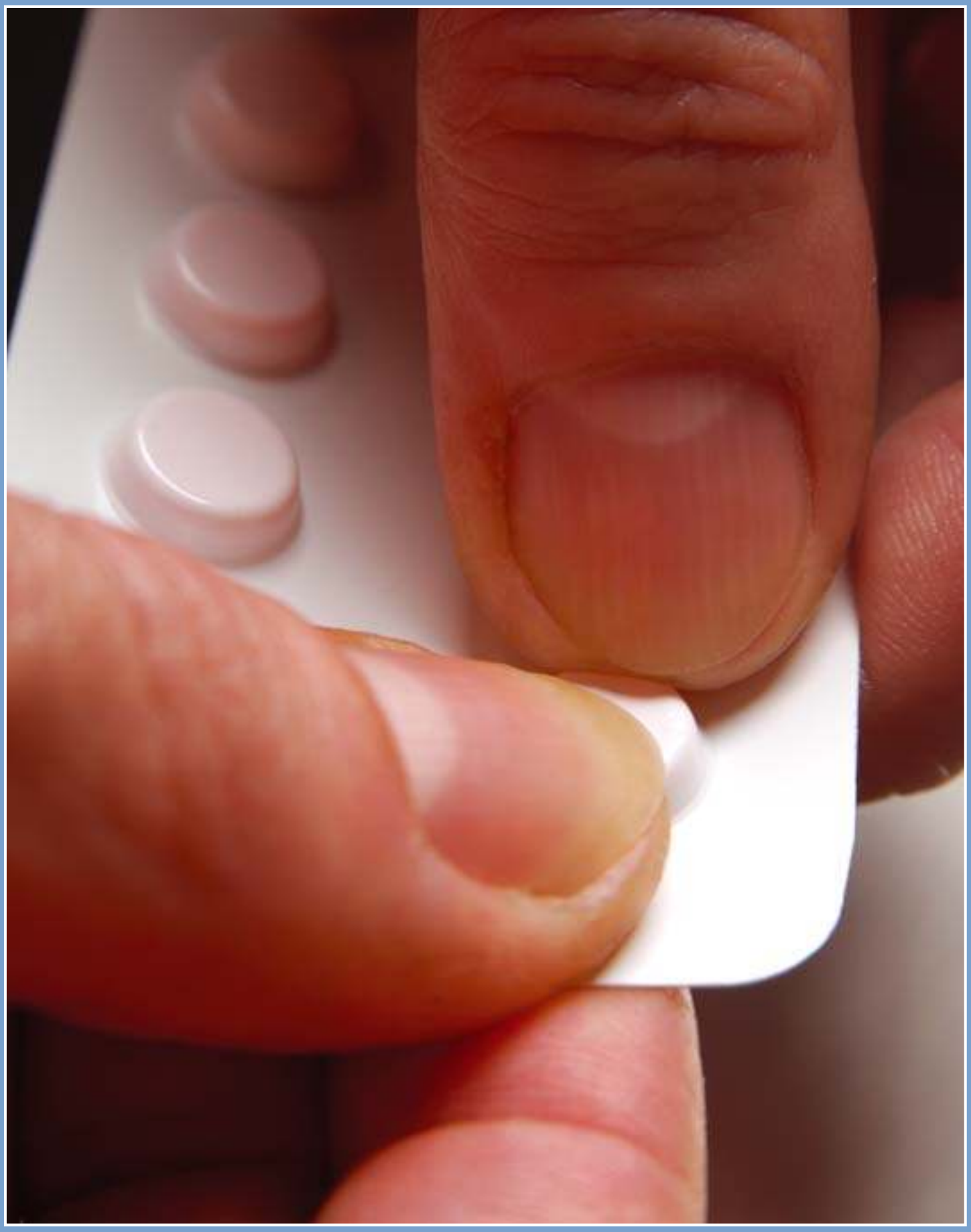
On 1 April 2003, the *British Pharmacopoeia* was incorporated into the Agency. The 2003 *British Pharmacopoeia* was published in September as a six-volume set, including 12 new national monographs and 68 new monographs reproduced from supplements 4.3, 4.4 and 4.5 of the *European Pharmacopoeia*. The 2003 edition also incorporated changes from British Approved Names (BANs) to recommended International Non-Proprietary Names (rINNs).

Service improvements

- Addition of MORE to the website
- GPRD Division launched a user group and rolled out customised on-line services for researchers working in clinical research, portfolio management, pharmacovigilance plus sales and marketing
- The Central Enquiry Point telephone service dealt with a record number of calls over the year with no extra resources
- The Agency outsourced its credit control function

See Annex 1 for a table showing performance against targets for 2003/04.

Above: Esther Fakeye, Andrea Johnson, Joanna Barrett, Shahnez Idrees and Mark Armstrong



Communications

COMMUNICATING WITH OUR STAKEHOLDERS AND THE PUBLIC IS AN ESSENTIAL PART OF OUR WORK. THE FOLLOWING SECTION SUMMARISES THE KEY COMMUNICATIONS ACTIVITIES FOR 2003/04.

Conferences and seminars

The Conference and Education function of the Agency organises regular MHRA-branded events, providing up-to-date information on the control of medicines and devices for its stakeholders. This year's topics included:

- the EU Clinical Trials Directive;
- pharmacovigilance;
- variations;
- unlicensed medicines;
- herbal medicines; and
- tissue banks.

These events recorded very high levels of customer satisfaction.

The website

The MHRA website is an important channel for communicating with our customers and stakeholders. This year we have added several new sections, covering the EU Clinical Trials Directive, the new European Variations Regulations, the changes in the naming of some medicines, and the manufacturer reporting of device-related incidents. Feedback on these developments has been very positive. Over the next year, the medicines and devices areas of the site will be fully integrated, and the site will be developed in order to provide a full range of information and on-line services.

Central Enquiry Point (CEP)

The CEP is the first point of contact for enquiries to the Agency. It receives over 500 telephone calls, 200 e-mails and 50 letters every week. The highly trained team either deal with queries themselves, or transfer them to an appropriate expert. We aim to reply to written requests within seven working days: in 2003/04, we dealt with 96 per cent within this timeframe. Where requests have to be transferred, we aim to send an acknowledgement within 24 hours. This year, we achieved this in 100 per cent of cases. The CEP's other main role is to provide public briefings on issues that attract media attention. Key issues this year included:

- HRT and osteoporosis;
- SSRIs;
- atypical antipsychotic drugs and stroke; and
- the recall of a pregnancy testing kit which was giving a higher than expected rate of 'false-negative' results.

Publications

Devices

The devices sector has produced a wide range of publications over the past year, including four *Device Bulletins*. The first gave an overview of device-related adverse event reports received by MHRA in 2003, together with an evaluation of recent developments in adverse incident reporting. Other bulletins covered:

- managing medical devices prior to repair, service or investigation;
- setting up safe systems of work and the various legal requirements associated with decontamination activities;
- decontaminating community equipment in loan stores;
- minimising the risk of cross-infection from the reuse of medical equipment issued by community equipment loan stores; and
- guidance for users, carers, healthcare professionals and manufacturers on wheelchair stability.

The Agency also published five editions of *One-Liners*, a one-sheet publication which highlights serious device-related problems. These have proved very popular. One issue was produced to coincide with the Diabetes UK Annual Conference, and covered user issues in relation to devices used in the diagnosis, monitoring or treatment of diabetes.

More and more devices are now being purchased over the counter, so we produced a leaflet outlining the Agency's role in investigating device-related adverse events and guidance on how to report them. This was distributed through pharmacies in England.

The Agency also continued to work with the British Orthopaedic Association (BOA) to improve rates of adverse incident reporting by orthopaedic surgeons, particularly for joint replacement implants that need to be revised after ten years. We worked with the BOA and the National Association of Theatre Nurses to produce a poster reminding surgeons and theatre staff of the need to report, which was circulated to all orthopaedic departments in England.

Medicines

MAIL (Medicines Act Information Letter) is the MHRA's medicines newsletter produced every other month. It contains substantial articles and news on current issues of concern for all those involved in licensing and manufacturing medicines. *MAIL* is available in print by subscription, and free of charge on our website. There is an e-mail alerting service to inform readers when it becomes available on our website.

Current Problems in Pharmacovigilance is the drug safety bulletin for doctors, dentists and pharmacists, produced by the CSM. This year's articles included:

- HRT: an update on the risk of breast cancer and long-term safety;
- topical vaginal oestrogens: endometrial safety;
- SSRI and venlafaxine use in children;
- salmeterol (Serevent) and formoterol (Oxis) in asthma management;
- methotrexate and pneumonitis;
- medicines containing peanut (arachis) oil;
- interaction between repaglinide (Novonorm) and gemfibrozil (Lopid);
- sodium valproate and prescribing in pregnancy;
- reactions in humans to veterinary medicines;
- sibutramine (Reductil): hypertension and tachycardia;
- pergolide (Celance) and cardiac valvulopathy;
- possible interaction between warfarin and cranberry juice;
- kava-kava and hepatotoxicity;
- the gastrointestinal toxicity of non-steroidal anti-inflammatories;
- safety of thiomersal-containing vaccines; and
- dopaminergic drugs and sudden sleep onset.

Device Safety Alert Broadcast System

Medical Device Alert safety warnings are the Agency's prime means of communicating safety information to health and social care medical device users. The Agency uses them to warn people about particular

problems and risks, and to recommend appropriate actions. They are distributed to the NHS and social care sectors for direct action, and for passing on to relevant healthcare professionals.

Each alert is designated as 'Immediate Action', 'Action' or 'Update'. They may also be used to request information and feedback. This year the Agency issued 52 alerts: 18 immediate action, 25 action, two update, two action/update, one immediate action/information, three action/information, and one information request. The Agency reviewed these alerts using positive feedback and suggestions from readers. The format influenced the design of the Safety Alert Broadcast System (SABS). This simple, streamlined mechanism for distributing safety alerts to the NHS was launched in April 2004. It e-mails new safety messages – including Medical Device Alerts and Drug Alerts – to nominated leads in all trusts who can then disseminate the message as needed.

Working with partners

Changing to internationally recognised names

The Agency has worked in co-operation with a wide range of external stakeholders representing healthcare professionals, medical software providers, community pharmacies and the pharmaceutical industry on an important initiative to make medicines in the UK safer for patients.

European Community law requires that medicines should be labelled using internationally recognised names under a system co-ordinated by the World Health Organization. Most medicines in the UK already use these recommended International Non-Proprietary Names (rINNs), but some are also available under their British Approved Names (BANs). This is potentially confusing for both healthcare professionals and patients, and increases the risk of medication errors.

The Agency consulted around 250 organisations before agreeing a programme of action for adopting the

Left: Janine Reed Above: Pauline Connolly and Yinka Olushola

internationally recognised names by the pharmaceutical industry and healthcare professionals. The initiative has been widely welcomed by stakeholders and the implementation programme, including a comprehensive communication strategy, should in future ensure that medicines are available under one name only, thereby safeguarding public health.

The device liaison officer focus group

Device liaison officers play a crucial role in disseminating Medical Device Alerts within their organisations and promoting the reporting of adverse incidents. The group meets at least once a year, and its members are drawn from the five areas targeted by the alerts:

- acute trusts;
- ambulance trusts;
- community/mental health trusts;
- primary care trusts; and
- social services departments.

It provides a forum for members to:

- receive support and encouragement in their role;
- share problems and exchange ideas;
- raise issues of concern;
- comment on initiatives and proposals;
- provide feedback on practice and experience in the field; and
- contribute to the best practice guidance published annually in a Medical Device Alert.

Focus group members have their contact details published on the liaison officer web page to help other liaison officers in their sector contact them for advice. They also help participate in the annual national liaison officer conference. A wider number get involved in the group's activities by e-mail. Membership of the focus group and wider circle currently totals 35.

Left: Caroline Ainsworth and George Thornton Above: Samantha Bedser, Stephen Harbron and Alison Long

Safeguarding public health

THE MHRA IS HERE TO SAFEGUARD PUBLIC HEALTH. THE FOLLOWING SECTION DESCRIBES ACTIVITIES UNDERTAKEN IN 2003/04 TO ACHIEVE THIS.

Reform of regulation for herbal medicines

In the UK, most herbal medicines reach the consumer as unlicensed herbal remedies that are not required to meet set safety or quality standards, nor to be accompanied by information necessary for their safe use. This regime does not adequately protect public health and the Agency has attempted to reform regulatory arrangements.

During the year negotiations on the Directive on Traditional Herbal Medicinal Products were successfully completed and the Agency plans that, in compliance with the Directive, it will introduce a traditional use registration scheme in the latter part of 2005. The Agency played an active role in negotiations and helped to secure additional flexibility over the scope of the scheme, which should extend patient choice and benefit the industry.

The Directive applies to manufactured, traditional herbal remedies suitable for use without the intervention of a medical practitioner. These will have to meet standards of quality and safety. In place of the normal requirement for medicines to demonstrate efficacy, remedies will be accompanied by minor indications based on evidence of traditional use. Systematic patient information will be required.

The Agency is working closely with the herbal sector in a programme to help the industry prepare for the start of the new scheme.

Reform of the regulation of unlicensed herbal remedies made up to meet the needs of individual patients

Existing legislation allows unlicensed herbal remedies to be made up and supplied to meet the needs of an individual patient following a one-to-one consultation. The very limited requirements as to the safety and quality of remedies supplied are widely regarded as a weakness in public health protection. The Agency therefore launched a consultation exercise with outline proposals for reform. It will continue to work in close partnership with the wider Department of Health, which has also carried out a parallel consultation on proposals for the statutory regulation of the herbal medicine profession.

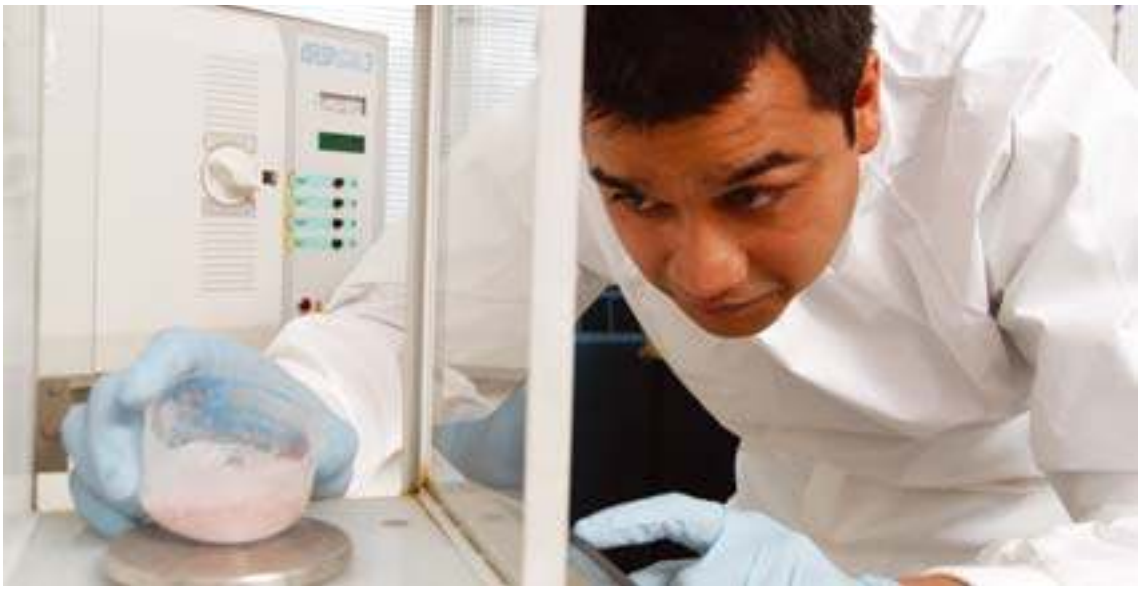
Summary of key safety issues

Devices

Medical devices are extremely diverse and safeguarding public health in this area demands in-house specialist knowledge, comprehensive information systems and access to up-to-date external advice. These enable the Agency to analyse the information received and issue appropriate advice. The Agency's advice may address device or user-related issues, or both. Summarised below are examples of important safety advice published by the Agency during the year, illustrating the breadth of guidance and warnings issued to the health service.

Non-active implants

The Agency received several reports of serious complications associated with the use of polymeric bone cement during spinal surgery procedures. After consultation with professional associations and royal colleges, the Agency issued best practice guidance in a Medical Device Alert, MDA/2003/021, to help prevent serious complications.



In vitro diagnostic medical devices (IVDs)

The Agency issued five Medical Device Alerts about problems with IVDs. Three of these concerned IVDs used by patients at home, either in the control of diabetes or to monitor anti-coagulation therapy. Two further alerts drew attention to false results from IVDs used in laboratory testing for sexually transmitted diseases.

Magnetic resonance imaging (MRI)

Helium-cooled MRI installations occasionally quench, causing liquid helium to boil off and generate huge amounts of helium gas in a few minutes. Normally quench pipes vent this rapid gas flow safely away. Reports of some quench systems not constructed to the manufacturer's specifications and posing a serious threat to patients and staff led the Agency to publish MDA/2003/014. This recommended that users check that all MRI quench venting systems meet the manufacturer's specifications.

Intravascular catheters

Reports of fatalities associated with the use of dialysis catheters, dilators and guidewires led to the issue of MDA/2003/020. This highlighted the need to select devices according to the insertion site to be used and to follow the manufacturer's instructions to avoid over-insertion. The Agency issued MDA/2003/045 on a neonatal sensor following reports of fragments left in a major blood vessel upon removal. The Agency provided advice on how to avoid damage by completely retracting the sensor before clamping the umbilical artery catheter.

Insulin pen injection system

The Agency received several reports from both patients and healthcare professionals concerning difficulties in operating an insulin pen injection system. The manufacturer had also received a significant number of complaints and these problems had led to uncertainty in the management of diabetes in some patients. The manufacturer believed that the problems were due to patients being unfamiliar with the device and established an education programme. However, the Agency noted a continued increase in complaints, so published MDA/2004/002 to highlight this issue to prescribers.

Guidance documents

Work on the subject of safe transportation of wheelchair users continued throughout the year following on from the *Device Bulletin* issued in 2001, DB2001(03). The Agency issued further guidance document DB2003(03) on the safe use of wheelchairs and vehicle-mounted passenger lifts in March 2003. Since the issue of both documents the Agency has noted a significant reduction in the number of fatalities reported.

Medicines

This section looks at some of the key medicine-related safety issues addressed during the year.

Safety of long-term hormone replacement therapy (HRT)

The Agency informed prescribers and patients of new information on the safety of long-term use of HRT, which is used in the treatment of menopausal symptoms and in the prevention of thinning of bones (osteoporosis). A large UK study provided evidence that the risk of breast cancer for combined (oestrogen and progestogen) HRT was substantially higher than with oestrogen-only therapy. The Agency communicated advice for health professionals and patients through the Chief Medical Officer's Public Health Link and the website to coincide with the publication of the study[1] in August 2003. An article published in *Current Problems in Pharmacovigilance* in September 2003 updated health professionals on the accumulating data on the risks of long-term treatment with HRT. Because of the accumulating evidence on the risks of long-term use, the Agency took action in December 2003 to inform prescribers and patients that HRT should not be used as first-line treatment in the prevention of osteoporosis.

Selective serotonin reuptake inhibitors (SSRIs) – use in children

The Agency and the CSM's Expert Working Group on SSRIs undertook a class review of the safety and efficacy of SSRIs in children and adolescents with depressive illness. No medicine is currently licensed for the treatment of depressive illness in children and adolescents; however, the SSRIs are used in this population off-licence. This review resulted in the Agency advising that the balance of risks and benefits for the treatment of depressive illness in patients under 18 years old was judged to be unfavourable for paroxetine (Seroxat), venlafaxine (Efexor), sertraline (Lustral), citalopram (Cipramil) and escitalopram (Cipralex) and unassessable for fluvoxamine (Faverin). Clinical trials demonstrated that only fluoxetine (Prozac) had a favourable balance of risks and benefits for the treatment of depressive illness in patients under 18 years old. The Agency provided information for health professionals and patients through the Public Health Link and placed on its website summaries of clinical trial data, questions and answers, and a press release.

[1] Beral V et al. *Lancet* 2003; 362:419–427

Left: Paras Shah Above: Ian Martin, Carolyn Greenwood and Charlotte Hawkins

Atypical antipsychotics and risk of stroke

The Agency issued advice on the risk of stroke associated with two antipsychotics, risperidone (Risperdal) and olanzapine (Zyprexa), in March 2004. The CSM had advised that there is clear evidence of an increased risk of stroke in elderly patients with dementia who are treated with these products, sufficient to outweigh benefits in the treatment of behavioural disturbances associated with dementia. Neither product has ever been licensed for treatment of behavioural symptoms of dementia, but both have been used off-licence in this indication. The Agency issued this advice through the Public Health Link, its website and a press release. Doctors were referred to clinical guidelines for the treatment of behavioural symptoms of dementia, which had been developed in response to the CSM advice by the Department of Health, in conjunction with the appropriate professional bodies.

Defective Medicines Reporting Centre (DMRC)

The DMRC investigated 298 reports of suspected defective medicinal products in 2003/04, of which 135 were confirmed. As a result, the Agency issued 15 Drug Alerts, of which two were Class 1 Drug Alerts.

The DMRC issued two Rapid Alerts and received 63 through the EU/PICS Rapid Alert procedure. This number has fallen compared with the last two years due to clarification of the EU procedure, such that only relevant Rapid Alerts are sent to each country.

The Centre is working with the Adverse Incident Centre at the Agency, NHS Estates, the National Patient Safety Agency and the Department of Health to introduce a new mechanism for distributing safety alerts to the NHS. This system goes live for most types of alerts in April 2004. Planning is currently under way to add Drug Alerts to the new system by the end of 2004. The new system will also allow the Centre to monitor the effectiveness of Drug Alerts more readily.

Enforcement

Devices

During the year the Agency started 210 proactive cases in the devices sector and 187 cases were completed, leaving 120 inspections under way. 199 reactive cases were opened and 200 cases completed, leaving 104 live cases under investigation. There were 82 on-site inspections.

The Agency also issued eight compliance notices, one warning letter and one notice of intent to remove products from the market.

Three prosecutions were also successfully concluded covering:

- a dental laboratory undertaking illegal dentistry (fined);
- an importer of non-CE marked condoms (fined); and
- an alternative therapy practitioner who was eventually sentenced to a year's imprisonment for selling illegal devices to cancer sufferers.

Medicines

The Agency opened investigations on 311 cases involving medicines, closed 300 and submitted 18 cases for prosecution for breaches of medicines regulations. A further 15 cases are being taken for prosecutions as joint actions with the Crown Prosecution Service, involving additional offences including Misuse of Drugs. The Agency issued 12 formal cautions and brought 157 offenders into compliance by giving written warnings and advice. The Agency referred 39 cases to other agencies to continue investigation and 56 cases showed no offence being committed. There were four successful prosecutions and one unsuccessful where, in a controversial decision after a retrial, the defendant was found not guilty of supplying Aristolochia.

Enforcement action carried out during the year covered:

- illegal activity related to the Internet;
- products involving Aristolochia, glibenclamide, fenfluramine and skin-lightening agents;
- herbal cream treatments adulterated with cortico-steroids;
- counterfeit Viagra and a variety of products ostensibly containing sildenafil citrate; and
- wholesale supply, unlicensed products, licensing infringements, importation, expired medicines and quality issues, advertising and borderline cases.

During the year investigators seized and removed from the market approximately 676,000 individual items with a further 70kg of medicinal products. The estimated retail/street value of items seized by the Agency relating to medicines-related investigations was £3.5 million.

The Agency has also undertaken joint enforcement activities with other UK government departments and other authorities, both UK based and overseas.

Left: Andrew Graham Above: Bill Cutts, Bosco Rapoz and Clare Headley

Working with Europe

IN 2003/04 WE CONTINUED TO WORK CLOSELY WITH OUR EUROPEAN PARTNERS. THIS SECTION DESCRIBES SOME OF OUR KEY ACTIVITIES.

Devices

Reforming the medical devices directives

This was a busy but successful year for the devices sector. In particular, we made significant progress on the (largely UK-inspired) reform agenda set following the 2002 review of medical devices directives.

The agenda addresses all the issues raised by the UK, and the MHRA has been active in all areas of implementation. We continued to chair the Notified Body Operations Group, which aims to improve the performance of Notified Bodies. This year, the group produced a range of guidance documents, including a handbook advising national authorities on the correct designation, auditing and control of Notified Bodies.

The Agency is also a member of both the Clinical Evaluation Task Force, which has produced guidance recommending that manufacturers' claims for devices be backed by clinical data, and the Market Surveillance Operations Group, which works to improve the effectiveness and consistency of national authorities' post-market surveillance activities.

In January, we successfully persuaded European companies to run a pilot project aimed at achieving greater transparency about the way the directives work and increasing the amount of information publicly available about specific devices.

We also contributed to discussions with the Commission and Member States about the changes that should be made to the medical devices directives. The Commission is expected to present its formal proposals for an amending directive in mid-2004.

Reclassification

During the year, we gained Member States' support for a UK proposal to reclassify some total joint replacement devices as class III medical devices. This means that they would need to undergo the most stringent controls allowed for in the directives before being placed on the market. Despite some fierce resistance from the industry, the Commission is expected to bring forward a directive to achieve the required reclassification in 2004.

Regulation

The MHRA is working with the Commission, other Member States and the industry to develop proposals for a regulatory regime for tissue-engineered products. The Commission is expected to produce formal proposals during 2004.

We have also continued to develop working relationships with various other regulatory authorities. We held our fourth annual benchmarking meeting with the French agency in November and, following a series of high-level discussions with the US FDA, both sectors have been designated as international collaboration centres.

The Agency has also helped in the expansion of the EU: in particular, by providing speakers at three workshops held to assist the accession countries. The Agency also gave a series of talks on the directives to the Turkish Department of Health in May. This was so successful that members of the Turkish authorities visited the Agency in June to follow up various issues raised and to see, at first hand, how the UK operated. The Agency has also participated in a number of other medical device conferences in the UK and abroad.

Medicines

Review of European legislation

Negotiations on this wide-ranging and detailed review continued throughout the year, with final adoption of

agreed texts in December 2003. Key changes include increasing the range of products that need to be authorised by the EMEA, introducing ten years' market exclusivity for new products across the EU, and accommodating the EU's new Member States. Other changes include a reduction in renewals, a requirement for user testing of patient information leaflets, new requirements for active ingredients used as starting materials to comply with GMP standards, and revised definitions of 'medicinal product' and 'generic'. Most of the changes will have to be in place by the end of 2005, so we have embarked on a comprehensive implementation programme.

Clinical Trials Directive

The Agency took the lead in preparing the regulations to implement the Clinical Trials Directive, which came into force in the UK on 1 May 2004. To get feedback on the practical implications from those who sponsor or conduct clinical trials, both in the commercial and non-commercial sectors, the Agency held conferences and workshops. We also provided speakers at a range of meetings about the Directive both in the UK and Europe.

Agency staff are involved in a joint project set up by the Medical Research Council and the Department of Health to encourage non-commercial investigators to share best practice. The project aims to ensure compliance with the requirements of the Directive, while supporting the valuable research carried out by this sector.

The new Directive calls for the regulation of healthy volunteer trials. In October, the Agency set up a voluntary pilot scheme so that sponsors could try out the new system. We have received 22 applications, all of which have been assessed within the Agency's 14-day target time limit.

Paediatric medicines

There is a clear need for new paediatric medicines, and for medicines which are currently used in children outside the licensing framework to be properly evaluated and formulated. A European regulation on medicines for paediatric use, which will make necessary changes to the regulatory structure, is currently being developed and should be finalised by the end of 2006.

In the meantime the Agency is working with the Department of Health to develop a short- to medium-term strategy aimed at increasing the number of appropriately labelled and formulated medicines for children, improving the quality of information for prescribers, carers and patients, and facilitating the conduct of paediatric clinical trials in the UK. We have asked companies to submit all completed paediatric clinical trial data. Other areas of action where we are also working with the pharmaceutical industry include discontinued medicines, imported medicines and the development of new paediatric formulations. Paediatric medicines will be a priority when the UK takes over presidency of the EU in July 2005.

EU enlargement

The Agency is currently involved in two twinning projects: one with the Czech regulatory agency (SUKL) and one with the Maltese Medicines Authority in partnership with the Irish Medicines Board. Twinning aims to help the countries preparing for accession into

the EU in their development of modern and efficient administrations, with the structures, human resources and management skills needed to implement the EU legislation (*acquis communautaire*) to the same standards as Member States.

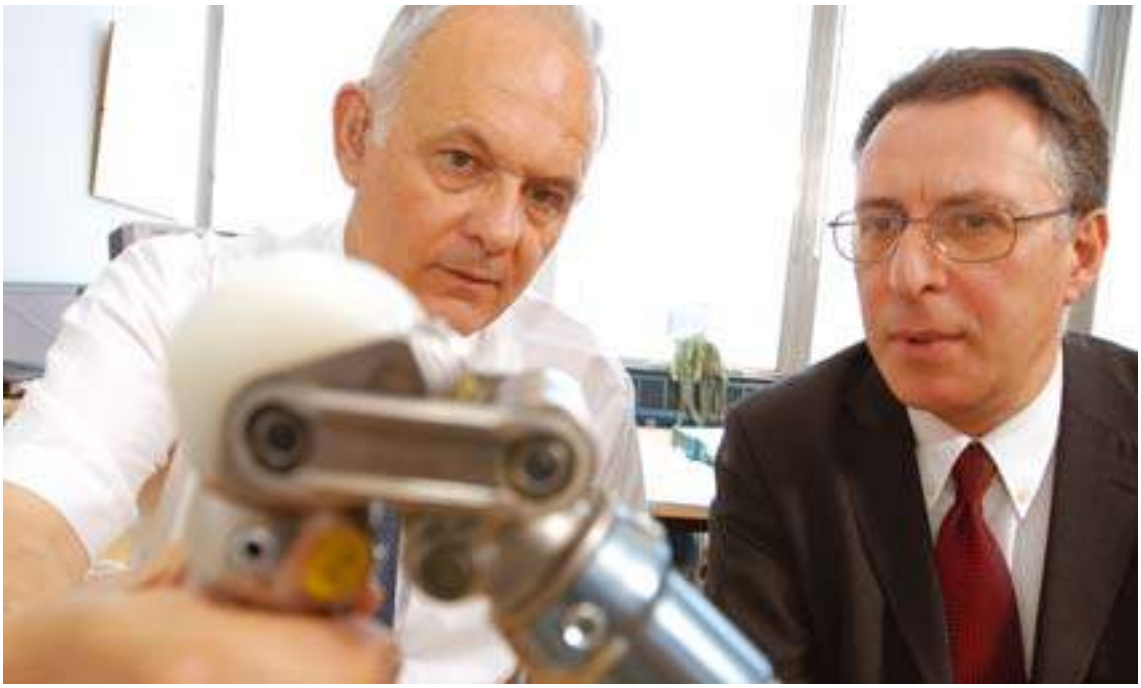
Since the launch of the project in November 2002, experts from the Agency have delivered around 600 working days of training for SUKL. Assistance has been provided in a wide range of areas, including licensing procedures, pharmacovigilance, inspection and enforcement, and human and financial resources. The project in Malta was launched in February 2003, and Agency experts have delivered around 95 working days of training, focused mainly in the areas of GMP inspections, governance issues, personal effectiveness, and business and operational planning.

European Directorate for the Quality of Medicines (EDQM): Official Medicines Control Laboratory (OMCL) Network

The Agency continues to participate in the activities of the Council of Europe EDQM, OMCL Network. There are MHRA representatives on the General Network and EU Network Advisory Groups, who also took part in their annual general meetings. In 2003/04, the Agency tested 23 products as part of the EDQM's co-ordinated programme of sampling and testing products authorised centrally by the EMEA. The Agency also worked with the OMCL Network to co-ordinate the analysis of medicinal products authorised under the mutual recognition procedure and to build a database of test results.

Mutual Recognition Agreement (MRA) with Japan

The MHRA supported the European Commission in negotiating an MRA on GMP with Japan. Over the past few years the Agency has reviewed the Japanese system for controlling the manufacture of medicines by observing Japanese GMP inspections, as well as taking part in the negotiations. The MRA, which became operational in May, means that companies will no longer need to fully test each batch of some medicines imported from Japan.



Left: Fred Huckle and Linda Oddotte Above: Chris Jones and Roy Saunders

Valuing and developing people

PEOPLE ARE THE MHRA'S MOST VALUABLE ASSET. THIS SECTION DESCRIBES THE DIFFERENT WAYS IN WHICH WE ENCOURAGE THEIR DEVELOPMENT.

The average number of staff employed during the year was 747. There were 66 external and 90 internal recruitment campaigns during the year. Turnover, although initially high in the devices sector, has steadily reduced.

The human resources teams

These teams work in partnership with managers and offer training, support, advice and guidance on a wide range of staffing issues. A recent survey of medicines managers showed they regarded the level of service provided by this team as excellent.

External consultants carried out a review of MHRA support services during the year. The report and recommendations for integration were discussed and agreed in principle by the Board in December. The Agency plans to implement a revised organisational structure early in 2004/05 following the appointment of a new Director of Human Resources in April 2004.

Learning and development

Management and leadership development

Forty-eight managers attended the Management and Leadership Development programme, which has now been extended to include new managers. A comprehensive review of the programme highlighted the need for a new course targeting supervisors and potential managers. Staff feedback suggests that the programme is having a positive effect on leadership behaviour within the Agency.

In-house training

A comprehensive programme of internal training was designed covering presentation skills, coaching, negotiation and influencing, and project management. The Agency has also improved its induction training to provide a three-level induction process for all new staff.

Equality and diversity

The medicines sector has established a Valuing Diversity Advisory Group. There are plans to extend this through the Agency to enable a strategy to be developed for promoting values, behaviour and working practices which recognise and value the differences between people, releasing their potential, enhancing performance and improving service standards.

Above: Debby Webb

Industrial relations

The Agency held regular meetings with trade union and staff representatives throughout the year, maintaining the constructive relationships built up over a number of years and promoting positive change. This year, the Agency agreed an Industrial Relations Constitution with the trade unions.

The Human Resources Information System

As part of the Sentinel programme, the medicines team has helped to develop and implement a new system that provides information direct to line managers and staff. This system went live in January 2004, and will be extended to the whole Agency next year.

Investors in People (IiP)

IiP is a national quality standard which provides a framework for improving business performance through a planned approach to setting and communicating business objectives and developing people to meet those objectives. Both the MCA and MDA were accredited as Investors in People, with the MCA implementing an action plan, championed by divisional representatives, to address areas in which it did not fully meet the standard. The MHRA was assessed in September 2003 and received IiP accreditation in January 2004. The assessment report identified examples of best practice in the Agency including:

- a commitment to training and encouragement to progress for staff at all stages of their careers;
- a genuine commitment to equality and diversity;
- clear aims and objectives; and
- improvements in management effectiveness as a result of the Agency's management and leadership courses.

Key areas identified for ongoing development included:

- harmonisation of human resource practices;
- evaluation of the impact of training; and
- improvements in communications and customer focus.

Doctor revalidation

By law, all UK medical practitioners must provide evidence of their fitness to practise if they wish to retain their licence and remain on the General Medical Council (GMC) register. The GMC has introduced a timetable for a five-year revalidation cycle, which will start in April 2005.

The MHRA, working with the wider Department of Health and the Faculty of Pharmaceutical Medicine, has agreed a format for revalidation with the GMC, which is based on the annual Senior Civil Service appraisal scheme and on the principles of continuing professional development. This should enable medical assessors and managers to hold their annual appraisal for both the Agency and GMC at the same time. However, doctors will still need to collect supportive evidence.

Continuing professional development for government pharmacists

Practising pharmacists in the UK will soon have to provide evidence of their ability to direct their own learning. To support its pharmacists, the Agency has developed a set of competencies for pharmacists working in the government environment, and agreed these with the Royal Pharmaceutical Society of Great Britain. The Agency also organised a series of facilitated workshops to explain the process to pharmacists and to provide a mentoring and coaching facility.

Left: Jennifer Cooke and Celina Cundy Above: Liz Perry, Anna Pipkin and Jemma Jaques

Valuing Individual Performance (VIP)

During the year the Agency relaunched the Personal Development and Performance Management project, and renamed it Valuing Individual Performance. Pilot studies were completed on three job families – administration/clerical, information capture/provision, and pharmaceutical assessment – which are currently being evaluated. Work is now under way on four more areas: medical assessors; inspectors; finance; and human resources.

Left: Nimo Ahmed and David Robinson Above: Mark Goddard, Richard Goldfinch, Jane Viner and Diane Leakey


60
100
140
180
220

Review of activities

THE VOLUME OF WORK COMPLETED BY THE MHRA IN 2003/04 IS SUMMARISED BELOW.

Evaluating devices

Device Evaluation Service

The Agency evaluated 505 devices during the year, producing 61 comparative reports and 15 single product reports. It also published three editions of *Diagnostic Imaging Review*. Budget constraints mean that the Service has had to reduce the number of evaluation centres it funds to 13. A strategic review has been set up to determine the future direction of device evaluation and establish new funding arrangements, and is due to report in summer 2004.

Adverse incident reports

	2000/01	2001/02	2002/03	2003/04
Incidents reported	7,352	8,180	8,735	9,037
Number investigated	1,651 (23%)	1,664 (20%)	1,663 (19%)	2,071 (23%)
Source of incident	**%**	**%**	**%**	**%**
Manufacturers	22.6	20.9	24.0	29.6
NHS	58.6	58.2	58.6	49.5
Non-government organisations	3.4	2.8	2.8	3.8
Other government departments	10.1	11.7	9.8	10.2
Overseas reporting organisation	4.1	4.9	3.5	5.4
Private healthcare	1.2	1.5	1.3	1.5
Outcomes*	**%**	**%**	**%**	**%**
No further action yet – trend only	46.7	47.5	50.5	56.1
Single faulty device	19.5	18.7	18.9	19.9
Design change of device, label or packaging	16.5	14.4	10.9	9.2
Manufacturer changed/improved QA	12.4	14.3	11.7	8.4
Device recall and field correction	9.9	8.4	8.0	7.9
Improved maintenance	1.2	1.5	1.5	1.1
Additional user training/publicity	3.5	5.7	5.5	5.2
Safety warning/manufacturer notice or letter	4.5	4.3	2.9	3.4
Production ceased	1.1	0.9	0.4	0.7

*Outcome totals exceed 100 per cent as some incidents fall into more than one category

Safety warning notices issued

Notices published	2000/01	2001/02	2002/03	2003/04
Device Alerts	9	8	10	–
Hazard Notices	11	7	8	–
Safety Notices	31	38	23	–
Pacemaker Technical Notes	7	–	1	–
Medical Device Alerts – Action	–	–	6	25
Medical Device Alerts – Immediate action	–	–	–	18
Medical Device Alerts – Action/Information	–	–	–	3
Medical Device Alerts – Immediate action/Information	–	–	1	1
Medical Device Alerts – Action/Update	–	–	–	2
Medical Device Alerts – Information	–	–	–	1
Medical Device Alerts – Update	–	–	–	2

Device Alerts, Hazard Notices and Safety Notices were replaced by Medical Device Alerts from January 2003.

Compliance investigations

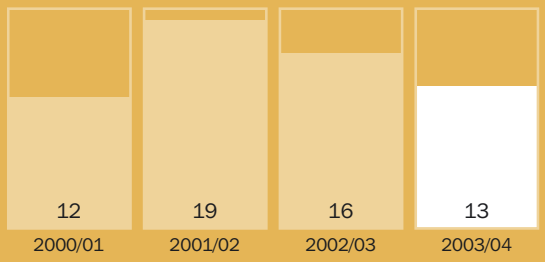
Reactive	Opened	Closed	Carried forward
2000/01	267	219	138
2001/02	237	267	108
2002/03	229	232	105
2003/04	199	200	104

Proactive	Opened	Closed	Carried forward
2000/01	102	102	62
2001/02	206	168	100
2002/03	168	171	97
2003/04	210	187	120

The Agency also carried out 82 on-site inspections.

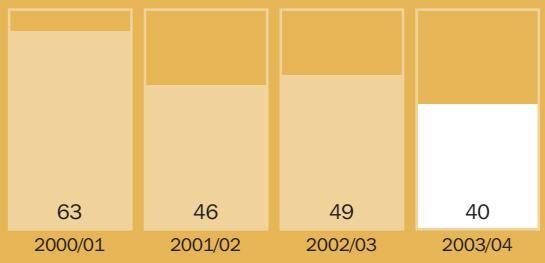
Notified Body audits

Of the 13 Notified Body audits undertaken this year, seven were on-site surveillance audits and six witnessed audits undertaken at the manufacturers' premises. All quantitative targets were met and all issues raised during the audits taken up with the relevant Notified Body.



Clinical investigations undertaken

Of the 40 clinical investigation notifications received for review, the Agency objected to five. Average time for review was 49 days, well within the statutory 60-day limit.



Medicines licensing

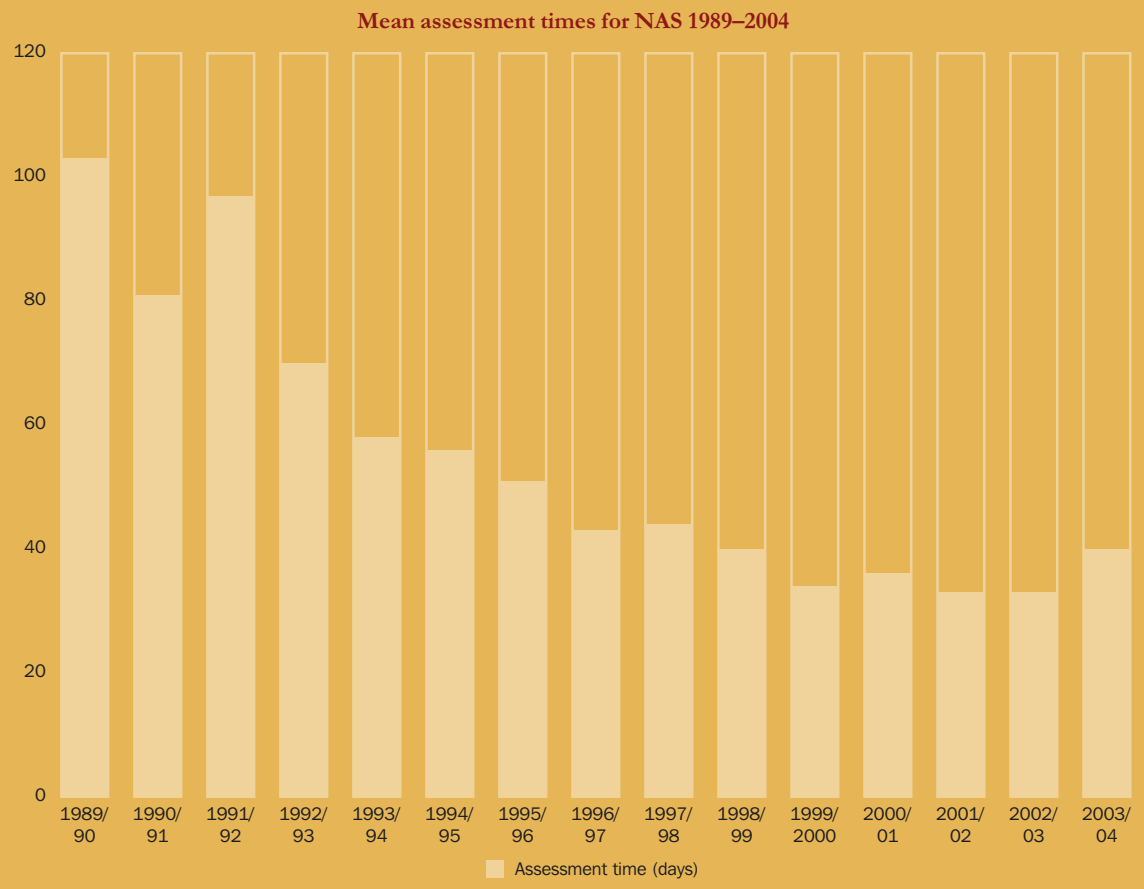
Clinical trials applications determined

The Agency has worked on a record number of trials as well as preparing the Regulations to implement the Clinical Trials Directive by 1 May 2004.

	2000/01	2001/02	2002/03	2003/04
New active substances	138	144	141	168
Abridged	78	71	72	65
Variations	1,619	1,668	1,607	1,607
Renewals	221	277	239	223
Clinical trials on marketed products	48	33	42	60
Doctors' and dentists' exemptions	958	816	968	1,038
Total	**3,062**	**3,009**	**3,069**	**3,161**

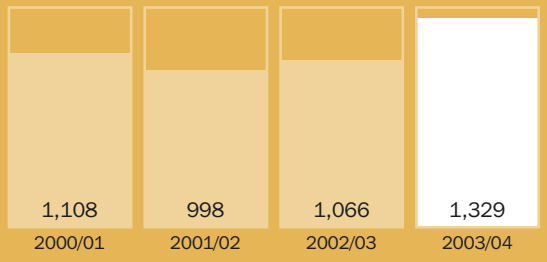
New active substances assessed

The Agency has progressively reduced the time taken to assess new active substances (NAS) since it was formed in 1989. Average assessment time is now 40 days.



Abridged licences assessed

The number of abridged applications was up nearly 25 per cent on last year.



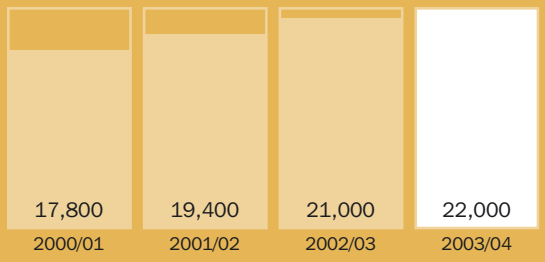
Parallel imports

	Applications received	Applications determined	Variations received	Variations determined
2003/04	**2,310**	**3,041**	**8,487**	**5,341**
2002/03	3,173	2,343	6,411	5,793
2001/02	2,851	1,575	5,617	5,131
2000/01	2,408	1,594	5,681	4,708

Contrary to predictions from the industry, the number of applications received in 2003/04 fell by 27 per cent. However, the number of applications determined rose by 30 per cent. The Agency also received a record number of variations of 8,487, up 32 per cent on last year.

Variations

New European Variations Regulations, which came into force in October, have established a new streamlined system for this high-volume area. The regulations introduced Type IA notifications, which require scientific validation only and are processed within 14 days. The UK is the first Member State to implement the full system, and has introduced a quality audit procedure for Type IA notifications, which is being used as a model by other Member States.



Overall performance has kept pace with the steady increase in numbers received over the last four years.

	Performance 2000/01	Performance 2001/02	Performance 2002/03	Performance 2003/04	Target 2004/05
Type IA[1] 100% within 14 days of receipt	–	–	–	achieved 100%	ongoing
Type I/IB[2] 100% within 30 days 85% within 20 days[3]	achieved 100% exceeded 98%	achieved 100% exceeded 95%	achieved 100% exceeded 96%	achieved 100% exceeded 91%	ongoing ongoing
Type II 100% within 90 days 85% within 60 days	accomplished 99% exceeded 94%	accomplished 99% exceeded 93%	accomplished 99% exceeded 95%	achieved 100% exceeded 90%	ongoing ongoing
Extended Type II[1] 100% within 120 days	–	–	–	achieved 100%	ongoing
Expedited Type II[1] 100% within 30 days	–	–	–	achieved 100%	ongoing

[1] Introduced 1 October 2003 [2] Type I replaced by Type IB from 1 October 2003 [3] 84% within 20 days for 2000/01 and 2000/02

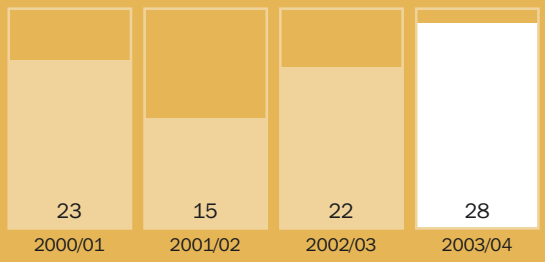
Renewals

In the past year, the UK acted as Reference Member State in 85 Mutual Recognition Procedures, and rapporteur or co-rapporteur for five Centralised products. The number of national renewals remained high at 194 per month, compared with 155 last year.

Working with European partners

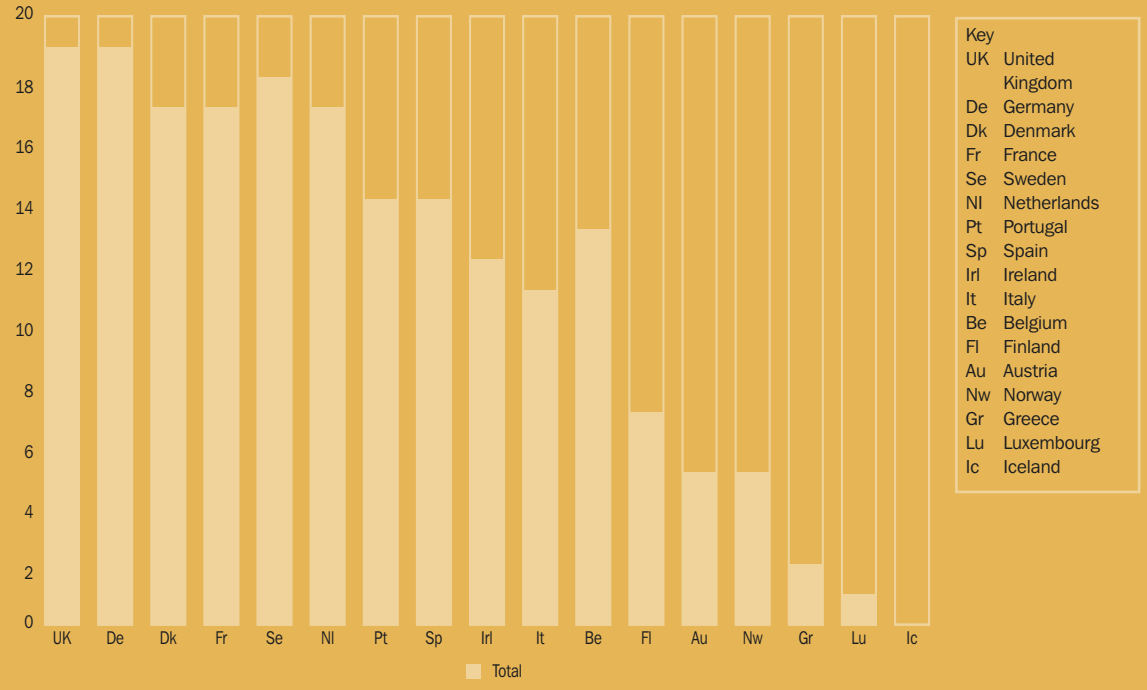
CPMP scientific advice

The UK provides more scientific advice to CPMP than any other EU Member State.



Centralised rapporteur and co-rapporteurships

Number of appointments for rapporteur and co-rapporteurs according to country from January 2001 to December 2003



By the end of December 2003, the UK was still the leading Member State for the appointment of rapporteur or co-rapporteurships for centralised applications.

Out-going mutual recognition

Assessment reports

Year	Number of reports	Average time to completion
2002/03	55	58 days
2003/04	67	44 days

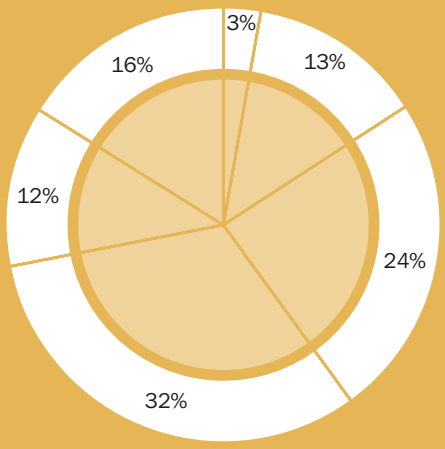
For the last two years the Agency has monitored the time for completion of these updated assessment reports, with the aim of reducing the target time of 90 days. As the figures illustrate, the time for production of the assessment report is well within the required 90 days.

Post-marketing surveillance

Pharmacovigilance

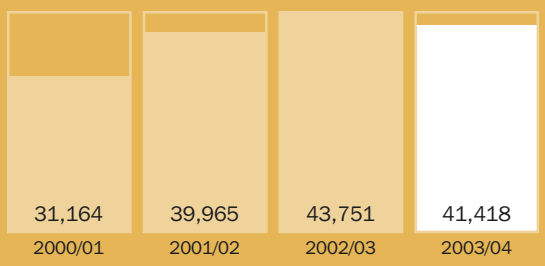
Reporting source of adverse drug reactions (ADRs) in the UK received in 2003/04

Community pharmacists	*3%*
Hospital pharmacists	*13%*
Hospital doctors	*24%*
General practitioners	*32%*
Nurses	*12%*
*Others**	*16%*



*Others = coroners, optometrists, dentists, radiographers and unspecified healthcare professionals

Non-UK reports of suspected adverse reactions



Spontaneous UK ADR reports received

	Total reports	Fatal	Serious reactions
2000/01	33,109	2%	44%
2001/02	19,254	3%	57%
2002/03	16,497	4%	70%
2003/04	**18,151**	**4%**	**67%**

This year's two per cent increase was largely due to the extension of the Yellow Card reporting scheme to include reports from nurses, midwives and health visitors. The Agency received 2,124 nurse reports during the year. We also set up a new website, www.yellowcard.gov.uk, to encourage health professionals to report ADRs electronically, and are currently in the process of linking it to other health-related websites. The Agency also received 305 electronic ADR reports this year.

Reclassification

The new reclassification strategy, which has now been in place for two years, has cut the time taken for medicines to be switched to pharmacy or general sale availability, whilst still maintaining patient safety. This year, there were two major changes in classification from prescription only medicines to pharmacy: a first proton pump inhibitor, omeprazole 10mg, for the relief of reflux-like symptoms; and a first statin, simvastatin 10mg, for patients at moderate risk of a cardiovascular event.

Medicines advertising investigated

	2000/01	2001/02	2002/03	2003/04
Number of complaints received	95	109	157	157
Number of advertisements withdrawn or amended as a result of action on complaints	35	81	98	102
Number of advertisements withdrawn or amended as a result of Agency scrutiny	5	50	28	28
Number of corrective statements published	0	1	3	9
Products for which advertising was reviewed prior to issue	14	16	15	17

The Agency strengthened its procedures to:

- effectively target vetting of advertising material before it is published;
- publish more corrective statements about misleading advertising;
- improve the handling of complaints; and
- report the outcomes of complaints investigated.

Maintaining standards

Accreditation of tissue banks

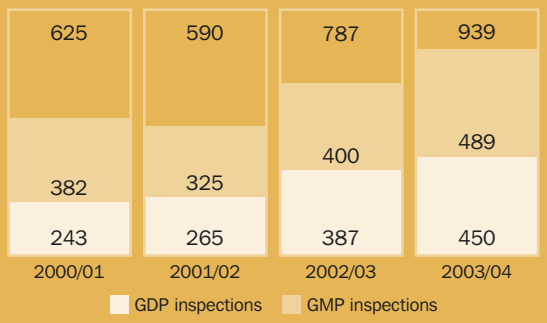
Voluntary accreditation for tissue banks started in 2001 and will become mandatory within the next two years. So far, 116 tissue banks have applied for accreditation, of which 61 have been inspected. Of these, 51 are accredited, 5 did not achieve accreditation and the remainder are working to achieve compliance.

Good Manufacturing Practice (GMP)

GMP inspectors met the high-level target to ensure that manufacturing sites are inspected at least once every 24 months. As well as carrying out 489 scheduled inspections in the UK, the unit undertook regular re-inspections, unannounced inspections, and 73 overseas inspections, of which 12 were on behalf of the EMEA.

Good Distribution Practice (GDP)

The Agency is responsible for ensuring continued compliance and adherence to GDP guidelines. During inspections the Agency found two critical deficiencies. These were followed up to ensure improvements were implemented.



Good Clinical Practice (GCP)

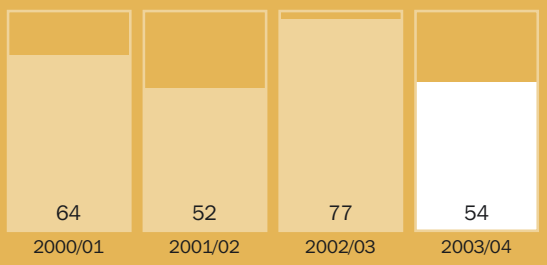
The GCP unit maintains the UK voluntary inspection programme. This year, the Agency carried out 19 inspections. From May 2004, the unit will also be responsible for maintaining the UK statutory GCP inspection programme as part of the implementation of the EU Directive on Clinical Trials (2001/20/EC), and for organising the transition from voluntary to statutory inspections.

Good Pharmacovigilance Practice (GPvP)

In July 2003, the Agency introduced a statutory pharmacovigilance inspection programme. So far, 18 have been carried out. The purpose is to examine the compliance of the systems with currently applicable EU and UK pharmacovigilance regulations and guidelines and ensure that appropriate action is taken for non-compliance.

Good Laboratory Practice Monitoring Authority (GLPMA)

During the year, three new test facilities joined the UK GLP compliance programme, and nine left. As well as carrying out routine inspections, the GLPMA audited two studies on behalf of the US FDA.



Manufacturers' and wholesale dealers' licences plus export certificates

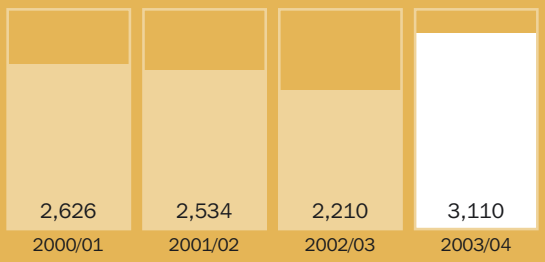
Licence certificates issued	2000/01	2001/02	2002/03	2003/04
Manufacturers' licences issued	37	44	36	36
Wholesale dealers' licences issued	162	138	156	196
Manufacturers' licence variations issued	268	320	396	337
Wholesaler dealers' licence variations issued	317	388	439	436
Export certificates issued	9,875	10,186	8,613	7,963

Applications for new licences remain steady, while the numbers of licences and variations actually issued increased. Demand for export certificates fell, reflecting fewer changes to details of marketing authorisations.

Medicines Testing Scheme

Source of samples	2000/01	2001/02	2002/03	2003/04
Defect samples	38	15	19	24
Medicines Inspectorate samples	48	41	20	9
Enforcement samples	245	226	371	463
Pre-approval (internal MHRA)	17	11	4	34
Market surveillance studies	2,273	2,231	1,774	2,505
EMEA centrally authorised products	5	10	22	23
Other (includes public, NHS and European collaboration)	–	–	–	52

This year saw a marked increase in the numbers of samples analysed, particularly market surveillance and enforcement samples. Analysis of enforcement samples provided confirmatory evidence for prosecution cases involving counterfeit medicines, traditional remedies adulterated with prescription only medicines and medicines containing illegal toxic chemicals such as heavy metals and nitroso-compounds.



Notification of unlicensed import

	2002/03	2003/04
Number of notifications received	94,974	123,505
Number assessed as a clinical emergency	708	441
Number of objections to importation	2,842	1,308

Workload in this area continued to increase rapidly. The Agency reviewed the processes for safety vetting of notifications, and implemented appropriate changes.

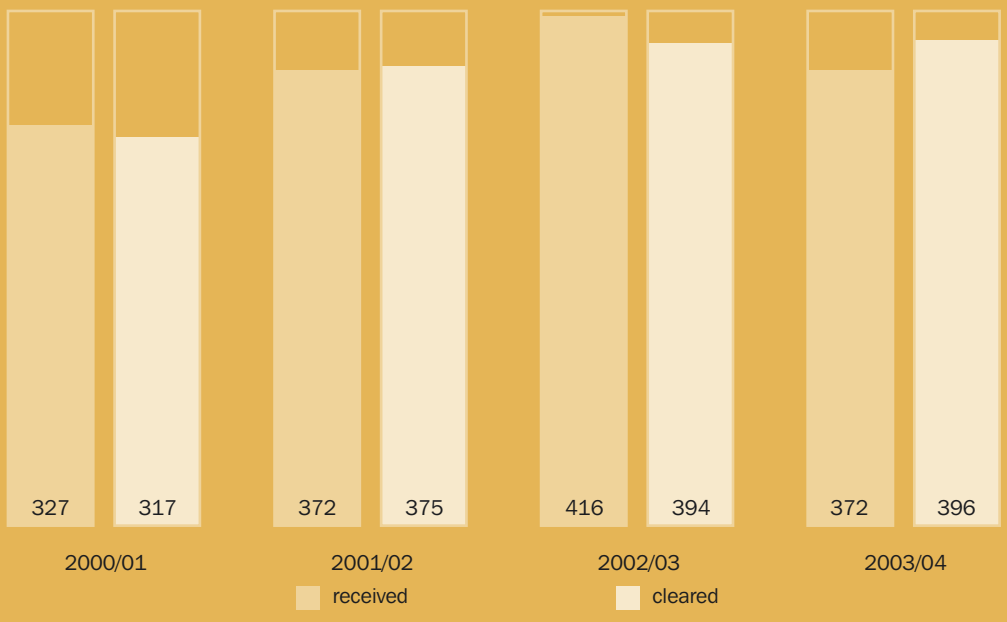
Intelligence unit

This unit provides a focal point for all intelligence-led enforcement activities in relation to ensuring the requirements of the Medicines Act 1968 and other relevant legislation and directives are met. During 2003, some 158 products were promulgated within the Agency and 156 outside the Agency. The unit's key strategic initiatives this year included targeting illicit ketamine, counterfeit medicines, and traditional Chinese medicines.

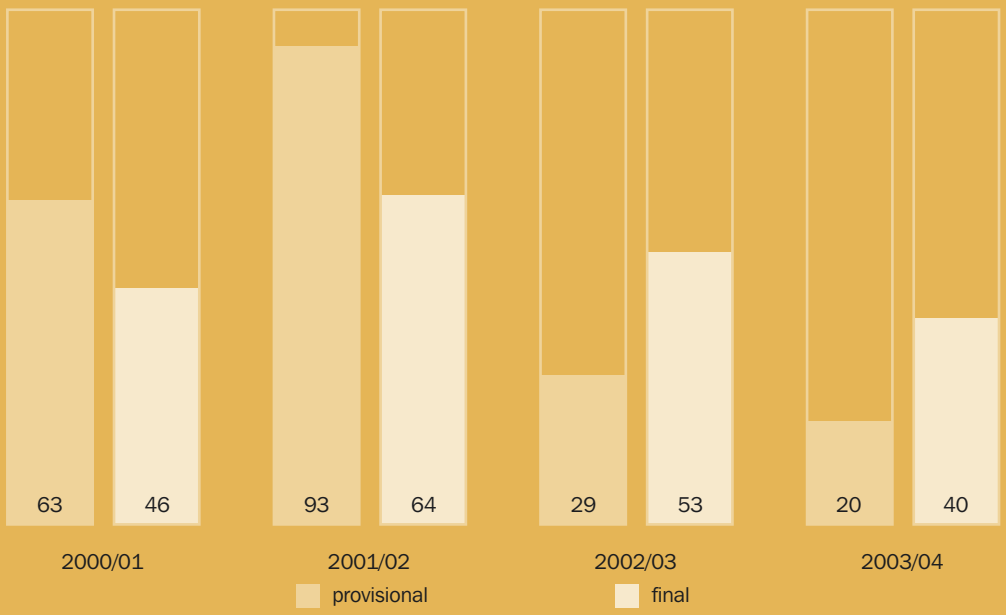
Borderline medicines considered

This section examines products that are not licensed as medicines but appear to be presented as such or have therapeutically active ingredients.

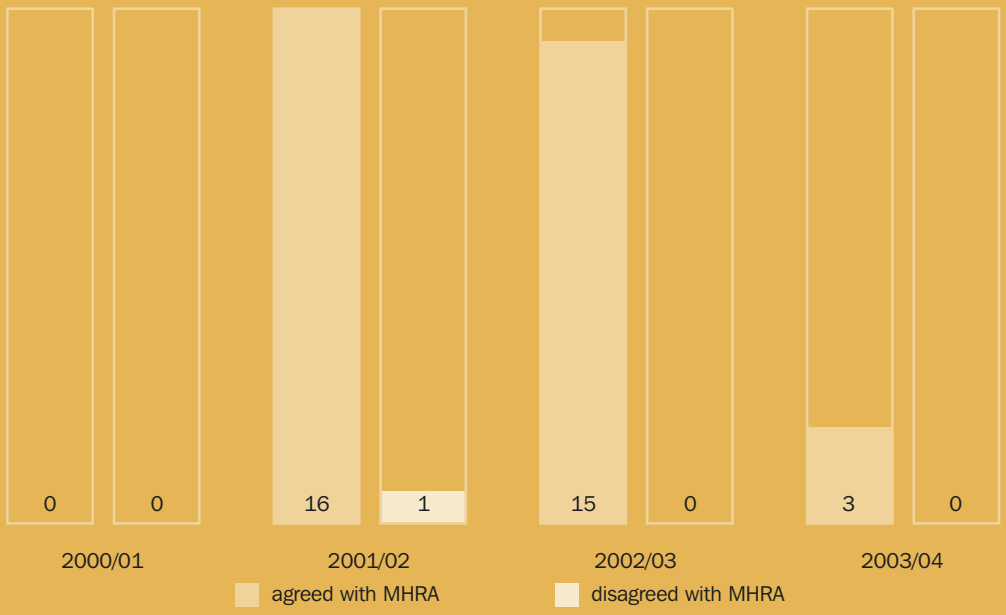
Advice requests



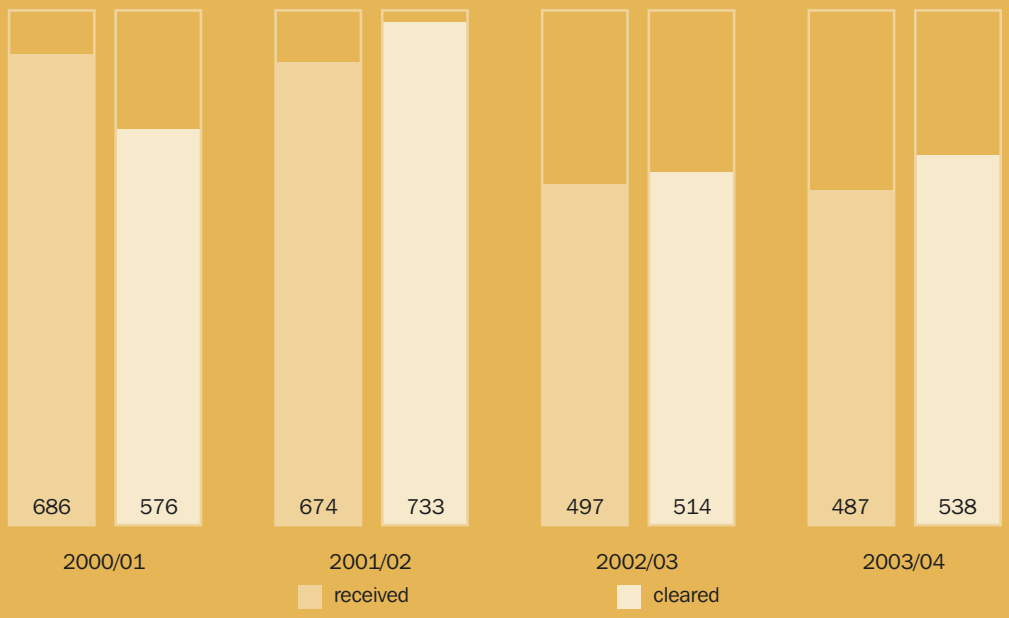
Statutory determinations issued

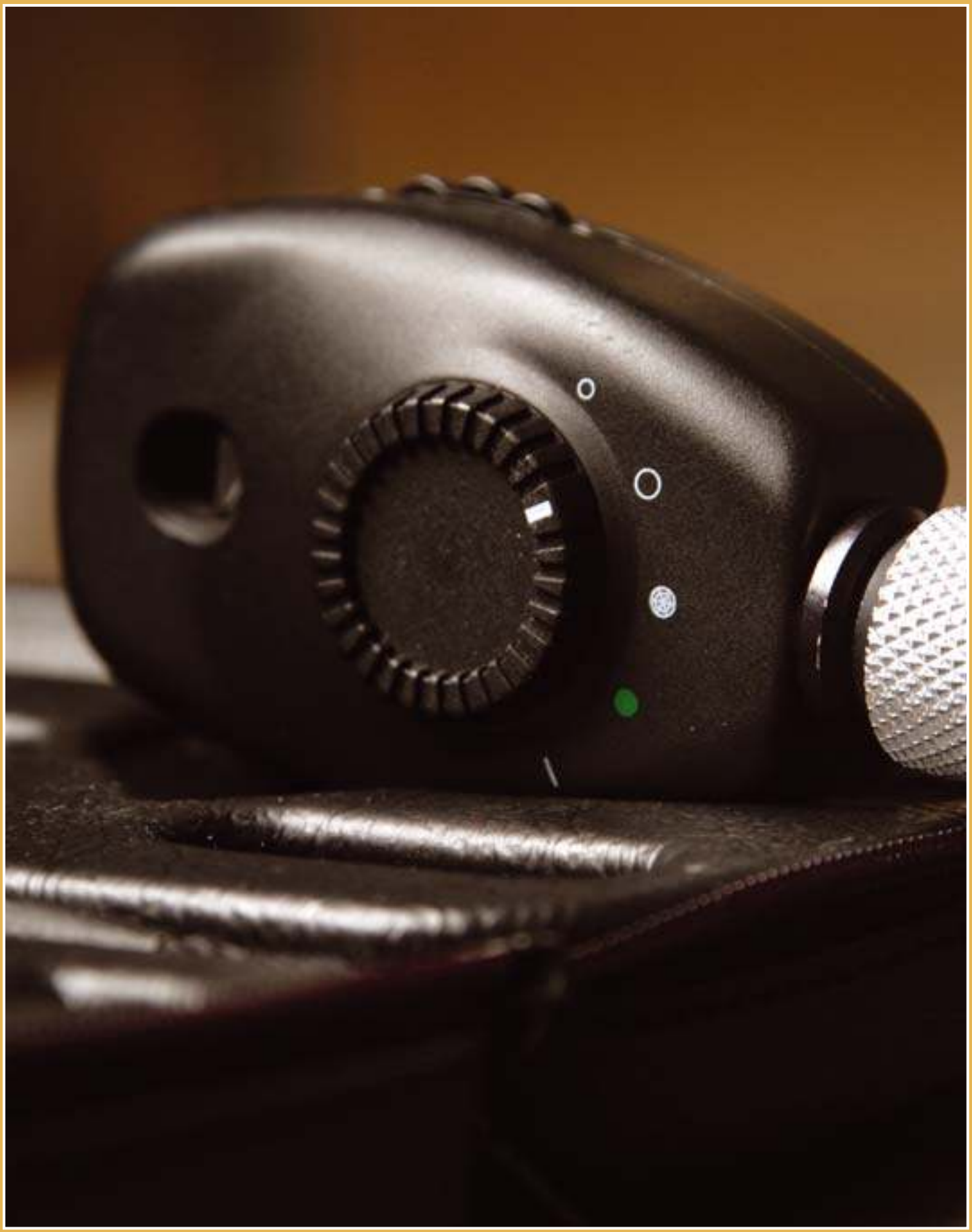


Independent Review Panel hearings



Complaints of breaches of legislation





Looking forward

THE SUCCESSFUL LAUNCH OF THE MHRA IN 2003/04 WILL GIVE US THE OPPORTUNITY TO CONSOLIDATE OUR POSITION OVER THE COMING YEAR.

If the merged Agency's first year has been one of continuity and change, the coming year will be one of consolidation.

Creating a new Executive Board was an important first step. It provides continuity of service and preserves the corporate memory; a single, coherent leadership team is the most effective way to deliver the full benefits of the merger.

The functions and responsibilities of the Agency are unlikely to change. However, how it carries out its tasks is likely to change, as the information management strategy progresses and staff start to work more closely together. Moving to a single building is a big step. It will give people more opportunities to learn from each other and work together on cross-cutting issues.

Protecting public health will remain our top priority. One way to achieve this is by ensuring that devices and medicines come to market as quickly and safely as possible. However, adverse reaction and event reporting systems, and databases such as the Yellow Card, MORE and GPRD, will grow and change so they can continue to meet the patient safety agenda.

Industry stakeholders are key to the long-term future of the Agency, so we will ensure that regulation is effective but not burdensome. Greater focus on customer needs will be built into our business processes. We are glad to be involved in the Healthcare Industry Task Force, and see it as a key driver for the future of device regulation.

Providing accessible, authoritative information must remain at the heart of our business if we are to achieve our overall mission. The information management strategy is an important – but not the only – tool we can use to become better providers of information.

To maintain high standards of protection for UK patients, and to ensure that the interests of the UK pharmaceutical and healthcare industries are represented, we need to continue to play an active, visible role in European and international regulatory affairs. The merger will ensure we are well placed to react to new regulatory issues, such as nanotechnology, and drug/device combination products.

Underpinning the consolidation process are the staff and management of the Agency. Making the merger happen in reality will involve physical relocation but it will also involve changes in attitude and behaviour. Establishing common support services is a significant step forward, but there is still a lot of exciting work ahead of us in this area.

Key targets for 2004/05

All these targets are scheduled for completion by 31 March 2005, unless otherwise stated.

1 Ensure that all fatal and serious adverse drug reactions received through the Yellow Card Scheme are captured and rapidly made available for the detection and analysis of possible drug safety hazards.

Fatal	**Serious**
100% within three working days	100% within seven working days
90% within one working day	95% within three working days

2 Develop better or additional measures and procedures for assuring and assessing the quality and effectiveness of our decision making.

3 Agree an outline communications strategy for 2004/05 (and the actions and resources needed to implement it) by the end of June 2004. The strategy should include establishing a dedicated communications function.

4 Issue timely Drug Alerts and Medical Device Alerts, which identify clear and appropriate action that recipients can achieve within realistic timescales, and review the effectiveness of these alerts.

5 Provide draft replies to 90 per cent of correspondence received by Ministers within 20 days.

6 Continue to lead the European Risk Management Strategy to ensure effective co-ordination of pharmacovigilance within Europe and support for the development of risk management plans.

7 Contribute to the creation of an effective regulatory regime for tissue-engineered products by effectively representing all relevant UK interests during negotiations following the Commission's proposals.

8 Review the Agency's contacts and forums for discussion with industry, and establish effective, transparent structures and lines of communication.

9 For introduction in 2005/06, as part of a longer programme of continuous improvement, develop better or additional measures and procedures for assessing the quality and effectiveness of the Agency's customer services.

10 Develop and implement an organisational structure and decision-making forums to meet the needs of the merged Agency by the end of July 2004.

11 Subject to approval of the business case, co-locate all London-based staff in a single building, keeping staff and service disruption to a minimum. On average, staff who move should lose no more than three days of productive working time. This does not apply to those supervising the move.

12 Ensure that the Agency achieves its agreed budgeted surplus.

Left: Jose Falcon Above: Bill Cutts

Accounts

Foreword

The Chief Executive, Chairman and Board of the Medicines and Healthcare products Regulatory Agency (MHRA) present their Report and Accounts for the year ended 31 March 2004. The accounts have been prepared in accordance with a direction given by the Treasury in pursuance of Section 4(6) of the Government Trading Funds Act 1973.

Formation of the Agency

The MHRA was set up on 1 April 2003 as an Executive Agency of the Department of Health and was created from a merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA). It was established as a Trading Fund by the Medicines and Healthcare products Regulatory Agency Trading Fund Order 2003 which came into force on 1 April 2003.

These accounts follow Financial Reporting Standard 6, 'Acquisitions and Mergers', and merger accounting has been used. The comparatives and opening balances are therefore a reflection of the results of all combining parties for 2002/03. The aggregate values of net assets appropriated into MHRA on 1 April 2003 were:

- Medicines Control Agency £22,342,000
- Medical Devices Agency £145,000
- Department of Health £251,000

Main Activities

The aim of the MHRA is to safeguard public health:

- by ensuring that medicines for human use, sold or supplied in the United Kingdom, are of an acceptable standard of safety, quality and efficacy;
- by ensuring that medical devices meet appropriate standards of safety, quality and performance;
- by promoting the safe use of medicines and devices.

In order to achieve this aim the Agency:

a. Operates a system of licensing, classification, monitoring and enforcement to ensure that medicines for human use, sold or supplied in the UK, are of an acceptable standard.

b. Discharges statutory obligations under the various UK regulations for medical devices and contributes, as necessary, to developing the safety and performance standards that support this work.

c. Ensures compliance with statutory obligations relating to the investigation of medicines in clinical trials and assesses notifications of proposals for clinical trials from manufacturers of medical devices.

d. Operates systems of post-marketing surveillance for:

- Reporting and monitoring of suspected adverse reactions to medicines and of suspected defective medicines and, where necessary, taking action to remove or restrict the availability of such products.
- Reporting adverse incidents with medical devices and, based on analysis and prompt investigation of reports, taking any necessary action to safeguard public health, e.g. issue safety warnings.

e. Promulgates good practice in the safe use of medicines and medical devices.

f. Ensures compliance, in the UK, with statutory obligations relating to the manufacture, distribution, sale, labelling, advertising and promotion of medicines.

g. Designates and monitors the performance of notified bodies that audit manufacturers of moderate and high-risk medical devices, and maintains a register of all other manufacturers placing medical devices on the UK market.

h. Monitors compliance with the medical devices regulations and, where necessary, takes enforcement action.
i. Provides advice and support on policy issues to Ministers in the Department of Health and the devolved administrations.
j. Represents the UK in European and other international Fora on matters concerning the regulation of medicines and medical devices.
k. Manages the activities of the General Practice Research Database (GPRD) of anonymised clinical records in support of a range of public health activities.
l. Manages the activities of the *British Pharmacopoeia* (BP) and work undertaken by BP staff relating to the *European Pharmacopoeia*.
m. Discharges the functions of the UK Good Laboratory Practice Monitoring Authority (GLPMA).

The report of the Chief Executive provides a more detailed review of the MHRA's activities during 2003/04 together with information on future developments.

Results

The results for the year are set out on page 69. There was an operating surplus of £8.3m (2002/03 operating surplus £0.3m). Income for the year was £67.0m (2002/03 £51.0m) and Expenditure was £58.7m (2002/03 £50.7m). Interest receivable was £0.79m (2002/03 £0.68m) and interest payable was £0.2m (2002/03 £0.09m). The dividend payable on public dividend capital was £0.246m (2002/03 £0.183m).

After the inclusion of interest and dividends the retained surplus for the year was £8.7m (2002/03 £4.0m). The retained surplus carried forward is £12.6m, (2002/03 £6.6m).

The increase in income of £16.0m is due to an increase in Department of Health funding of £6.1m, consisting of £3.5m for the Device Evaluation Service and a one-off subsidy of £2.6m. The remaining income increases arise from an improved trading performance in licensing, service fees, *British Pharmacopoeia* and other income sources.

Other operating costs have increased due to the transfer from the Department of Health of the budget for the Device Evaluation Service and an increase in the revenue costs of computing expenditure due to the ongoing Sentinel programme.

Fees for MHRA's medicine regulation activities were increased by 8% from April 2003. For 2004/05 a fee increase of 3.7% has been agreed. The Agency plans its future fee strategy so as to achieve a return averaged over the period 1 April 2003 to 31 March 2008 of at least 3.5% in the form of a surplus on ordinary activities before interest and dividends expressed as a percentage of average capital employed.

MHRA management carried out an impairment review of the GPRD assets operated by the Agency. The intention of the review, which has been carried out in compliance with the Financial Reporting Standard II, Impairment of Fixed Assets and Goodwill, was to establish whether the current cash flow projections for the GPRD operations supported the carrying value of the assets recognised in the Agency's balance sheet.

During the early phases of operating GPRD, effectively in start up mode, past budgets, forecasts and projections have been inherently more uncertain than would be the case in more established operations. Current projections of expenditure are believed to be more reliable, and whilst there is also a degree of uncertainty about income, these projections form a better base for estimating the asset value.

The projections show that the net present value of future cash flows arising from operating the GPRD asset is £10.1m. The carrying value of the asset has therefore been written down to £10.1m, an impairment of £7.5m. This impairment charge has been deducted from the revaluation reserve.

During the year assets under construction increased in value by £6.5m. This represents new expenditure relating to Sentinel – our continuing Information Management Strategy.

The auditor of the MHRA is the Comptroller and Auditor General and the costs of the audit were £0.1m (2002/03 £0.1m).

Creation of MHRA Opening Balances 1 April 2003

The creation of PDC (public dividend capital) and medium-term loans has arisen due to the merger of the MCA with the MDA and the transfer of the Department of Health Budget for the *British Pharmacopoeia* to form the MHRA on 1 April 2003. Under the terms of the Trading Fund Order, the MHRA was permitted to bring forward £3.9m as a retained surplus reserve. As the constituent parts of the new Agency ended 2002/03 with a retained surplus of £6.557m, the difference of £2.657m was designated as PDC and medium-term loans.

In order to strengthen the new Agency's balance sheet and to fund an extensive Information Technology capital project, a working capital subsidy of £2.6m was received from the Department of Health. In addition a medium-term loan of £3.4m was also agreed.

Payment of Suppliers

The MHRA complies with the Better Payment Practice Code. Unless the amounts charged are considered to be wrong, Agency policy is to settle invoices within contractual periods, and in the absence of contractual provisions, within 30 days of the date of receipt of goods and services or receipt of a valid invoice, whichever is later.

For invoices received between April 2003 and March 2004, 98% of invoices by number (2002/03 97%) were paid in accordance with these terms.

MHRA Senior Management

In the year the senior management arrangements included the Agency Board and separate Senior Management Teams for each of the Medicines and Devices sectors.

The Agency Board comprises the Chairman, Chief Executive and six Non-executive Directors.

Professor Sir Alasdair Breckenridge	Chairman	
	Chief Executive	from 1/4/03 until 31/12/03
Professor Kent Woods	Chief Executive	joined 1 January 2004
Ms Lisa Arnold	Non-executive Director	joined 1 June 2003
Miss Shelley Dolan	Non-executive Director	joined 1 June 2003
Mr Michael Fox	Non-executive Director	joined 1 June 2003
Mr Charles Kernahan	Non-executive Director	joined 1 June 2003
Professor Angus Mackay	Non-executive Director	joined 1 June 2003
Mr Garry Watts	Non-executive Director	joined 1 June 2003

The members of the Medicines sector Senior Management Team during the year were:

Mr R K Alder	
Miss D Hepburn	
Dr I Hudson	
Dr G Munro	
Dr J M Raine	
Mr G Savage	
Dr L Wood	
Ms R Sandby-Thomas	Legal Adviser until July 2003
Mr S Rogers	Legal Adviser from August 2003

The members of the Devices sector Senior Management Team during the year were:

Mr C Bray	
Mr K M Cornelius	
Mr T Crawley	retired 5 May 2003
Dr D Jefferys	
Dr S Ludgate	
Mr S Owen	
Mr J Watkins	from 5 May 2003 to 17 November 2003
Mrs S Wilkins	from 17 November 2003
Mr M Woods	from 17 November 2003

Employee Policies

We are an equal opportunities employer and we are positive about employing suitably qualified people regardless of gender, sexual orientation, marital status, race, religion, politics or disability.

The MHRA has systems in place to ensure that recruitment is carried out in accordance with the Recruitment Code published by the Civil Service Commissioners. These systems are subject to an annual independent check.

We have an active communications programme with staff including intranet-based and written communications, and employee meetings.

Outside Bodies

Opinions of industry trade associations and organisations representing public and professional interests were canvassed on a range of proposed statutory changes and other matters of importance.

Kent Woods
Chief Executive and Accounting Officer
15 July 2004

Statement of Agency's and Chief Executive's Responsibilities

Under Section 4(6) of the Government Trading Funds Act 1973 the Treasury have directed the MHRA to prepare a statement of accounts for each financial year in the form and on the basis set out in an accounts direction. The accounts are prepared on an accruals basis and must give a true and fair view of the Agency's state of affairs at the year end and of its income and expenditure, total recognised gains and losses and cash flows for the financial year.

In preparing the accounts the Agency is required to:

- observe the accounts direction issued by the Treasury, including the relevant accounting and disclosure requirements, and apply suitable accounting policies on a consistent basis;
- make judgements and estimates on a reasonable basis;
- state whether applicable accounting standards have been followed, and disclose and explain any material departures in the financial statements;
- prepare the financial statements on the going concern basis, unless it is inappropriate to presume that the Agency will continue in operation.

The Treasury has appointed the Chief Executive of the MHRA as the Accounting Officer for the Agency. His relevant responsibilities as Accounting Officer, including his responsibility for the propriety and regularity of the public finances for which he is answerable and for the keeping of proper records, are set out in the Accounting Officers' Memorandum, issued by the Treasury and published in *Government Accounting*.

Statement on Internal Control Year End 31 March 2004

1. Scope of responsibility

As Accounting Officer, I had responsibility for maintaining the sound system of internal control that supported the achievements of the Medicines and Healthcare products Regulatory Agency's policies, aims and objectives whilst safeguarding public funds and assets for which I was personally responsible in accordance with the responsibilities assigned to me in *Government Accounting*.

The Medicines and Healthcare products Regulatory Agency (MHRA) was formed on 1 April 2003 when the Medicines Control Agency (MCA) and Medical Devices Agency (MDA) were merged. I took up appointment as Chief Executive Officer on 1 January 2004. Between 1 April 2003 and 31 December 2003, the Chairman of MHRA also acted as temporary Chief Executive and Accounting Officer. The Agency has been housed in two separate locations for the period of the report. In addition, both sectors of the Agency retained separate internal auditors for 2003/04. Similar processes of risk management were in place for each building and were based on guidance produced by the Department of Health, National Audit Office and Treasury. The risk management programmes operated independently of the Department of Health but the Department was kept informed through the departmental representative's attendance at the Risk and Audit Committees.

2. The purpose of the system of internal control

The Agency's systems of internal control were designed to manage risk to a reasonable level rather than to eliminate all risk of failure to achieve policies, aims and objectives, and could only therefore provide reasonable, and not absolute, assurance of effectiveness. The systems of internal control were based on an ongoing process designed to identify and prioritise the risks to the achievement of the overall policies, aims and objectives of the Agency, to evaluate the likelihood of those risks being realised and the impact should they be realised, and manage them efficiently, effectively and economically. The MHRA systems of internal control have been in place for the year ended 31 March 2004 and accord with Treasury guidance.

3. Capacity to handle risk

The systems of internal control and risk management were endorsed by the relevant Accounting Officers and the Risk and Audit Committees, and were in existence throughout the year.

A Risk Management framework and Standard Operations Procedure (SOP) with an Agency Guide to Risk Management were in place. Information about Corporate Governance and Risk Management was incorporated into the induction procedure. All these documents were on the MHRA Intranet and were available to all staff. A Risk Management Co-ordinator was also available for facilitating risk management training and providing risk management support.

Senior Management Teams at both locations were responsible for reviewing the risk registers on a regular basis and maintaining a corporate responsibility for the identification and monitoring of the Risk Management system.

4. The risk and control framework

Risk Management

As part of the stewardship reporting process for the end of the year Divisional Heads (medicines) completed a statement of accountability, confirming that systems of effective internal control were in place, within their areas of responsibility, throughout the period. It was not the practice to obtain individual statements from Divisional Heads (devices) but each owned and managed individual risks. The risks were collectively reviewed and monitored by the Senior Management Team (SMT), as a group. The SMT took corporate responsibility, and this was recorded.

Risk registers were maintained at operational level, which recorded the risks identified and action being

taken to mitigate the risks. These were dynamic working documents, which were updated regularly in order to ensure that the risk register reflected the most up-to-date position. The information in the risk registers was analysed and high level risks identified. Directors were required to report any significant changes to individual risks or any new risks immediately. The identification and management of risks was integrated into the Agency's planning system via regular reports to the Operations Management Team (medicines), the Senior Management Teams and the Risk and Audit Committee. Independent internal audit reports on risk management for the Agency, gave assurance that risks were adequately managed and controlled in both locations.

The most common means of undertaking risk assessments was through round table discussions. Identification of the context of risk included the safety, quality and efficacy of all medicines and devices, Ministerial interests, public interests, service user interests and aspects of relationships both inside and outside of government. The main area of priority was around the successful implementation of the merger of the two agencies; this included producing a single Business Plan and setting up a single Risk Management strategy.

5. Review of effectiveness

As Accounting Officer, I have responsibility for reviewing the effectiveness of the system of internal control. My review of the effectiveness of the system of internal control in place is informed by the work of the internal auditors and the executive managers within the MHRA, who have responsibility for the development and maintenance of the internal control frameworks, and comments made by external auditors in their management letter and other reports. I have been advised on the implications of the result of my review and effectiveness of the systems of internal control by the Board and the Risk and Audit Committee. A plan to address weaknesses and ensure continuous improvement of the MHRA system is in place for 2004/05.

- *Corporate governance management structure*

The Agency Board, consisting of Chairman, six non-executive members and the Chief Executive Officer (CEO) of the Agency was in place from June 2003. From June 2003 to December 2003 the Chairman also acted as temporary Chief Executive Officer. A register of interests was held and as a Civil Servant the CEO was answerable to the Civil Service Code of Conduct. The Board met monthly to discuss the Agency's plans and strategic direction and to take action as appropriate.

The Senior Management Teams (SMTs) met monthly to discuss plans for the Agency and to take appropriate action. As part of the SMTs' programme the systems of the Risk Management strategy were monitored on a regular basis. The Operations Management Team (medicines) reviewed the risk register, ensuring a consistent approach from an operational point of view. Operational issues for medicines and devices issues were discussed monthly.

Quarterly reports were sent to me and the senior management, setting out the key performance and risk indicators. In addition, the reports brought to our attention any control issues by the early warning processes embedded within the Agency's business operations.

- *The Risk and Audit Committees*

The Risk and Audit Committees were an important part of the Agency's Risk Management process. In the first half of the year there were two Committees overseeing the production of the last Annual Accounts for the MCA and MDA. Following the dissolution of the Risk and Audit Committees in July 2003, a single new MHRA Risk and Audit Committee was set up. A legacy report was produced by the outgoing Committees flagging up issues to be taken forward as part of the agenda for the new MHRA Committee. The inaugural meeting of the new Committee was in October 2003. It met three times during the period of this report. It looked at the issues raised in the legacy report, the effectiveness of the Agency's Risk Management processes, the internal

and external audit plans, discussed and considered reports from internal and external audit and management on internal control and any material control weaknesses, and gave advice on the level of assurance given by the internal and external audit reports via the Chairman's end of year report.

- *Internal Audit*

The internal audit service for the MHRA has been provided by Bentley Jennison and Department of Health Internal Audit, both of whom operated to the standards defined in the Government Internal Audit Manual. During 2003/04 a joint audit programme was produced which was based on the risks identified in the relevant risk registers, with due regard being given to areas of commonality. For 2004/05 the Agency has appointed Bentley Jennison as the single internal audit service provider.

An Acting Head of Internal Audit was appointed for 2003/04 and regular reports on the adequacy and effectiveness of the systems of internal control together with recommendations for improvement were produced and monitored. The Acting Head of the Joint Internal Audit Team provided an independent opinion in an end of year report. The report stated that the MHRA did have adequate and effective risk management, control and governance processes to manage the achievement of the organisation's business objectives as reflected by the sound risk management, corporate governance and internal controls within the two legacy agencies. Notwithstanding this the auditors considered that the absence of an overarching and consistent framework limited the extent to which full assurance could be given.

During 2003/04 Internal Audit completed 20 audits. Action plans, agreed by the internal auditors, were put in place for recommendations made in all the audit reports. The implementation of recommendations made in a number of reports was subject to 'in-year' follow-up audits. Where the implementation of recommendations has not been achieved before the end of the period of this report the action plans have been carried forward into the new year.

Half the areas audited were given substantial assurance and eight areas were considered to have adequate procedures in place. Only two areas were given a limited assurance, those dealing with Enforcement (devices) and Temporary and Agency Staff. An action plan to implement recommendations made in the Enforcement report has been agreed with Internal Audit. As a result of the Temporary and Agency Staff audit, the Agency is to review this area and recommendations made in the report will be addressed by the review. It is expected that the review will be completed by December 2004.

The procurement of a contractor for the implementation of the Agency's Information Management Strategy was audited as was the adequacy of the controls for the contract now in place and operational. Substantial assurance was given on both audits. Action plans on recommendations were agreed and taken forward as part of the development of the new system. Rollout of the Agency's new IT system is under way and scheduled to be completed in 2005.

Two audits carried out on Risk Management procedure gave the processes adequate assurance. However, reviewing the Risk Management strategy has been a key task for the new Agency. Action plans to implement recommendations made in the reports were agreed with the auditors and included in the new strategy which was finalised in March 2004. Rollout started on 1 April 2004. The new Risk Management system will be fully implemented by March 2005.

An audit carried out in June 2003 made a number of recommendations to improve the Business Continuity and Disaster Recovery Plan in Market Towers. Following the co-location of the Agency to a single building, a strategy will be produced which will address the recommendations made in the June report. Central

control and communications will be prime areas for attention. The MHRA is taking this work forward vigorously to ensure that in the event of a serious interruption to normal daily operations or an actual disaster the work of the MHRA will continue to operate effectively.

6. Significant internal control problems

The MHRA Risk and Audit Committee reviewed the Internal Audit progress reports produced in the 2003/04 year which included audits which monitored the implementation of key recommendations made in reports. The Committee, having made reasonable enquiries, has been able to assure me that the risks identified to delivery of the business objectives, had been managed to a reasonable level within the various action plans.

Kent Woods
Chief Executive and Accounting Officer
15 July 2004

The Certificate and Report of the Comptroller and Auditor General to the Houses of Parliament

I certify that I have audited the financial statements on pages 69 to 84 under the Government Trading Funds Act 1973. These financial statements have been prepared under the historical cost convention as modified by the revaluation of certain fixed assets and the accounting policies set out on pages 73 and 74.

Respective responsibilities of the Medicines and Healthcare products Regulatory Agency, the Chief Executive and Auditor

As described on page 63, the Medicines and Healthcare products Regulatory Agency and Chief Executive are responsible for the preparation of the financial statements in accordance with the Government Trading Funds Act 1973 and Treasury directions made thereunder and for ensuring the regularity of financial transactions. The Medicines and Healthcare products Regulatory Agency and the Chief Executive are also responsible for the preparation of the other contents of the Annual Report. My responsibilities, as independent auditor, are established by statute and I have regard to the standards and guidance issued by the Auditing Practices Board and the ethical guidance applicable to the auditing profession.

I report my opinion as to whether the financial statements give a true and fair view and are properly prepared in accordance with the Government Trading Funds Act 1973 and Treasury directions made thereunder, and whether in all material respects the expenditure and income have been applied to the purposes intended by Parliament and the financial transactions conform to the authorities which govern them. I also report if, in my opinion, the Foreword is not consistent with the financial statements, if the Accounting Officer has not kept proper accounting records, or if I have not received all the information and explanations I require for my audit.

I read the other information contained in the Annual Report and consider whether it is consistent with the audited financial statements. I consider the implications for my certificate if I become aware of any apparent misstatements or material inconsistencies with the financial statements.

I review whether the statement on pages 64 to 67 reflects the Agency's compliance with Treasury's guidance on the Statement on Internal Control. I report if it does not meet the requirements specified by Treasury, or if the statement is misleading or inconsistent with other information I am aware of from my audit of the financial statements. I am not required to consider, nor have I considered whether the Accounting Officer's Statement on Internal Control covers all risks and controls. I am also not required to form an opinion on the effectiveness of the Medicines and Healthcare products Regulatory Agency corporate governance procedures or its risk and control procedures.

Basis of audit opinion

I conducted my audit in accordance with United Kingdom Auditing Standards issued by the Auditing Practices Board. An audit includes examination, on a test basis, of evidence relevant to the amounts, disclosures and regularity of financial transactions included in the financial statements. It also includes an assessment of the significant estimates and judgements made by the Medicines and Healthcare products Regulatory Agency and Chief Executive in the preparation of the financial statements, and of whether the accounting policies are appropriate to the Agency's circumstances, consistently applied and adequately disclosed.

I planned and performed my audit so as to obtain all the information and explanations which I considered necessary in order to provide me with sufficient evidence to give reasonable assurance that the financial statements are free from material misstatement, whether caused by error, or by fraud or other irregularity and that, in all material respects, the expenditure and income have been applied to the purposes intended by Parliament and the financial transactions conform to the authorities which govern them. In forming my opinion I have also evaluated the overall adequacy of the presentation of information in the financial statements.

Opinion

In my opinion:

- the financial statements give a true and fair view of the state of affairs of the Medicines and Healthcare products Regulatory Agency at 31 March 2004 and of the surplus, total recognised gains and losses and cash flows for the year then ended and have been properly prepared in accordance with the Government Trading Funds Act 1973 and directions made thereunder by Treasury; and
- in all material respects the expenditure and income have been applied to the purposes intended by Parliament and the financial transactions conform to the authorities which govern them.

I have no observations to make on these financial statements.

John Bourn
Comptroller and Auditor General
National Audit Office
157–197 Buckingham Palace Road
Victoria
London SW1W 9SP
20 July 2004

Income and Expenditure Account for the Year Ended 31 March 2004

Continuing Operations

Notes		2003/04 £000	2002/03 £000
3	Trading income	64,432	51,065
	Department of Health subsidy	2,600	–
		67,032	51,065
4	Staff costs	31,012	29,617
6	Other operating costs	24,840	17,184
8,13	Depreciation	2,856	3,063
11	Exceptional items – asbestos	–	889
		58,708	50,753
	OPERATING SURPLUS BEFORE INTEREST AND FINANCING CHARGES	8,324	312
	Exceptional items – credit arising from repayment of loans/PDC	–	3,292
7	Interest receivable	790	679
	Interest payable	(199)	(94)
	Redemption interest	–	(37)
	Dividend payable on public dividend capital	(246)	(183)
	RETAINED SURPLUS FOR THE YEAR	8,669	3,969
	Retained surplus brought forward		2,588
	Opening retained surplus	3,900	
13	RETAINED SURPLUS CARRIED FORWARD	12,569	6,557

NOTE: There were no discontinued operations.

The notes on pages 73 to 84 form part of these accounts.

Statement of Total Recognised Gains and Losses for the Year Ended 31 March 2004

	2003/04 £000	2002/03 £000
Retained surplus for the year excluding dividend payable	8,915	4,152
GPRD impairment	(7,500)	
DoH loans	3,400	
Unrealised surplus on revaluation	53	73
Total recognised gains/(losses)	4,868	4,225

The notes on pages 73 to 84 form part of these accounts.

Balance Sheet as at 31 March 2004

Notes		31 March 2004 £000	31 March 2003 £000
8	FIXED ASSETS Tangible fixed assets	26,668	30,238
	CURRENT ASSETS		
9	Debtors	6,142	4,794
16	Cash at bank and in hand	22,276	12,730
		28,418	17,524
10	Creditors: amounts falling due within one year	(10,882)	(10,559)
	Net current assets	17,536	6,965
	Total assets less current liabilities	44,204	37,203
	FINANCED BY:		
11	Provisions for liabilities and charges	998	1,546
12	Deferred revenue	16,846	12,899
		17,844	14,445
13	CAPITAL AND RESERVES:		
	Public dividend capital	1,329	–
	Medium-term loans	4,728	–
	Revaluation reserve	7,734	16,201
	Retained surplus	12,569	6,557
		26,360	22,758
		44,204	37,203

The notes on pages 73 to 84 form part of these accounts.

Kent Woods
Chief Executive and Accounting Officer

15 July 2004

Cash Flow Statement for the Year Ended 31 March 2004

Notes		2003/04 £000	2002/03 £000
14	NET CASH INFLOW/(OUTFLOW) TO OPERATING ACTIVITIES	12,497	(6,672)
	RETURNS ON INVESTMENTS AND SERVICING OF FINANCE		
	Interest received	759	663
	Interest paid	(142)	(88)
	Dividend paid on public dividend capital	–	(344)
	Net cash inflow from returns on investments and servicing of finance	617	231
	CAPITAL EXPENDITURE		
	Payments to acquire fixed assets	(6,968)	(2,962)
	MANAGEMENT OF LIQUID RESOURCES		
	Net cash inflow from short term deposits with National Loans Fund	–	–
	FINANCING		
	Further medium-term borrowings	3,400	–
	Net cash inflow from financing	3,400	–
16	(DECREASE)/INCREASE IN CASH FOR YEAR	9,546	3,941

The notes on pages 73 to 84 form part of these accounts.

Notes to the Accounts

1. Accounting Policies

The financial statements have been prepared in compliance with the accounting principles and disclosure requirements of the edition of *Trading Funds – Accounts Guidance* issued by HM Treasury which is in force for 2003/04. The accounting policies contained in the Guidance follow UK generally accepted accounting practice for companies (UK GAAP) to the extent that it is meaningful and appropriate to the public sector. Where the Guidance permits a choice of accounting policy, the accounting policy which has been judged to be most appropriate to the particular circumstances of the MHRA for the purpose of giving a true and fair view has been selected. The MHRA's accounting policies have been applied consistently in dealing with items considered material in relation to the accounts.

a. Accounting conventions

The accounts have been prepared under the Historical Cost Convention, modified to allow for the revaluation of fixed assets, at their value to the business by reference to their current costs.

b. Going concern

On 13 June 2002 the Government announced the formation of the MHRA via a merger of the Medicines Control Agency with the Medical Devices Agency from 1 April 2003. Most assets and liabilities of the two agencies, plus some from the DoH were transferred to the new trading fund at the value shown in the balance sheet, and as a result the accounts have been prepared on a going concern basis.

c. Fixed assets

Fixed assets include tangible fixed assets and the costs of acquiring or creating computer systems or software. The threshold for capitalising expenditure is £5,000. Only items or groups of related items with a combined value in excess of £5,000 are capitalised.

All assets excepting assets under construction and GPRD data are revalued annually using the Central Statistical Office and appropriate Health Services Cost indices.

Assets under construction are shown at Historic Cost. Modified Historic Cost valuations are applied at the point the asset comes into use.

GPRD data assets are valued via an assessment of the future cash flows arising from exploitation of these assets discounted to net present values. Impairments arising from valuations are offset against the revaluation reserve.

Surpluses and deficits arising on revaluation on non-GPRD data assets are treated in accordance with financial reporting standards. Where deficits occur these are taken to the revaluation reserve as long as there is sufficient balance in the reserve otherwise they are taken to other operating costs in the Income and Expenditure Account.

Depreciation is provided on a straight line basis on all fixed assets, excepting assets under construction, at rates calculated to write off the cost or valuation (less any estimated residual value) of each asset over its expected useful life as shown below. Depreciation commences when assets are brought into use.

Personal computers and faxes	3 years
Laboratory equipment	5 years
Computer servers, laptops and associated applications, software, office equipment, furniture, fixtures and fittings	5 years
GPRD equipment	6 years
Office refurbishment costs	10 years
GPRD data	20 years

d. Recognition of income

The proportion of the fees receivable for licence applications, representing the work estimated to be outstanding to complete the processing of such applications, is carried forward to future periods.

e. Foreign currencies

Transactions denominated in foreign currencies are translated into sterling at the rates of exchange ruling at the date of the balance sheet. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are translated at the rates ruling at that date. The resulting exchange differences are dealt with in the Income and Expenditure Account for the year.

f. Staff terms and conditions

The Agency's staff are civil servants in the Department of Health and are subject to centrally determined terms and conditions. Staff who are members of the Senior Civil Service (SCS), including Members of the Board of Management, are covered by SCS central arrangements and the Department of Health's terms and conditions and other procedures governing implementation of the SCS, including the Senior Salaries Review Body's performance-related pay recommendations.

Past and present employees are covered by the provisions of the Principal Civil Service Pension Scheme (PCSPS) which is a defined benefit scheme and is unfunded and non-contributory. The Agency recognises the expected cost of providing pensions on a systematic and rational basis over the period during which it benefits from employees' services by payment to the PCSPS of amounts calculated on an accruing basis. Liability for payment of future benefits is a charge on the PCSPS.

g. Bad debt and credit note provision

The bad debt and credit note provision is reviewed each year and reflects the level of trade debtors that it is anticipated may result in either a bad debt or a requirement to issue a credit note.

h. Operating leases

Operating lease rentals are charged to the Income and Expenditure Account on a straight line basis.

2. Financial Objectives

The MHRA's financial objectives are set out in full in a Treasury Minute dated 9 February 2004, which is reproduced on page 84. The objectives are that the MHRA should be managed so that its revenue:

a) consists principally of receipts in respect of goods and services provided in the course of its funded operations;

b) is sufficient, taking one year with another, to meet outgoings which are properly chargeable to revenue account and to achieve an operating surplus equivalent to a 3.5% average return on net assets employed at current values.

Net assets are taken to be total assets less total liabilities, excluding an agreed proportion of the GPRD database. For 2003/04 a return of 3.5% equates to £0.445m and is reflected in the amounts of interest and dividend payable. The actual operating surplus for the year was £8.324m (2002/03 operating surplus of £0.312m).

3. Income

	2003/04 £000	2002/03 £000
Licence and inspections income invoiced during the year	31,489	25,521
Service fee income invoiced during the year	17,632	15,176
	49,121	40,697
Add income deferred from previous periods *(see Note 12)*	12,264	10,070
Less income deferred to future periods *(see Note 12)*	(16,433)	(12,264)
Income relating to work done in the year	44,952	38,503
Income from miscellaneous activities	7,497	4,073
DoH funding	11,983	8,489
	64,432	51,065

The miscellaneous income for the year is shown net of £0.413m deferred to future periods (31 March 2003 £0.541m).

3B. Segmental Analysis

Treasury Guidance on Fees and Charges is applied when setting fee levels for the MHRA. Fees are set following consultation with Industry, the Department of Health and the Treasury, and are intended, taking one year with another, to cover the costs of the Agency. DoH funding in relation to devices activities is also intended to cover the costs of providing this specific service.

Income (net of deferred revenue)		**2003/04 £000**	**2002/03 £000**
Medicines –	Licence fees	27,320	23,327
	Service fees	17,632	15,176
	British Pharmacopoeia	1,767	893
	Remote Access to Marketing Authorisations	784	713
	Seminars	547	266
	Miscellaneous	3,415	1,807
Devices –	DoH funded services	11,983	8,489
	Miscellaneous	584	394
Corporate –	DoH recharge	400	–
		64,432	51,065
Expenditure	Medicines	46,141	41,870
	Devices	12,167	8,883
	Corporate	400	–
		58,708	50,753

It is currently not possible to provide a detailed segmental report of expenditure. This detailed disclosure will not be available until the planned replacement of IT systems intended for 2004/05 has taken place.

4. Staff Costs

	2003/04 £000	**2002/03 £000**
Salaries and wages	24,249	22,857
Social security costs	2,130	1,757
Pension contributions	3,532	3,360
	29,911	27,974
Agency and other staff costs	1,058	784
Early retirement and redundancy costs	43	859
	31,012	29,617

Pension

The employees of the MHRA, excluding the Chief Executive, are covered by the provisions of the Principal Civil Service Pension Scheme. The PCSPS is an unfunded multi employer defined benefit scheme but the MHRA is unable to identify its share of the underlying assets and liabilities. A full actuarial valuation was carried out at 31 March 2000 and details can be found in the separate scheme statement of the PCSPS. For 2003/04, normal employer contributions of £3.5m were payable to the PCSPS (2002/03 £3.4m) at rates in the range 12 to 18.5% of pensionable pay. It has been agreed that contributions will remain at that level for the next year. Employer contribution rates are reviewed every three years following a scheme valuation by the Government Actuary. The contribution rates reflect benefits as they are accrued, not when the costs are actually incurred, and they reflect past experience of the scheme.

Pension benefits are provided through the Civil Service pension arrangements. From 1 October 2002, civil servants may be in one of three statutory based 'final salary' defined benefit schemes (**classic**, **premium**, and **classic plus**). New entrants after 1 October 2002 may choose between membership of **premium** or joining a good quality 'money purchase' stakeholder based arrangement with a significant employer contribution (**partnership pension account**).

(a) Classic Scheme

Benefits accrue at the rate of 1/80th of pensionable salary for each year of service. In addition, a lump sum equivalent to three years' pension is payable on retirement. Members pay contributions of 1.5% of pensionable earnings. On death, pensions are payable to the surviving spouse at a rate of half the member's pension. On death in service, the scheme pays a lump sum benefit of twice pensionable pay and also provides a service enhancement on computing the spouse's pension. The enhancement depends on length of service and cannot exceed 10 years. Medical retirement is possible in the event of serious ill health. In this case, pensions are brought into payment immediately without actuarial reduction and with service enhanced as for widow(er) pensions.

(b) Premium Scheme

Benefits accrue at the rate of 1/60th of final pensionable earnings for each year of service. Unlike **classic**, there is no automatic lump sum, but members may commute some of their pension to provide a lump sum up to a maximum of 3/80ths of final pensionable earnings for each year of service or 2.25 times pension if greater (the commutation rate is £12 of lump sum for each £1 of pension given up). For the purposes of pension disclosure the tables assume maximum commutation. Members pay contributions of 3.5% of pensionable earnings. On death, pensions are payable to the surviving spouse or eligible partner at a rate of 3/8ths of the member's pension (before any commutation). On death in service, the scheme pays a lump sum benefit of three times pensionable earnings and also provides a service enhancement on computing the spouse's pension. The enhancement depends on length of service and cannot exceed 10 years. Medical retirement is possible in the event of serious ill health. In this case, pensions are brought into payment immediately without actuarial reduction. Where the member's ill health is such that it permanently prevents them undertaking any gainful employment, service is enhanced to what they would have accrued at age 60.

(c) Classic Plus Scheme

This is essentially a variation of **premium**, but with benefits in respect of service before 1 October 2002 calculated broadly as per **classic**.

Pensions payable under **classic**, **premium**, and **classic plus** are increased in line with the Retail Prices Index.

(d) Partnership Pension Account

This is a stakeholder-type arrangement where the employer pays a basic contribution of between 3% and 12.5% (depending on the age of the member) into a stakeholder pension product. The employee does not have to contribute but where they do make contributions, these will be matched by the employer up to a limit of 3% (in addition to the employer's basic contribution). Employers also contribute a further 0.8% of pensionable salary to cover the cost of risk benefit cover (death in service and ill health retirement). The member may retire at any time between the ages of 50 and 75 and use the accumulated fund to purchase a pension. The member may choose to take up 25% of the fund as a lump sum.

5. Employee Details

The average number of full time equivalent persons employed by the Agency during the year was:

	2003/04	2002/03
Senior Management	14	15
Civil Service staff	664	637
Secondees	2	1
Short term contracts	67	57
Total staff	747	710

The Chairman's total remuneration, excluding pension contributions, for the year was £110,250; this includes payment for the role of Chief Executive

from 1 April to 31 December 2003. The Chief Executive from 1 January 2004 is on secondment to the Agency and the salary element of secondment costs were £40,000. Neither the Chairman, Chief Executive nor Agency Board Members have any pension entitlement arising from their service with the MHRA.

The fees of the remaining Board Members were as follows:

Fees	£
Ms Lisa Arnold	0–5,000
Miss Shelley Dolan	0–5,000
Mr Michael Fox	0–5,000
Mr Charles Kernahan	0–5,000
Professor Angus Mackay	0–5,000
Mr Garry Watts	0–5,000

The following members of the Senior Management Teams have exercised their rights not to disclose salary and pension rights; such information is not included in the table above:
Mr R K Alder, Mr C Bray, Mr K M Cornelius, Mr T Crawley, Miss D Hepburn, Dr I Hudson, Dr D Jefferys, Dr S Ludgate, Dr G Munro, Mr S Owen, Dr J M Raine, Mr G Savage, Mr J Watkins, Mrs S Wilkins, Dr L Wood, Mr M Woods.

The emoluments for the year of the members of the Senior Management Teams fell within the following ranges:

Number of Employees

	2003/04	2002/03
£0–£9,999	1	1
£10,000–£19,999	1	–
£20,000–£29,999	1	–
£40,000–£49,999	1	–
£60,000–£69,999	1	3
£70,000–£79,999	1	2
£80,000–£89,999	3	2
£90,000–£99,999	1	3
£100,000–£109,999	2	3
£110,000–£119,999	4	1

During 2003/04 no payment was made to any member of the Management Board in respect of allowances (except to the extent that they were a reimbursement of expenses directly incurred in the performance of his or her duties) or expenses (insofar as these sums were chargeable to UK income tax).

6. Other Operating Costs

	2003/04 £000	2002/03 £000
Consultancy	615	305
Contracted out personnel & payroll services	392	214
Contracted out administration services	664	640
Legal services	877	768
Marketing	145	20
Training	572	516
Travel and subsistence	978	957
Committee costs	425	480
Accommodation	5,848	5,229
Medicines testing & laboratory expenses	751	763
Device evaluation services	3,507	84
Computing	6,497	4,209
Pharmacovigilance database and other costs	347	200
Printing, stationery and distribution	1,323	766
Other administration costs	1,283	2,011
Audit fee	103	104
(Decrease)/increase in debt provision	321	(236)
Charge for permanent impairment in value of fixed assets	221	(160)
Foreign exchange (gain)/loss	(100)	30
Debt write off	50	266
Loss (profit) on disposal	3	(5)
Clinical assessment	18	23
	24,840	**17,184**

a) Costs include irrecoverable Value Added Tax.

b) The budget for Device Evaluation Services was transferred from the Department of Health on 1 April 2003.

c) The audit fee represents the cost for the audit of the financial statements carried out by the Comptroller and Auditor General. This amount does not include fees in respect of non-audit work. No such work was undertaken.

d) Operating surplus is stated after charging the following for operating leases:

	2003/04 £000	2002/03 £000
Rent	3,141	3,137
Catering equipment	29	28
Photocopiers	11	11
IT equipment	1	–
	3,182	3,176

7. Interest Receivable

	2003/04 £000	2002/03 £000
Bank accounts	790	679
	790	679

Funds held in the Paymaster General's Account earn interest at the rate payable on Ways and Means advances.

8. Tangible Fixed Assets

	Totals	Computer & Telecom. Equipment	Computer Systems & Software	Laboratory Equipment	Fittings, Furniture & Office Equipment	Assets under Construction	GPRD Data
	£000	£000	£000	£000	£000	£000	£000
Cost or valuation:							
At 1 April 2003	54,315	4,050	17,670	935	7,188	2,243	22,229
Additions	8,131	690	221	61	8	6,467	684
Disposals	(881)	(508)	(208)	–	(165)	–	–
Revaluation	(8,122)	(408)	(299)	(15)	100	–	(7,500)
Accounting Policy Alignment	(512)	(327)	–	(93)	(92)	–	–
Transfers	–	–	–	–	87	(87)	–
At 31 March 2004	52,931	3,497	17,384	888	7,126	8,623	15,413
Depreciation:							
At 1 April 2003	24,077	2,830	12,913	396	3,747	–	4,191
Disposals	(878)	(505)	(208)	–	(165)	–	–
Revaluation	(458)	(278)	(227)	1	46	–	–
Charge for the year	3,856	420	1,299	157	851	–	1,129
Accounting Policy Alignment	(334)	(181)	–	(88)	(65)	–	–
At 31 March 2004	26,263	2,286	13,777	466	4,414	–	5,320
Net Book Value:							
At 1 April 2003	30,238	1,220	4,757	539	3,441	2,243	18,038
At 31 March 2004	26,668	1,211	3,607	422	2,712	8,623	10,093

1. The GPRD data asset was valued at 31 March 2004 by consultants from the Agency's internal audit contractor Bentley Jennison in May 2004 on the basis of value in use. This has resulted in an impairment of £7.5m which has been charged against the balance held in the revaluation reserve.
2. The above note includes an adjustment to asset values arising from the need to ensure the accounting policies of the merged bodies are aligned.

9. Debtors

	31 March 2004 £000	31 March 2003 £000
Trade debtors	2,866	526
Accrued income	1,556	2,209
Prepayments	238	322
Other debtors	1,482	1,737
	6,142	4,794

Trade debtors are shown net of a provision for irrecoverable debts of £0.864m (31 March 2003 £0.543m) and of a provision for credit notes of £2.116m (31 March 2003 £0.298m).

10. Creditors – Amounts Falling Due Within One Year

	31 March 2004 £000	31 March 2003 £000
Payments received on account	2,127	1,707
Trade creditors	313	42
Other creditors	1,688	6,040
Accrued expenses	6,650	2,726
Taxation and social security	104	44
	10,882	10,559

11. Provision for Liabilities and Charges

	31 March 2004 £000	31 March 2003 £000
Early retirement/Voluntary severance		
Opening position	617	409
Utilised during year	(125)	(170)
Provided in year	128	378
Transfer to DoH	(93)	–
Closing balance	527	617
Other provisions		
Opening position	929	–
Utilised during year	(438)	–
Reversed unused	(20)	–
Provided in year	–	929
Closing balance	471	929
Total provisions	998	1,546

Early Retirement/Voluntary Severance

The provision is to cover the MHRA's estimated liability for pensions, until normal retirement date of employees who, at the year-end, had retired before normal retirement date. We anticipate the utilisation of around £0.1m in 2004/05. £0.09m of the provision has been transferred to the Department of Health to cover the liabilities arising from Devices retirements prior to 1 April 2003.

Other Provisions

A provision has been established for the anticipated costs of asbestos safety work within the Agency's Market Towers head office to be completed in 2004/05.

12. Deferred Revenue

	31 March 2003 £000	Movement £000	31 March 2004 £000
Major fees	10,083	4,601	14,684
Minor fees	1,130	249	1,379
Outgoing mutual recognition	284	86	370
EMEA	767	(767)	–
Subtotal (Note 3)	**12,264**	**4,169**	**16,433**
Miscellaneous	541	(128)	413
Total	**12,805**	**4,041**	**16,846**

The net movement in deferred revenue is £4.041m. Revenue deferred at 31 March represents the value of outstanding applications received prior to that date. The opening balance is shown net of exchange rate movements of £0.094m. There is no deferral for EMEA income at 31 March 2004 as this income is paid in arrears and will therefore be excluded from deferred revenue.

13. Capital and Reserves

		Government Funds		Reserves	
	Total £000	Public Dividend Capital £000	Medium Term Loans £000	Revaluation Reserve £000	Retained Surplus £000
Balance at 1 April 2003	22,738	1,329	1,328	16,181	3,900
Movements 2003/04:					
Further borrowings	3,400	–	3,400	–	–
Revaluation of data assets	(7,500)	–	–	(7,500)	–
Transfer to other operating costs of permanent impairment in value	53	–	–	53	–
Realised depreciation	(1,000)	–	–	(1,000)	–
Retained surplus for year	8,669	–	–	–	8,669
Balance at 31 March 2004	26,360	1,329	4,728	7,734	12,569

The realised depreciation offsets the charge for the year shown in Note 8. The creation of PDC and loans has arisen due to the merger of the Medicines Control Agency with the Medical Devices Agency to form the MHRA on 1 April 2003.

The opening balances shown above are defined in the Trading Fund Order creating MHRA, and they differ from the aggregate closing balances of the predecessor agencies which are shown as comparatives in the balance sheet.

An analysis of the maturity and interest rates of the medium term loans is as follows:

	Total £000	Within three years £000	Between three and four years £000	Between four and six years £000
Fixed interest rate (%):				
4.00	1,000	1,000	–	–
4.15	1,000	–	1,000	–
4.30	1,000	–	–	1,000
4.35	1,728	–	–	1,728
At March 2004	4,728	1,000	1,000	2,728

14. Reconciliation of Surplus to Net Cash Inflow from Operating Activities

	31 March 2004 £000	31 March 2003 £000
Operating surplus/(deficit)	8,324	312
Depreciation	2,856	3,063
Revenue deferred to future periods (note 12)	16,846	12,899
Revenue deferred from past periods (note 12)	(12,899)	(10,157)
Decrease/(increase) in debtors	(1,415)	(38)
(Decrease)/increase in creditors	(961)	(584)
(Decrease)/increase in provisions	(548)	1,307
Other non-cash items	294	(130)
Net cash inflow/(outflow) from operating activities	12,497	(6,672)

15. Reconciliation of Net Cash Flow to Movement in Net Funds

	31 March 2004 £000	31 March 2003 £000
(Decrease)/increase in cash for year	9,546	3,941
Cash released from liquid resources	–	–
Repayment of PDC and loans	–	3,292
New loans granted	3,400	–
Creation of PDC and loans	2,657	–
Movement in net funds	15,603	7,233
Net funds at end of previous year	12,730	5,497
Net funds at end of year	28,333	12,730

16. Analysis of Net Funds as shown in the Reconciliation of Net Cash Flow

	Total £000	Cash at Bank and in hand £000	Public Dividend Capital £000	Medium Term Loans £000
Balance at 1 April 2003	12,730	12,730	–	–
Movements 2003/04:				
Loans	4,728	–	–	4,728
PDC	1,329	–	1,329	–
Increase in cash at bank	9,546	9,546	–	–
Balance at 31 March 2004	28,333	22,276	1,329	4,728

17. Capital Commitments

	31 March 2004 £000	31 March 2003 £000
Contracted	6,220	7,480
Authorised by the Board of Management but not contracted	1,749	790

The above capital commitments represent capital expenditure commitments for the Medicines and Healthcare products Regulatory Agency in 2003/04.

18. Contingent Liabilities

There are no contingent liabilities for the year.

19. Related Party Transactions

As a Trading Fund of the Department of Health, the Department is regarded as a related party within the definition of FRS8. During 2003/04, the MHRA has had a significant number of material transactions with the Department.

In addition, the MHRA has had various material transactions with other Government departments and other central Government bodies. Most of these transactions have been with the Department for Work and Pensions and the Veterinary Medicines Directorate of the Department for Environment, Food and Rural Affairs.

During 2003/04, none of the Board Members, members of the key management staff or other related parties has undertaken any material transactions with the MHRA.

20. Losses and Special Payments

There were no losses or special payments during the year.

21. Financial Commitments

The MHRA has the following financial commitments:

	2004/05 £000	2003/04 £000
Land and buildings		
Leases expiring within 5 years	856	842
Leases which expire after 5 years	2,982	2,299
Other	277	41

22. Financial Instruments

FRS13 – 'Derivatives and Other Financial Instruments' requires disclosure of the role which financial instruments have had during the period in creating or changing the risks an entity faces in undertaking its activities. Because of the nature of its activities, financial instruments play a much more limited role in

creating or changing risk than is typical of the listed companies to which the FRS mainly applies.

The MHRA has very limited powers to borrow or invest surplus funds. Financial assets and liabilities are generated by day-to-day operational activities and are not held to change the risks facing the Agency in undertaking its activities.

As permitted by FRS13, debtors and creditors which mature or become payable within 12 months from the balance sheet date have been omitted from the currency profile.

Fair value is not significantly different from book value.

Liquidity risk

The MHRA's resource and capital expenditure requirements are financed by revenues generated from its activities, with the exception of a loan facility with the Department of Health of £10.0m. This requires the Agency to ensure it has sufficient reserves of cash to enable it to undertake its statutory activities.

The table below provides details of cash balances held at the end of the year and the average rate during the year. Balances held in the Commercial Account are denominated in euros.

Account	2003/04 £000	Interest rate*	2002/03 £000	Interest rate*
Paymaster	22,169	3.1%	12,297	3.2%
Commercial	107	0.25%	433	1.0%
	22,276		12,730	

* The interest rates for both types of account are variable.

Interest rate risk

The MHRA is not exposed to significant interest rate risk; the average total of loans held throughout the year was £4.7m. This resulted in interest payable of £0.199m out of total expenditures in excess of £58m.

Currency risk

The level of currency risk is determined by the level of income generated by activity undertaken on behalf of the EMEA. For 2003/04 this was £2.1m (3.1m euros). This represents 3% of the total gross income for the year. The Agency is potentially exposed to significant falls in the value of this currency, however the risk of this occurring is not significant and is mitigated by the regular transfer of funds to the sterling accounts of the Agency.

Credit risk

The Agency is not exposed to significant credit risk.

23. Post-Balance Sheet Events

As an Executive Agency of the Department of Health, MHRA is classed as an 'arm's-length body'. In October 2003 the Secretary of State for Health announced his intention to review the Department of Health's arm's-length bodies. On 20 May 2004, the Secretary of State for Health outlined the first stage of this review.

There are 42 separate arms length bodies which employ 22,000 staff with a combined budget of £2.5bn. The Secretary of State announced that by 2007/08 there will be a 50% reduction in the number of arm's-length bodies reducing total expenditure by £0.5bn and staff posts by 25%.

The final outcome of the review should be announced before the Parliamentary summer recess. As at the date of signing these financial statements, the implications of the review for the MHRA have not yet been announced.

Medicines and Healthcare products Regulatory Agency Trading Fund

Treasury Minute dated 9 February 2004

1. Section 4(1) of the Government Trading Funds Act 1973 ('the 1973 Act') provides that a trading fund established under that Act shall be under the control and management of the responsible Minister and, in the discharge of his function in relation to the fund, it shall be his duty:

a) to manage the funded operations so that the revenue of the fund:
   i) consists principally of receipts in respect of goods or services provided in the course of the funded operations; and
   ii) is not less than sufficient, taking one year with another, to meet outgoings which are properly chargeable to revenue account; and

b) to achieve such further financial objectives as the Treasury may from time to time, by minute laid before the House of Commons, indicate as having been determined by the responsible Minister (with Treasury concurrence) to be desirable of achievement.

2. A Trading Fund for the Medicines and Healthcare products Regulatory Agency was established on 1 April 2003 under the Medicines and Healthcare Products Regulatory Agency Trading Fund Order 2003 (SI 2003 No. 1076).

3. The Secretary of State for Health, being the responsible Minister for the purposes of section 4(1)(a) of the 1973 Act, has determined (with Treasury concurrence) that a further financial objective desirable of achievement by the Medicines and Healthcare products Regulatory Agency Trading Fund for the five-year period from 1 April 2003 to 31 March 2008 shall be to achieve a return, averaged over the period as a whole, of at least 3.5% in the form of a surplus on ordinary activities before interest (payable and receivable) and dividends expressed as a percentage of average capital employed. Capital employed shall equate to the total assets from which shall be deducted the total liabilities with the exception of the long-term element of the voted loans. However, in determining the value of the total assets, the following proportion of the value of the General Practice Research Database may be disregarded:

2003/04:	100%
2004/05	75%
2005/06	50%
2006/07	25%
2007/08	0%

4. Let a copy of this Minute be laid before the House of Commons pursuant to section 4(1)(b) of the Government Trading Funds Act 1973.

Above: Sam Delahay, John Watkins, Debbie Sargeant and Ade Orhiere

Annex 1: Performance against targets 2003/04

1. Safety

High-level target		Standard achieved
1.1	Assess the quality of professional decision-making by checking the concordance of outcomes arising from review by the appropriate Advisory Committee with recommendations made by the Agency	Achieved. 39 products considered, 95% concordance
1.2	Ensure that all serious and fatal spontaneous adverse drug reactions received through the Yellow Card Scheme are captured and rapidly made available for the detection and analysis of possible drug safety hazards	
Fatal:	100% within three working days 90% within one working day	Achieved (100%) Exceeded (100%)
Serious:	100% within seven working days 95% within three working days	Achieved (100%) Exceeded (100%)
1.3	Issue Device Alerts soon after identifying that they are needed	Achieved. 100% immediate action issued within 20 days, 94% other categories issued within 60 days
1.4	Ensure that medicines and medical devices meet the appropriate regulatory requirements	Achieved. Average time between inspections of medicines' manufacturing sites no more than 24 months; all active UK Notified Bodies for medical devices audited at least annually

2. Standards of service

High-level target		Performance standard
2.1	Deliver efficient and effective services to users	Achieved. Satisfaction surveys of the Agency's users are being used to set a baseline for future improvements
2.2	Ensure that timely and effective briefing and advice is provided to Ministers on regulatory, policy and parliamentary matters, working in conjunction with the relevant parts of the Department of Health	83% answered within 20 working days

3. Agency development

High-level target		Performance standard
3.1	Progress the merger of the MCA and MDA by establishing a single corporate culture focused on the strategic aims and objectives of the MHRA	Achieved. We published statements on our strategic aims, mission, vision and values, and achieved IiP accreditation
3.2	Meet the Agency's financial commitments	Achieved
3.3	Prepare a plan for accommodating all London-based staff at a single site	Achieved
3.4	Continue implementation of the Sentinel programme and undertake a strategic review of the information management operating environment	Achieved

4. Adding value

High-level target		Performance standard
4.1	Establish and promote the agreed aims, values and brand of the Agency	Achieved. Communication strategy for the Agency delivered
4.2	Develop further guidance and education strategies to promote the safe and effective use of medicines and medical devices with healthcare professionals	Achieved. We helped to educate healthcare professionals in the safe use of medicines and medical devices

Annex 2: Glossary

ADR	Adverse Drug Reaction
BANs	British Approved Names
BOA	British Orthopaedic Association
BP	*British Pharmacopoeia*
CSM	Committee on Safety of Medicines
CDRH	Centre for Devices and Radiological Health
CEP	Central Enquiry Point
CPMP	Committee on Proprietary Medicinal Products
DMRC	Defective Medicines Reporting Centre
EMEA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration (US)
FOI	Freedom of Information
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GLPMA	Good Laboratory Practice Monitoring Authority
GMP	Good Manufacturing Practice
GPRD	General Practice Research Database
GPvP	Good Pharmacovigilance Practice
ICH	International Conference on Harmonisation
IVDs	In Vitro Diagnostic medical devices
MAIL	Medicines Act Information Letter
MCA	Medicines Control Agency
MDA	Medical Device Agency
MDA	Medical Device Alert
MHRA	Medicines and Healthcare products Regulatory Agency
MORE	Manufacturers' On-line Reporting Environment
MRI	Magnetic Resonance Imaging
NAO	National Audit Office
NBOG	Notified Body Operations Group
NHS	National Health Service
OST	Office of Science and Technology
Pharmacovigilance	Post-marketing surveillance of medicines
rINNs	recommended International Non-Proprietary Names
SABS	Safety Alert Broadcast System
SSRIs	Selective Serotonin Reuptake Inhibitors

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