Medicines and Healthcare products Regulatory Agency

Annual Report and Accounts

2004/05

"2004/05 has been a challenging year for the MHRA. The Agency is young, and although we have achieved a huge amount, there is still a great deal to do."

Professor Sir Alasdair Breckenridge

Medicines and Healthcare products Regulatory Agency

Annual Report and Accounts

2004/05

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 2005 together with the Report of the Comptroller and Auditor General thereon

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Contents

Agency Board

From left to right: Lisa Arnold, Sir Alasdair Breckenridge, Michael Fox, Angus Mackay, Garry Watts, Damien Bishop, Charles Kernahan, Shelly Dolan, Simon Rogers and Kent Woods

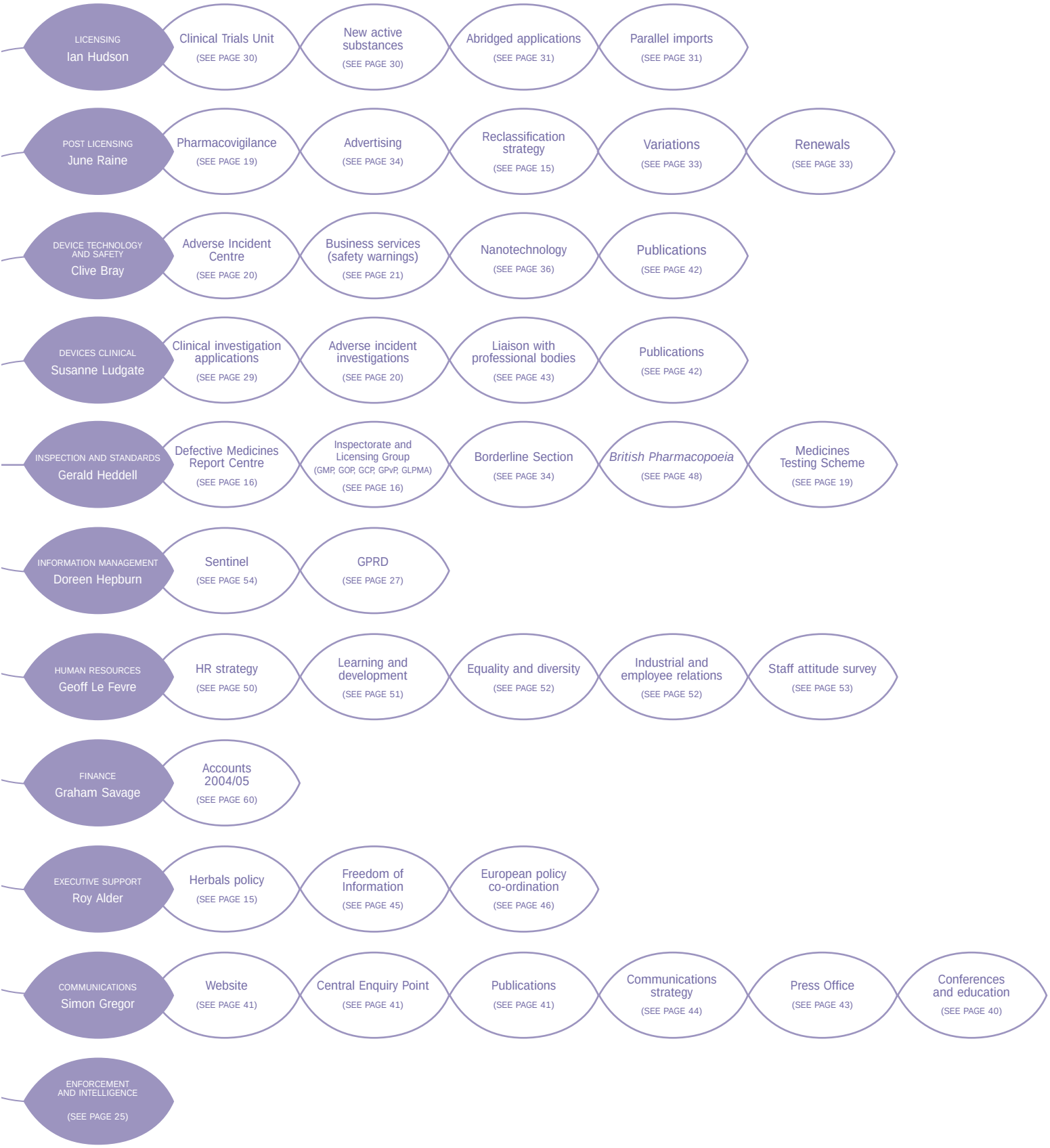
CHAIRMAN
Professor Sir Alasdair Breckenridge

CHIEF EXECUTIVE
Professor Kent Woods

Executive Board

From left to right, clockwise: Simon Rogers, Gerald Heddell, Susanne Ludgate, Roy Alder, Ian Hudson, Clive Bray, Kent Woods, Louise Loughlin, Doreen Hepburn, Geoff Le Fevre, Simon Gregor, Graham Savage and June Raine

Organogram


LICENSING
Ian Hudson
Clinical Trials Unit
(SEE PAGE 30)
New active substances
(SEE PAGE 30)
Abridged applications
(SEE PAGE 31)
Parallel imports
(SEE PAGE 31)
POST LICENSING
June Raine
Pharmacovigilance
(SEE PAGE 19)
Advertising
(SEE PAGE 34)
Reclassification strategy
(SEE PAGE 15)
Variations
(SEE PAGE 33)
Renewals
(SEE PAGE 33)
DEVICE TECHNOLOGY AND SAFETY
Clive Bray
Adverse Incident Centre
(SEE PAGE 20)
Business services (safety warnings)
(SEE PAGE 21)
Nanotechnology
(SEE PAGE 36)
Publications
(SEE PAGE 42)
DEVICES CLINICAL
Susanne Ludgate
Clinical investigation applications
(SEE PAGE 29)
Adverse incident investigations
(SEE PAGE 20)
Liaison with professional bodies
(SEE PAGE 43)
Publications
(SEE PAGE 42)
INSPECTION AND STANDARDS
Gerald Heddell
Defective Medicines Report Centre
(SEE PAGE 16)
Inspectorate and Licensing Group
(GMP, GOP, GCP, GPvP, GLPMA)
(SEE PAGE 16)
Borderline Section
(SEE PAGE 34)
British Pharmacopoeia
(SEE PAGE 48)
Medicines Testing Scheme
(SEE PAGE 19)
INFORMATION MANAGEMENT
Doreen Hepburn
Sentinel
(SEE PAGE 54)
GPRD
(SEE PAGE 27)
HUMAN RESOURCES
Geoff Le Fevre
HR strategy
(SEE PAGE 50)
Learning and development
(SEE PAGE 51)
Equality and diversity
(SEE PAGE 52)
Industrial and employee relations
(SEE PAGE 52)
Staff attitude survey
(SEE PAGE 53)
FINANCE
Graham Savage
Accounts 2004/05
(SEE PAGE 60)
EXECUTIVE SUPPORT
Roy Alder
Herbals policy
(SEE PAGE 15)
Freedom of Information
(SEE PAGE 45)
European policy co-ordination
(SEE PAGE 46)
COMMUNICATIONS
Simon Gregor
Website
(SEE PAGE 41)
Central Enquiry Point
(SEE PAGE 41)
Publications
(SEE PAGE 41)
Communications strategy
(SEE PAGE 44)
Press Office
(SEE PAGE 43)
Conferences and education
(SEE PAGE 40)
ENFORCEMENT AND INTELLIGENCE
(SEE PAGE 25)

Chief Executive Officer's report

My foreword in last year's Annual Report described how the two themes of continuity and change underpinned the first year of the Agency's operations. I also looked forward to a period of further change and consolidation. This report tells the story of last year.

Making an effective contribution to public health

Some things do not change: the Agency's overriding duty is to safeguard public health through the effective regulation of medicines and devices. Last year saw a number of significant safety issues, three of which deserve particular mention.

The publication reviewing the safety and efficacy of selective serotonin reuptake inhibitors (SSRIs) in December 2004 marked the completion of some 18 months' work by an expert working group of the Committee on the Safety of Medicines (CSM). A second area of concern during the year was the emerging evidence of cardiovascular side effects in patients using anti-inflammatory drugs of the COX-2 inhibitor class. Following the withdrawal of Vioxx, a widely used COX-2 inhibitor, the entire class is now the subject of a review at European level. The third issue related to the manufacturing quality of the influenza vaccine Fluvirin. Immediate suspension of the manufacturing licence caused supply problems for vaccination programmes in the United States in particular but was a necessary regulatory action to protect public health. Agency staff have supported the manufacturing company in carrying out remedial work and the suspension has now been lifted. Although these three headline-making topics have all been related to medicines, there have also been challenging public health issues relating to medical devices. For example, Heaf testing devices used for tuberculosis screening have been the subject of several Medical Device Alerts.

Supporting scientific innovation

Public health is promoted by the Agency's role in supporting scientific innovation. Patients in the UK require the quickest access to effective new medicines and devices consistent with safety. An efficient and effective service to industry (in terms of scientific advice, support during product development and the speed with which licences are issued) is important. The first major review of the scientific advisory committees for medicines, and forthcoming reforms, will also contribute to this aim.

The publication of the report of the Healthcare Industries Task Force (HITF) in November 2004 demonstrated the Government's commitment to the device sector. The Agency contributed substantially to the report and will be responsible for implementing a number of its recommendations. Among other things, the report recommended transferring the Device Evaluation Service from the Medicines and Healthcare products Regulatory Agency (MHRA) to the NHS Purchasing and Supply Agency (PASA), with increased funding. This will expand the scope of a widely respected service which makes a valuable contribution to the NHS.

> The MHRA helped write the Healthcare Industries Task Force report and will be responsible for **implementing** some of its recommendations.

Providing authoritative information

The year marked a change in the way the MHRA handles the information it holds on medicines and devices. The Agency published the clinical and scientific data on which it based its judgements, for example on hormone replacement therapy (HRT) and SSRIs, together with the safety advice. The early introduction of European Union (EU) legislation requiring user testing of Patient Information Leaflets, ahead of other legislative changes due in late 2005, will lead to an increase in the quality of these important documents.

Perhaps the largest change is the introduction of better ways in which the Agency communicates both internally and externally. A wide consultation with stakeholder groups preceded the development of a communications strategy and the setting up of a separate Communications Division within the MHRA. This has resulted in the transfer of media relations responsibility from the Department of Health (DH) to the Agency in March 2005. A major project to redevelop the website has also started.

Influencing European and international regulation

The Agency has continued to play a major role in European and international affairs. It has ensured that the 2001 Review of medicines legislation is implemented on time, and taken an active part in negotiations on the regulation of paediatric medicines. The Agency has also helped influence the initial work in the review of the medical device directives and regulation on tissue engineering.

Legislation aside, the Agency has also encouraged an enhanced surveillance of notified bodies in Europe, contributed substantially to the European licensing system and been active in the development of a European risk management strategy for medicines.

The Agency has good relations with other regulators, particularly the United States Food and Drug Administration (FDA), where co-operative links on medicine and device safety issues are becoming increasingly important.

Operating as a successful business

Setting up the Executive Board on 1 April 2004 created an integrated management team under the leadership of the Chief Executive. Over the past year, the Board has helped to foster a single Agency view on key issues.

After a period of some uncertainty in the first year of the Agency's life, a MORI survey was commissioned to explore the views and priorities of staff. It confirmed that staff were proud to work for an organisation committed to the protection of public health but wanted strong leadership in a time of change. Work is now in hand to help address these issues. The information management strategy has moved on quickly, with yet more to come. The Agency continues to meet its financial objectives, an important prerequisite for the developments described here.

Staff contribution

None of the Agency's achievements would have been possible without an outstanding contribution from its staff. I would like to thank them and look forward to working together with them over the coming year.

Professor Kent Woods
Chief Executive

A MORI survey confirmed that staff were proud to work for an organisation committed to the **protection** of public health.

Chairman's foreword

Sir Alasdair Breckenridge

Nothing that we have achieved, and no **challenges** yet to come, are possible without our staff who work under **enormous pressure** and deliver **excellent results**.

The past year has been a challenging one for the MHRA. With the publication of our report and recommendations on SSRIs, we have concluded the largest ever independent expert review of a class of drugs, and have set a new standard in international drug regulation by publishing the evidence on which our recommendations were made. We have opened up the data in our adverse incident reporting scheme so that anyone can now view the information we hold, on the Internet, and we have piloted a scheme to allow patients and carers to report suspected adverse reactions for the first time. We have set up the Agency's Communications Division to help us interact much more proactively with all our stakeholders and in particular with patients and the public. And there are many more examples I could give of the challenges we have faced over the past year; the fact that the Agency has risen to them is no mean achievement for an organisation that we sometimes forget is just two years old.

The pace we have set ourselves will not relent in 2005/06. The Health Select Committee has now published its report on the influence of the pharmaceutical industry[1] and, at the time of writing, the Government is preparing its response. The report flagged up many areas where the Agency is already focusing its attention – the need to open up decision-making processes which in the past have appeared opaque; the importance of a greater dialogue with the public and with patients; and the development of greater openness and transparency in general around the work of the Agency. We are already engaged in work on these, which is reflected in this report, but we have heard and will act upon the Committee's call to do more, and not let the pace of change slide.

The coming year will be one in which we start to realise more fully the benefits of merging the medicines and devices sides of the business. The fact that medicines and devices staff are now located in the same building will allow us to exploit the opportunities for joined-up working which the merger was designed to achieve. In new and developing areas, such as the regulation of nanotechnology or of blood and blood products, the ability to work across these traditional boundaries will be vital.

Our advisory committee structure will also change over the coming year. There have been significant changes in the membership of the Committee on Safety of Devices (CSD), a relatively new committee that has already made major contributions to the regulation of medical devices. The medicines regulation committees are also undergoing significant reform: not only will these changes create an even more rigorous approach to the management of interests, but they will also open up our decision-making processes much more by increasing lay representation. With the Health Select Committee report very much in the forefront of our minds, we see this as the beginning rather than the end of a process, but it is a significant first step nonetheless.

In a short, introductory letter, I can hope to touch on only a few of the achievements of the last year, and highlight a handful of challenges for the next. The Agency is still young and, although we have achieved a huge amount, there is a great deal still to do. Nothing that we have achieved, and no challenges yet to come, are possible without our staff who work under enormous pressure and deliver excellent results. I would like to conclude by thanking them for the vital role they have played for delivering on the work set out in this report.

Professor Sir Alasdair Breckenridge
Chairman

About the MHRA

Executive Board from left to right, clockwise: Simon Rogers, Gerald Heddell, Susanne Ludgate, Roy Alder, Ian Hudson, Clive Bray, Kent Woods, Louise Loughlin, Doreen Hepburn, Geoff Le Fevre, Simon Gregor, Graham Savage and June Raine

Mission

The MHRA's mission is to enhance and safeguard the public's health by ensuring that medicines and medical devices meet the required standards of safety and effectiveness in use.

Values

In pursuing its mission, the Agency will strive to act with:

- integrity;
- openness;
- courtesy;
- responsiveness;
- timeliness;
- professionalism;
- impartiality; and
- consistency.

Aims

MHRA aims to safeguard public health by:

- ensuring, through regulation, that medicines and devices have an acceptable balance of risks and benefits;
- helping people understand the benefits and risks of medicines and devices; and
- encouraging and facilitating the development of medicines and devices that will benefit all.

Objectives

The Agency's key objectives are to:

- maintain rigorous authorisation and inspection programmes;
- maintain and develop proactive surveillance and enforcement programmes;

- communicate authoritative and reliable information and advice to improve public and professional awareness;
- engage with and influence other government bodies and European and worldwide regulators concerned with medicines or medical devices;
- support innovation and product development, offering constructive and impartial advice to scientific communities and health services;
- minimise the cost of regulation so far as is compatible with our public health role; and
- run a successful business with a skilled and equipped workforce dedicated to the Agency's aims.

Activities

The Agency's main activities are:

- assessing the safety, quality, efficacy, and the authorisation of medicines sold or supplied in the UK for human use;
- overseeing the UK notified bodies which audit medical 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 proactive compliance programme for medical devices;
- 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 medical devices through inspection, taking enforcement action where necessary;
- promoting good practice in the safe use of medicines and medical devices;
- managing the General Practice Research Database (GPRD) and the *British Pharmacopoeia* (BP) and contributing to the development of performance standards for medical devices;
- offering scientific, technical and regulatory advice on medicines and medical devices; and
- providing the public and professions with authoritative information to enable informed dialogue on treatment choices.

Corporate governance

The MHRA has an Agency Board, an Executive Board and a Risk and Audit Committee. Together these three entities oversee the Agency's corporate governance and risk management systems to ensure that the highest standards of integrity, accountability and operational capability are maintained.

- The Agency Board consists of a Chairman, six non-executive members and the Chief Executive Officer of the Agency. The Agency Board meets monthly to discuss the Agency's plans and strategic direction and to take action as appropriate.

- The Executive Board comprises the Chief Executive Officer and the Heads of Divisions. This group convenes monthly and takes executive responsibility for the strategy, operational management and service delivery of the Agency, including risk management. As the Accounting Officer, the Chief Executive Officer also has responsibility for the Agency's resources.

- The Risk and Audit Committee reports independently to the Accounting Officer and the Agency Board on the effectiveness of the operation of the Agency's corporate governance and risk management systems. The Committee is chaired by a non-executive Agency Board member, and is supported by the Agency's Risk Management Team.

Highlights and successes

From left to right: Daren Jones, Brian Pocknall, Graham Savage, Mary Forskitt, Caroline Lloyd, Richard Humphreys, Finance

Public health

- launched patient reporting of suspected adverse drug reactions (ADRs) through the Yellow Card scheme
- completed detailed review of the safety of SSRIs and related antidepressants in adults and children
- increased number of appropriately labelled and formulated medicines for children
- took action to ensure the quality standards of influenza vaccine were maintained
- reclassified Simvastatin 10mg (Zocor Heart-Pro) from a prescription only medicine (POM) to a pharmacy medicine (P)
- reached agreement with Europe on reclassification of some total joint replacements
- issued 64 Medical Device Alerts (MDAs) and received 8,490 adverse incident reports
- created a new system to review transmissible spongiform encephalopathy (TSE) information supplied by notified bodies on medical devices
- withdrew co-proxamol from UK market

Working for Ministers

- continued work on the registration scheme to be launched in October 2005 for traditional herbal medicinal products

- extended the prescribing of POMs
- extended supplementary prescribing to podiatrists, physiotherapists and radiographers
- prepared regulations setting up a new advisory committee – Commission on Human Medicines
- provided evidence and information to the Health Select Committees on the pharmaceutical industry and new technologies in the NHS

Communications

- completed external review of communications with presentation of report to Agency Board
- started preparations on establishing Communications Division ready for April 2005
- launched in-house media relations function in March
- developed proposals to improve risk communication in patient information leaflets and user testing guidance

Industry

- launched Export Certificates system on Agency IT system, Sentinel
- published HITF report, aimed at stimulating innovation in medical device manufacture in the UK
- received record number of variations (25,000) and processed to tight European targets
- assessed nine new medicines in average of 37 days, compared to previous average of 40 days
- worked to ensure that the first elements of the new integrated IT system, Sentinel, became operational

Quality

- created cross-Agency Inspection Action Group to review Good Clinical Practice (GCP) and Good Pharmacovigilance Practice (GPvP) inspections
- relocated BP Laboratory to Laboratory of the Government Chemist
- ensured that the Wheeled Mobility and Seating Centre received its continued accreditation
- evaluated almost 500 device products in 81 various reports
- completed Breast Implant Registry research project

Staff

- developed Human Resources (HR) and Learning Strategy
- harmonised staff employment terms and conditions plus HR policy and procedure
- developed training plan and delivered comprehensive programme of training
- rolled out new upgraded PCs and desktop IT equipment to over 600 staff

Making an effective contribution to public health

There was a 22% drop in suicidal deaths from paracetamol and salicylates in the year after the reduction in pack size.

The MHRA's positive impact on public health: reducing morbidity and mortality from paracetamol overdose

Legislation was introduced in September 1998 to limit the size of packs of paracetamol with the aim of reducing morbidity and mortality associated with paracetamol overdose. The unrestricted sale limit for pharmacies was reduced to a maximum of 32 tablets, and for other retail outlets from 24 to 16 tablets. Pack sizes of aspirin were also reduced. The main objective was to reduce household stocks and ease of access for impulsive overdosing.

A number of papers have appeared on the impact of this legislation on mortality, hospital admission and related liver transplants for paracetamol. The most recent (2004) and comprehensive publication from Oxford[2] reported a 22% reduction in England and

Above, from left to right: Sue Harris, Elaine Godfrey, Siu Ping Lam, Maureen Riach, Linda Anderson, Herbal Policy

Wales in suicidal deaths from paracetamol and salicylates in the year after the change in legislation, and a reduction over the next two years. Liver unit admissions and liver transplants for paracetamol-induced liver toxicity in England and Scotland were reduced by about 30% in the few years after 1998. The total number of fatal overdoses was also reduced. These results are very encouraging and will be followed up by the Oxford unit.

Rigorous authorisation and inspection

Regulation of herbal medicines

The Agency has worked towards improving public health protection for patients using unlicensed herbal medicines. Until now, these products have not been required to meet specific standards of safety or quality, nor to be accompanied by the necessary information for their safe use.

The Directive on Traditional Herbal Medicinal Products

Following the successful completion of negotiations on the European Directive on Traditional Herbal Medicinal Products, the Agency planned for the launch of a registration scheme in October 2005. The scheme covers manufactured, traditional herbal remedies which will need to meet set standards of safety and quality and be accompanied by systematic patient information. Minor claims will be permitted based on evidence of traditional use. The Agency has undertaken an extensive programme of work to help the herbal sector prepare for this, including practical workshops, training and meetings with individual companies.

Herbal practitioners

A consultation exercise was run outlining proposals for the reform of the regulation of unlicensed herbal remedies made up by, or for, practitioners to meet the needs of individual patients. The Agency has worked closely with the Department of Health (DH) as related proposals for the statutory regulation of the herbal medicine profession have progressed. Further consultation is planned later in the year.

Extending the prescribing, sale, supply and administration of medicines

There were a number of changes to medicine legislation last year to extend responsibilities for the prescribing, sale, supply and administration of medicines.

These included:

- extending the range of POMs prescribable by Nurse Prescriber's Extended Formulary;
- extending supplementary prescribing to podiatrists, physiotherapists and radiographers;
- updating the range of medicines that can be sold, supplied or administered by registered ophthalmic opticians; and
- introducing the use of electronic signatures on prescriptions.

In addition, other changes enabled specified prison staff to supply single doses of General Sales List (GSL) medicines to prisoners during periods when qualified healthcare staff are not available.

Further changes are being considered. For example, optometrists will become supplementary prescribers. Also, the Agency and DH have issued public consultations seeking views on the future of the Nurse Prescribers' Extended Formulary and on the introduction of independent prescribing by pharmacists. The outcome of those consultations will be considered later in 2005 by the CSM, who will help Ministers in the usual way on further changes to medicines legislation.

POM to P switching

The Agency consults widely and takes into consideration all points of view before undertaking changes in the legal classification of medicines. Safety and the potential for public health benefit are always the primary concerns. There were 29 POM to P and P to GSL switches approved during the year. The most important POM to P switch was simvastatin 10mg for persons at risk of coronary heart disease. This set new standards for applications and pharmacy

protocols. Other key POM to P switches included omeprazole 10mg for relief of reflux. The Agency also consulted on the POM to P switch of chloramphenicol 0.5% eye drops for acute bacterial conjunctivitis. To encourage companies to apply for significant switches, the Agency prepared guidance on the regulations governing exclusivity and held regular meetings with key stakeholders to discuss strategy on potential switches.

Defective Medicines Report Centre (DMRC) and unlicensed imports

The unit provides 24-hour coverage, including weekends and public holidays, for dealing with reports of potentially defective medicines and, when necessary, provides support for product recalls by marketing authorisation (MA) holders.

During the last year, the Agency received reports of approximately 340 potential product defects and issued 15 drug alerts involving product recalls. Of these, two were particularly unusual as they involved the first recalls in about ten years of counterfeit products that had entered the legitimate UK supply chain. The products affected were Cialis 20mg tablets (Lilly ICOS) and Reductil 15mg capsules (Abbott). Close liaison between Agency Inspectorate, Medicines Testing Scheme, Intelligence, Enforcement and DMRC was effective in the handling of these incidents.

The DMRC is also responsible for running the Import Notification System for importation of medicines unlicensed in the UK. During the last year, it received and processed about 124,000 such notifications.

Inspection and standards

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 461 scheduled inspections in the UK, the inspectors undertook regular re-inspections, unannounced inspections and 65 overseas inspections, of which seven were for the European Medicines Agency (EMEA).

GMP inspectors carried out 461 inspections in the UK and 65 overseas.

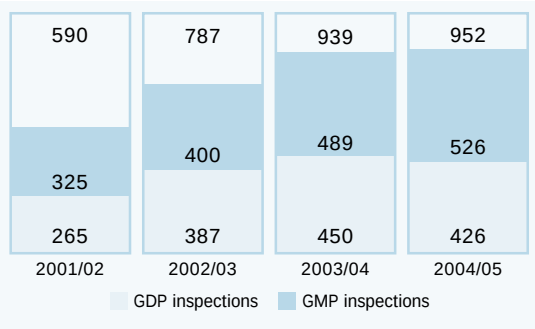
From left to right: Ian Holloway, Sarah Lee, Graham Matthews, Defective Medicines Report Centre

The scope of the work of the GMP Inspectorate continues to widen. The Agency undertook inspections of manufacturers and importers of investigational medicinal products (IMPs) implementation following the Clinical Trials Directive. The Agency also undertook voluntary inspections of active pharmaceutical ingredient (API) manufacturers, and inspections of tissue banks under the DH Code of Practice for Human Tissues, in readiness for Directive 2004/23/EC, coming into force in April 2006.

The GMP Inspectorate provided input into the Blood Directive, for which the Agency is now the Competent Authority, the implementation of Directive 2004/27/EC, and the forthcoming draft directive on tissue-engineered products. The Agency has also run a number of presentations and symposiums on APIs, herbals and stem cells.

Good Distribution Practice (GDP)

GDP inspectors performed 426 inspections to ensure the continued compliance of existing licence holders and to assess new licence applications and variations. Inspectors also carried out monitoring inspections to check the satisfactory implementation of corrective actions following the identification of deficiencies.



The Agency also undertook a number of joint inspections with other European inspectorates with the aim of harmonising inspection standards within the EU.

Did you know?

The MHRA has been busy. Last year, we issued 64 MDAs and received 8,490 device adverse incident reports. We received 20,410 spontaneous UK ADR reports. We have assessed nine new medicines in an average of 37 days and evaluated nearly 500 device products.

Good Clinical Practice (GCP)

A statutory inspection programme for GCP inspections was introduced in May 2004. During this first year, the Agency carried out 39 routine statutory inspections; an additional four were triggered in response to 'whistle blowers'.

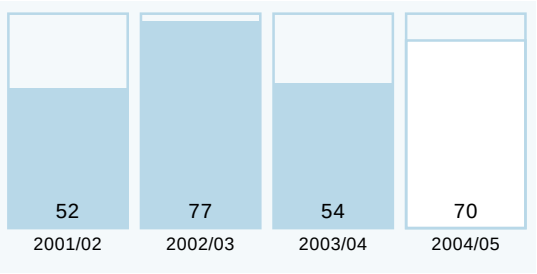
Good Pharmacovigilance Practice (GPvP)

Pharmacovigilance inspectors undertook 25 statutory inspections. One of these was at the request of the CHMP and several inspections were for a monitoring programme for a specialist medicinal product.

GPvP inspectors undertook 25 statutory inspections – one at the request of the CHMP.

This new team also gained ISO accreditation in September.

Good Laboratory Practice Monitoring Authority (GLPMA)



The GLPMA undertook 70 routine facility inspections, including seven interim inspections of very large test facilities. Eight facilities applied for membership of the programme, all of which were accepted following implementation inspections, and seven facilities left the compliance programme. The Agency undertook a number of post-inspection surveillance visits plus visits to assess the impact of major organisational changes.

The GLPMA also participated in two EU working groups set up to provide guidance on archiving and cross-contamination respectively.

Quality Management System

The Inspection and Standards Division and the Enforcement and Intelligence Group continued to maintain their certification to the international standard ISO 9001. The scope of certification was extended during the year to include the Pharmacovigilance Inspectorate, the Import Notification Section and the Intelligence Unit.

Manufacturer's and wholesale dealer's licences plus export certificates

Licence certificates issued	2001/02	2002/03	2003/04	2004/05
Manufacturer's licences issued	44	36	36	176
Wholesale dealer's licences issued	138	156	196	161
Manufacturer's licence variations issued	320	396	337	412
Wholesaler dealer's licence variations issued	388	439	436	487
Export certificates issued	10,186	8,613	7,963	7,129

The number of manufacturer's licences issued is high due to the introduction of IMP licences.

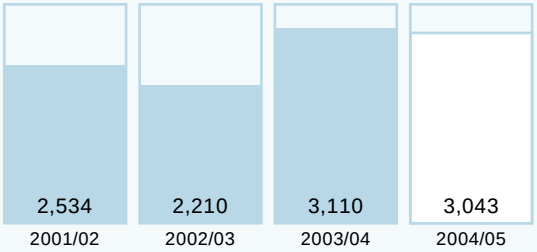
Notification of unlicensed imports

	2002/03	2003/04	2004/05
Number of notifications received	94,974	123,505	124,000
Number assessed as a clinical emergency	708	441	278
Number of objections to importation	2,842	1,308	1,900

The number of notifications of intention to import unlicensed medicinal products under SI 1999/4 was about 124,000. The number of objections to importation was 1,900 and the number of importations in respect of clinical emergencies was 278.

Medicines Testing Scheme

Source of samples	2001/02	2002/03	2003/04	2004/05
Defect samples	15	19	24	44
Medicines Inspectorate samples	41	20	9	26
Enforcement samples	226	371	463	544
Pre-approval (internal MHRA)	11	4	34	75
Market surveillance studies	2,231	1,774	2,505	2,273
EMEA centrally authorised products	10	22	23	17
Other (includes public, NHS and European collaboration)	-	-	52	64



This year saw a substantial increase in the numbers of samples analysed on demand for inspection, licensing assessments and particularly enforcement samples; overall, the total numbers of samples was on a par with two years ago.

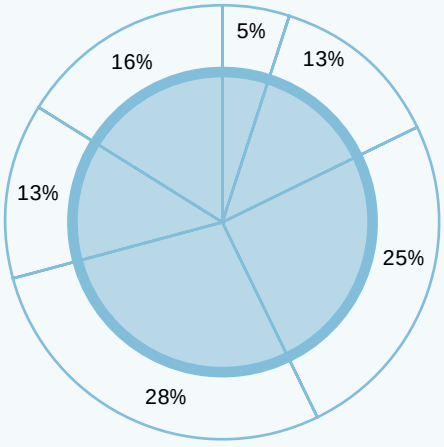
Proactive surveillance and enforcement

Pharmacovigilance

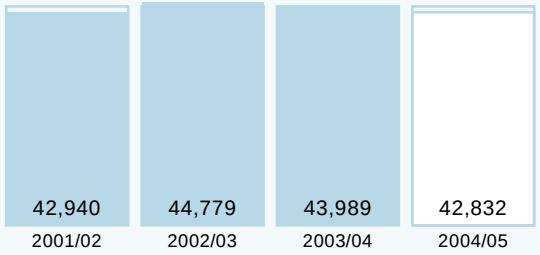
Reporting source of ADRs
in the UK received in 2004/05

Community pharmacists	5%
Hospital pharmacists	13%
Hospital doctors	25%
General practitioners	28%
Nurses	13%
Others*	16%

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



Non-UK reports of suspected ADRs



Spontaneous UK ADR reports

	Total reports	Fatal	Serious reactions
2004/05	20,410	5%	58%
2003/04	19,552	4%	53%
2002/03	18,409	4%	31%
2001/02	19,011	3%	16%

This year saw a 4% increase in Yellow Card reporting from health professionals. This rise was largely due to an increased number of electronic reports received through the new website at www.yellowcard.gov.uk

Devices

Adverse incident reports, numbers received, sources and outcomes

	2001/02	2002/03	2003/04	2004/05
Incidents reported	8,180	8,735	9,037	8,490
Number investigated	1,664 (20%)	1,663 (19%)	2,071 (23%)	1,868
Source of incident	%	%	%	%
Manufacturers	20.9	24.0	29.6	28.9
NHS	58.2	58.6	49.5	51.7
Non-government organisations	2.8	2.8	3.8	2.9
Other government departments	11.7	9.8	10.2	8.6
Overseas reporting organisation	4.9	3.5	5.4	6.6
Private healthcare	1.5	1.3	1.5	1.3
Outcomes*	%	%	%	%
No further action yet - trend only	47.5	50.5	56.1	59.1
Single faulty device	18.7	18.9	19.9	16.5
Design change of device, label or packaging	14.4	10.9	9.2	8.2
Manufacturer changed/improved QA	14.3	11.7	8.4	7.0
Device recall and field correction	8.4	8.0	7.9	9.1
Improved maintenance	1.5	1.5	1.1	1.3
Additional user training/publicity	5.7	5.5	5.2	5.4
Safety warning/manufacturer notice or letter	4.3	2.9	3.4	3.7
Production ceased	0.9	0.4	0.7	1.0

*Outcome totals exceed 100% as some incidents fall into more than one category.

Safety warning notices issued

Notices published	2001/02	2002/03	2003/04	2004/05
Device Alerts	8	10	-	-
Hazard Notices	7	8	-	-
Safety Notices	38	23	-	-
Pacemaker Technical Notes	-	1	-	-
Medical Device Alerts - Action	-	6	25	30
Medical Device Alerts - Immediate action	-	-	18	21
Medical Device Alerts - Action/Information	-	-	3	3
Medical Device Alerts - Immediate action/Information	-	1	1	1
Medical Device Alerts - Action/Update	-	-	2	6
Medical Device Alerts - Information	-	-	1	3
Medical Device Alerts - Update	-	-	2	1

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

Summary of key safety issues

Medicines

Withdrawal of co-proxamol

There was growing concern, prompted by recently published UK research,[3] showing that co-proxamol alone was implicated in almost one-fifth of drug-related suicides, and was second only to tricyclic antidepressants as an agent of fatal drug overdose. In April 2004, the MHRA and CSM re-evaluated the risk:benefit of co-proxamol products in the light of the new data on overdose, the National Suicide Prevention Strategy and concerns in other EU Member States on the dangers of co-proxamol. The Agency also held a public consultation, looking for evidence on the risks and benefits of co-proxamol, which included organisations representing healthcare professionals, patient groups and other stakeholders. A CSM Working Group on pain management gave guidance on various treatment strategies for different patient groups. The CSM, after considering all the available evidence on co-proxamol, concluded that co-proxamol should be withdrawn from the market on the grounds that the benefits did not outweigh the risks. The Agency accepted this advice and made a public announcement on 31 January 2005. This message, together with the CSM's overview of alternative analgesic options, was communicated though the Chief Medical Officer's Public Health Link to all healthcare professionals.

COX-2 inhibitors – cardiovascular safety

The Agency led a Europe-wide review of the safety of COX-2 inhibitors following the withdrawal of rofecoxib (Vioxx) in September 2004 because new clinical trial data showed an increased risk of heart attack and stroke. COX-2 inhibitors are used in the treatment of pain and inflammation. Concern was increased by a clinical trial involving celecoxib (Celebrex), which showed an increased risk of heart attack, stroke and death relative to placebo. The Agency issued interim precautionary advice to healthcare professionals in December 2004 that patients with established heart disease should be switched from COX-2s to alternative treatments. This advice was updated in February 2005 following the Europe-wide review of the available data. The Agency provided information for health professionals and patients through the Public Health Link and on its website.

Depo-Provera contraceptive injection and bone mineral density

The Agency provided updated prescribing advice for medroxyprogesterone acetate (Depo-Provera) following review of several new studies, including studies in adolescents, which provided further information on its known effect in reducing bone mineral density. The Agency communicated the advice of the CSM that Depo-Provera should only be used in adolescents, or those with risk factors for osteoporosis, if alternative contraceptive measures were considered unacceptable, and that there should be careful re-evaluation of the risks and benefits of treatment for all women after two years of use. The advice was communicated to healthcare professionals through the Public Health Link and information was provided on the website for patients.

Yasmin (ethinylestradiol with drospirenone) and venous thromboembolism (VTE)

The Agency issued advice on the risk of VTE in association with the oral contraceptive Yasmin (ethinylestradiol with drospirenone). Preliminary data from a UK Prescription Event Monitoring study suggested that there might be an unexpectedly high rate of VTE associated with Yasmin. Interim data from a large comparative study in a number of countries suggested that the rate of VTE with Yasmin is of the same order of magnitude as that for other oral contraceptives.[4] The Agency updated the product information for Yasmin to reflect this new information and published an article in *Current Problems in Pharmacovigilance* focusing on appropriate prescribing of Yasmin and other oral contraceptives.

Crestor (rosuvastatin) – risk of muscle toxicity

The Agency reviewed the safety of a new product for the treatment of high cholesterol, rosuvastatin (Crestor), following concerns about the risk of muscle toxicity and evidence that some patients were started on higher doses than necessary. Following discussions with the Agency, the manufacturer reminded healthcare professionals of the prescribing information, that the highest dose of rosuvastatin should only be prescribed under specialist advice, and that certain specific contraindications were appropriate to ensure that patients at risk of myopathy do not receive the highest dose of rosuvastatin. The Agency put this information on its website and health professionals were again reminded of this advice in a general article on statins published in the bulletin *Current Problems in Pharmacovigilance*.

Devices

Blood collection tubes

Blood collection tubes are essential for many laboratory tests. The Agency discovered that some tubes, when used in combination with selected test systems, produced incorrect test results that could cause a misdiagnosis or inappropriate patient management. The Agency issued two MDAs to instruct laboratories not to use the tubes with the affected test systems and to seek up-to-date information from the manufacturers.

Decontamination of endoscopes

The Agency issued an MDA relating to the risk of transmission of infection because of inadequate decontamination of endoscopes. Parallel alerts were issued in Scotland, Northern Ireland and Wales. As a result, the Chief Medical Officers asked that a task force, co-ordinated by the Health Protection Agency, be set up to investigate. The task force identified several issues relating to processes and equipment management which are being addressed.

Implantable defibrillators

The manufacturer of an implantable defibrillator advised the Agency that some batteries could develop an internal short circuit leading to rapid battery depletion. The company had received only a small number of reports of total failure. However, failure analysis and identification of the actual cause indicated that the problem could be widespread and occur without warning. The Agency, therefore,

issued an MDA in conjunction with the manufacturer, to advise clinicians of specific patient follow-up and device monitoring. The three models affected were implanted in about 800 UK patients.

Electrical installation guidance

Work has continued on a set of *Medical Electrical Installation Guidance Notes* (MElGaN). This guidance document is based on IEC 60364-7-710 and IEE Guidance Note 7 and is to supersede those documents, and supplement other existing guidance documents. It is intended for use by healthcare establishments and medical device suppliers involved in the permanent electrical installation of diagnostic imaging and radiotherapy rooms/suites and associated equipment. It may also prove a useful document for people installing other permanently installed medical devices. This guidance will be for new buildings and refurbished rooms and will not be retrospective. It is due to be published as a web-based document later in 2005.

Nasogastric tubes

An MDA was issued to advise clinicians to use pH rather than litmus paper to confirm the placement position of nasogastric tubes in the stomach. The Agency continues to work closely with the National Patient Safety Agency (NPSA) on this issue. The Agency also published a series of frequently asked questions on its website, to provide further information.

Physiological measurement devices

The Agency continued to receive adverse incident reports on a variety of physiological measurement issues. These resulted in several MDAs during 2004. September saw the introduction of peak expiratory flow meters manufactured to the new European Standard EN 13826. These will replace the traditional Wright scale models. The Committee on Blood Pressure Monitoring in Clinical Practice held a series of meetings during 2004 and is due to report in 2005. The Committee's remit is to evaluate whether mercury sphygmomanometers should continue to be used in the clinical environment and to consider the evidence regarding the accuracy of alternative devices.

Electrically operated beds

The Agency became aware of a risk of entrapment and crushing involving the accidental operation of the foot controls of an electrically operated bed. It published an MDA to highlight this issue and raise awareness of the need for a proper risk assessment of the likelihood of accidental operation of foot controls. It also identified factors that may need to be considered when deciding on the use of an electrically operated bed. This issue continues to be discussed with the manufacturers via the British Healthcare Trades Association and it is anticipated that further advice will be published in 2005.

Stability of wheelchairs

The Agency published a guidance document on the stability of wheelchairs, DB2004 (02), in March 2004. The content is aimed at improving the general understanding of the potential serious safety implications of using a wheelchair on slopes, ramps or uneven ground, especially when accessories or other assistive technology equipment have been fitted to or carried on the wheelchair. This guidance document was used in discussions with Department for Transport on the access requirements for vehicles adapted to carry wheelchairs. It was also used as the basis for discussions with wheelchair and seating manufacturers to improve the detail provided in their usage information concerning the maximum safe slopes for their wheelchairs.

Safety of SSRIs

The Agency set up an expert working group of the CSM in April 2003 because of continuing concerns about the safety of SSRIs. They issued advice as work progressed; in particular, in December 2004 on the risks and benefits of SSRIs in children, and in March 2005 on the recommended dose for paroxetine (Seroxat).

The Agency issued a reminder in the October 2004 edition of *Current Problems in Pharmacovigilance* of the key prescribing advice. In parallel with the national review, the Agency led a Europe-wide review of the risks and benefits of paroxetine and participated in a class review of the safety of all SSRIs in children and adolescents.

The Agency completed the detailed review of the safety of SSRI antidepressants and related antidepressants in adults and children, publishing the full report of the CSM expert working group in December 2004,[5] to coincide with the publication of National Institute for Clinical Excellence (NICE) guidelines on the treatment of depression and anxiety. The key findings of the expert working group were that the balance of risks and benefits of all SSRIs in adults remains positive in their licensed indications, but that clear advice was to be given in all SSRI product information in three areas:

- withdrawal reactions;
- dose changes; and
- suicidal behaviour.

An additional key finding was that there is no dose-response relationship for Seroxat, making it illogical to increase the dose for non-responders.

In children and adolescents the risk : benefit of all SSRIs, with the exception of fluoxetine (Prozac), is unfavourable for the treatment of depressive illness. The key findings of the expert working group and headlines from the NICE guidelines were sent to health professionals in a letter from the Chairman of the CSM through the Chief Medical Officer's Public Health Link.

The report of the expert working group, which is available on the MHRA website, outlines the key areas of concern examined. It provides a summary of the data considered, including clinical trial data, spontaneous reporting data from health professionals and patients, and a study conducted in GPRD[6] on the risk of suicidal behaviour in patients exposed to SSRIs and tricyclic antidepressants. The report also looks forward to consider what lessons were learned during the process of the review and what further research is required into the safety of SSRIs.

Yellow Card scheme

In May 2004, the *Report of an Independent Review of Access to the Yellow Card Scheme* was published, to coincide with the 40th anniversary of the scheme.

The report recommended that Yellow Card data should be made publicly available, especially for public health research, but that the release of data should be subject to scientific and ethical safeguards to protect the confidentiality that is inherent to the scheme.

Following advice from the CSM, the Government accepted all the main recommendations on access to data made by the Independent Review. An interim committee was set up under the chairmanship of Dr Jeremy Metters to advise the MHRA on the development of arrangements for the release of Yellow Card data. The interim committee will be replaced in the near future by a substantive committee to consider requests for Yellow Card data.

One of the recommendations of the Review was that, in addition to healthcare professionals, patients should also be able to directly report suspected ADRs. To advise on the development of a patient-reporting scheme, a working group of the CSM was set up, with representatives from patient and consumer groups, academia, pharmacy and medicine.

The review into SSRIs also considers what **further research** is required into their safety.

Did you know?

The Yellow Card is 40 years old. But it's more active than ever. This year saw a 4% increase in Yellow Card reporting from health professionals. This includes electronic reports received through the new website, at www.yellowcard.gov.uk.

Since January 2005, patients can report suspected ADRs by completing a paper patient Yellow Card reporting form, or an electronic form on the MHRA website at www.yellowcard.gov.uk. More widespread pilots, using a range of reporting mechanisms, will be rolled out later this year across the UK. The Agency expects that permanent patient-reporting systems will be put in place in 2006.

Enforcement

Medicines

The MHRA Enforcement and Intelligence Group is now the largest in Europe. The Enforcement Unit opened investigations on 250 cases and closed 158, submitting 18 files for possible prosecution. A further 41 cases had joint prosecutions with the Crown Prosecution Service (CPS). The Agency issued 20 formal cautions and brought 58 offenders into compliance by giving warnings and advice. During the year, the Agency had six successful prosecutions, and exercised its powers under the Proceeds of Crime Act to confiscate £320,000 from two individuals convicted of Medicines Act offences.

Enforcement action carried out during the year included:

- the first prosecution for non-compliance of a determination issued by the Borderline Unit;
- an importer of unlicensed sildenafil citrate products receiving a custodial sentence of 18 months' imprisonment and £150,000 confiscated;
- the confiscation of £170,000 from a mail order and Internet distributor of Viagra;

From left to right: Suzie Ekins-Daukes, Naashika Quarcoo, Kavita Chadda, Andrew Black, Yellow Card Scheme

Did you know?

The MHRA can bring criminals to justice. Last year, we issued 20 formal cautions and had six successful prosecutions. This included a double conviction under the Medicines Act that allowed us to confiscate £320,000.

- a joint prosecution with the CPS against a counterfeiter of medicinal products who received a five and a half year prison sentence for Trademarks and Medicines Act offences; and
- a £50,000 fine for a licensed wholesaler illegally diverting AIDS drugs.

The year has seen a marked increase in the complexity of cases, many of which involve liaison with overseas regulatory and law enforcement counterparts. Summer 2004 saw the first cases of counterfeited products reaching patients for ten years, and cases are currently under investigation.

The newly-formed Intelligence Unit provides the focal point for information-gathering activities in the Agency as a whole and provides operational and strategic support to the Enforcement and Intelligence Group's Criminal Investigation Unit. Key areas of Intelligence Unit work have included:

- leading the MHRA anti-counterfeiting strategy, which involves working closely with other regulators, industry and law enforcement bodies at UK, European and global levels to develop innovative solutions in order to ensure the integrity of the UK medicines distribution chain;
- playing a key role in the organisation of a Council of Europe anti-counterfeiting seminar, which will be the largest global conference on the subject. The Agency, on behalf of the UK, is the biggest financial donor for this seminar, which is reliant on voluntary contributions; and
- the production of an in-house bi-monthly intelligence bulletin on pharmaceutical crime trends and cases.

Devices

The Agency started 227 proactive cases and completed 248 cases. It opened 269 reactive cases and completed 226. (There was a rise of 35% in allegations of non-compliance received this year due, in part, to the end of the transitional period for IVD medical devices.) There are currently 246 live cases under investigation. There were 101 on-site inspections.

The Agency issued nine compliance notices and removed three unsafe devices from the market. These were:

- an IVD analyser for monitoring new-born babies;
- a back pain heat patch; and
- a tuberculosis-testing device.

Additionally, a prosecution is continuing against an importer and manufacturer of a Chinese-manufactured laryngeal airway device. The Agency has also co-operated with the Irish and Dutch competent authorities in an investigation into counterfeit condoms on the EU market. About 1.5 million counterfeit condoms were seized in Eire, The Netherlands and the UK. This investigation is ongoing.

Finally, as a result of the Directive coming into force for medical devices utilising tissues of animal origin, the Agency has checked that all affected devices are compliant. This year it reviewed 86 Supplementary Evaluation Reports prepared by notified bodies, which has resulted in a number of devices being removed from the market.

General Practice Research Database (GPRD)

During the year, the GPRD Division continued to maintain the database, with three million active patients ensuring it remains the largest of its kind in the world. The publication of the Agency report on SSRIs and suicidal behaviour in the *British Medical Journal (BMJ)* further enhanced the profile of the research capability of GPRD. Additionally, the division's Research Services Team collaborated with colleagues across the pharmaceutical industry, UK Government and international academia to deliver a range of services for the benefit of public health research. Areas of research where GPRD was the data source included:

- stroke and transient ischemic attack (TIA);
- Botox;
- body piercing;
- gastro-enteritis and flu-like illnesses;
- alcohol use disorders;
- asthma; and
- the epidemiology of respiratory syncytial virus infections in primary care.

Additionally, it held two symposia, one of which was hosted by Lord Warner, to increase use of GPRD by DH.

The implementation of a fully integrated business development and customer relationship management strategy enabled GPRD to deliver increased awareness of the database to a wide international audience.

New licences for online access were taken out in the year by the US Food and Drug Administration (FDA), Boots Healthcare, Bristol-Myers Squibb, Sanofi Aventis and the Boston Collaborative Drug Surveillance Programme. The division also embarked upon a strategy to widen the use of GPRD data in academia and intends to take this work further forward in the coming year.

From left to right: Nageen Hashmi, Jeremy Mean, Beryl Keeley, Advertising

Supporting scientific and industry innovation

The UK healthcare industry is **highly innovative** and has the potential to grow into one of our most **successful industrial sectors.**

Review of activities

Devices

Device evaluations undertaken and reports produced

Operating with 13 evaluation centres, the Device Evaluation Service evaluated 493 devices and produced 81 evaluation reports.

Above, from left to right: Susan Delaney, David Brown, Ian Hirsch, David Wright, Statistics Unit

Compliance investigations

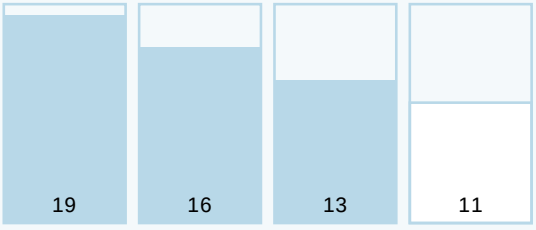
Reactive	Opened	Closed	Carried forward
2004/05	269	226	147
2003/04	199	200	104
2002/03	229	232	105
2001/02	237	267	108

Proactive	Opened	Closed	Carried forward
2004/05	227	248	99
2003/04	210	187	120
2002/03	168	171	97
2001/02	206	168	100

The Agency also carried out 101 on-site inspections.

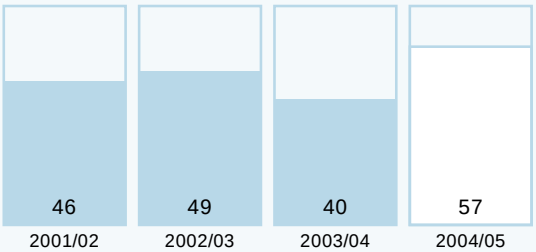
Notified body audits

The Agency undertook 11 notified body audits during the year: eight on-site surveillance audits and three witnessed audits of notified bodies undertaking assessments at manufacturers' facilities. The Agency met all quantitative targets, and all issues raised during the audits were taken up with the relevant notified body.



Clinical investigations undertaken

The Agency reviewed 57 clinical investigation applications during the year, with 14 of these objected to; all were reviewed within the statutory 60-day period with an average time of 52 days.



Medicines

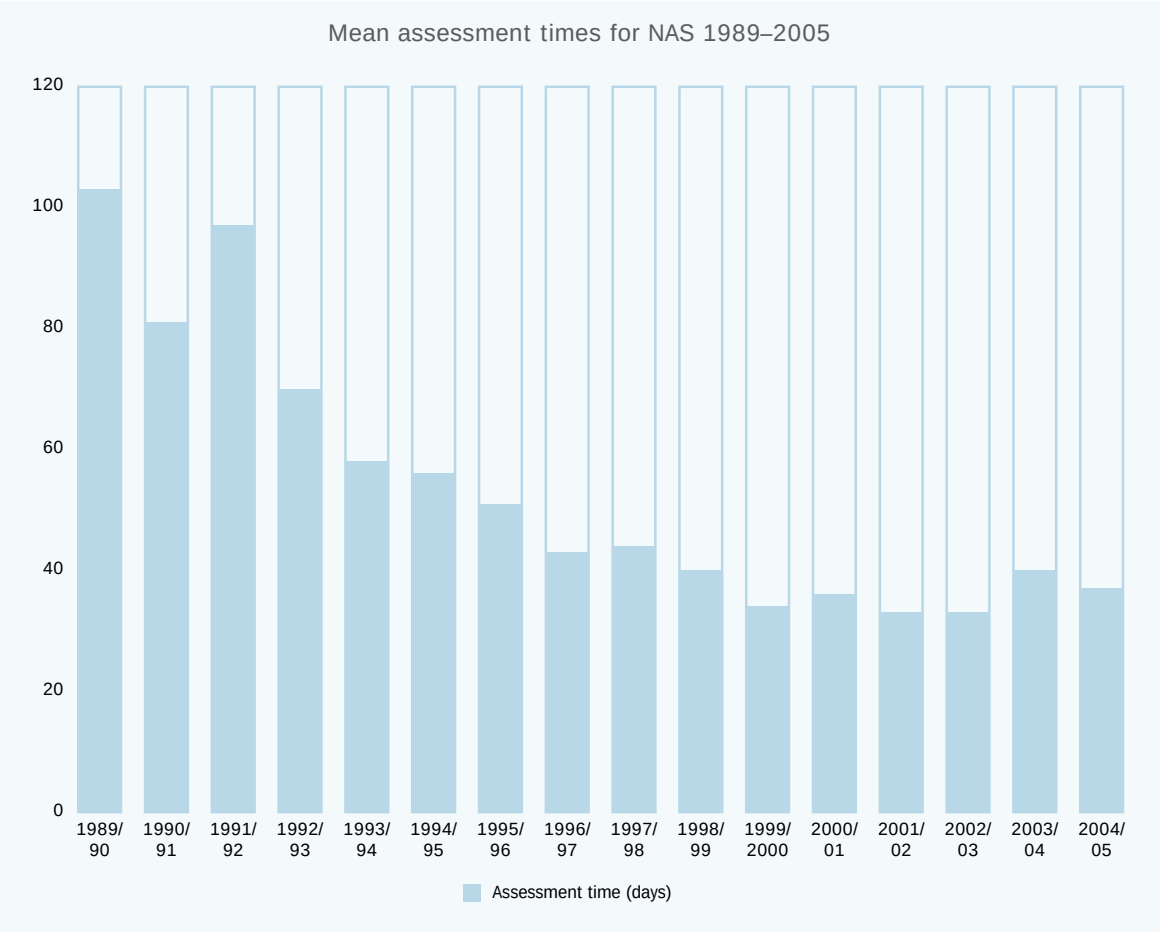
Clinical trial authorisations (CTA) 2004/05

	Number of Phase 1 applications received	Average assessment time	Number of CTA applications	Percentage assessed in 30 days
2004/05	257	13.1 days	561	87%

Following the implementation of the Clinical Trials Directive in May 2004, all applications are now approved as clinical trial authorisations. The authorisation of Phase 1 healthy volunteer trials is a new type of work resulting from implementation of the Directive.

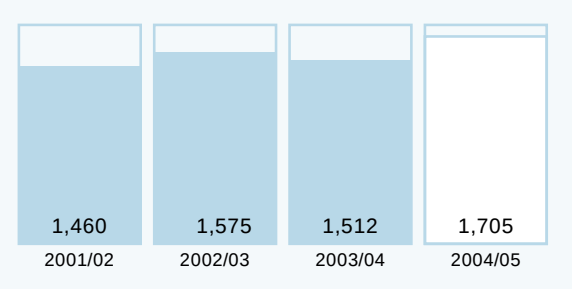
New active substances (NAS) assessed

The Agency continues to maintain a very fast mean assessment time: completion of assessment report for new active substance applications is achieved in less than 40 days.



Abridged applications determined

The Agency determined a record number of abridged applications, almost 13% higher than the previous year.



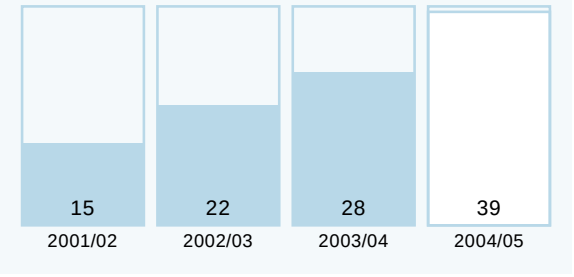
Parallel imports

	Applications received	Applications determined	Variations received	Variations determined
2004/05	2,867	3,380	8,848	8,846
2003/04	2,310	3,041	6,903	5,341
2002/03	3,173	2,343	6,411	5,793

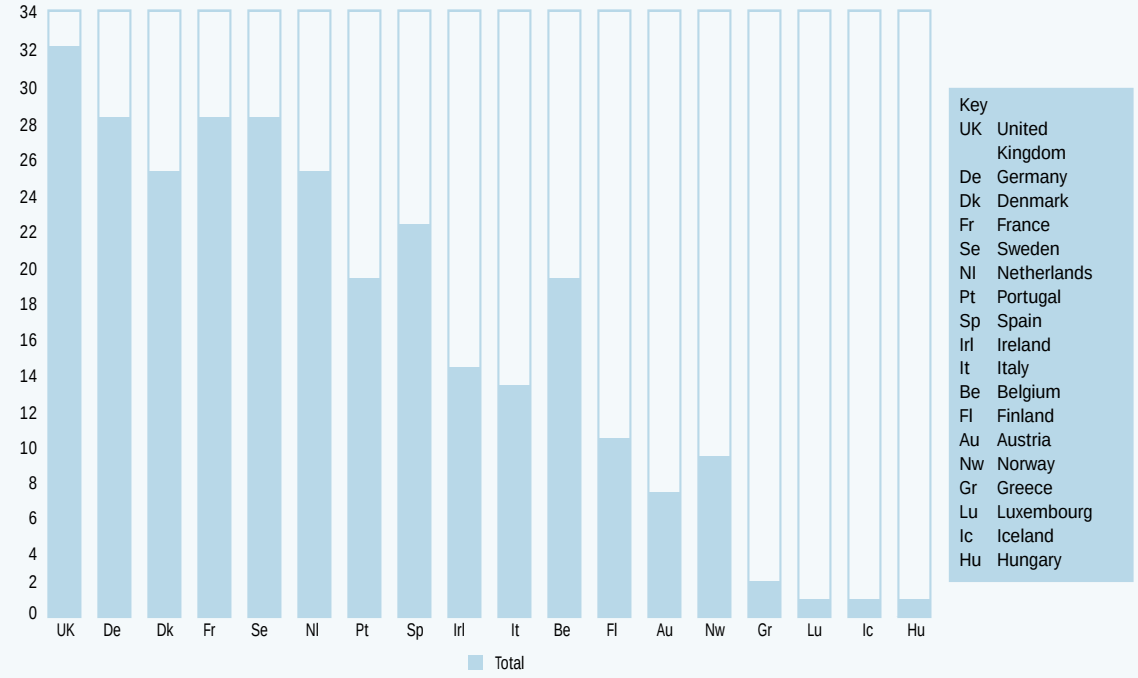
Throughput of parallel import applications has increased significantly again this year.

CHMP scientific advice

The UK continues to provide more scientific advice to the CHMP than any other regulatory authority.



Centralised rapporteur and co-rapporteurships



By the end of December 2004, the UK remained the leading Member State for the appointment of rapporteur or co-rapporteurships for centralised applications.

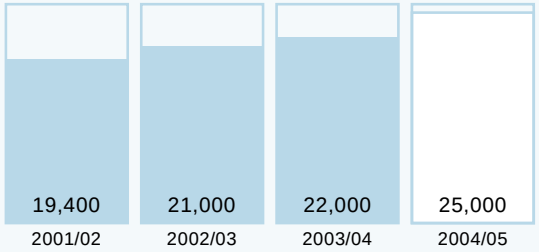
Outgoing Mutual Recognition

	Assessment reports	
Year	Number of reports	Average days to completion
2004/05	122	26
2003/04	67	44

The Agency has produced a record number of outgoing Mutual Recognition assessment reports, and has reduced the time to prepare the reports. The average time to completion of the report at 26 days is well within the required 90 days.

Variations

The number of variation applications received this year has risen by 13%, twice the rate of increase seen in recent years as shown in the chart. Overall, the Agency has maintained assessment performance (see table) in parallel with this record number of 25,000 variations. Applications received covered a spectrum of changes to marketing authorisations (MAs), from minor manufacturing amendments to the addition of significant new clinical indications in therapeutic areas such as oncology and cardiovascular disease.



	Performance 2001/02	Performance 2002/03	Performance 2003/04	Performance 2004/05	Target 2005/06
Type IA[1] 100% within 14 days of receipt	-	-	achieved 100%	achieved 100%	ongoing
Type I/IB[2] 100% within 30 days 85% within 20 days[3]	achieved 100% exceeded 95%	achieved 100% exceeded 96%	achieved 100% exceeded 90%	achieved 100% exceeded 91%	ongoing ongoing
Type II 100% within 90 days 85% within 60 days	accomplished to 99% exceeded 93%	accomplished to 99% exceeded 95%	achieved 100% exceeded 89%	accomplished to 99% exceeded 90%	ongoing ongoing
Extended Type II[1] 100% within 120 days	-	-	achieved 100%	achieved 100%	ongoing
Reduced Type II[1] 100% within 30 days	-	-	achieved 100%	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 2001/02

Renewals

In the past year, the UK has acted as Reference Member State in 140 Mutual Recognition procedures (compared with 85 last year) and rapporteur or co-rapporteur for five centralised procedures. In addition, the Agency processed 110 national applications per month (a decrease from 194 last year, reflecting the increased involvement of European work).

As a result of the 2001 Review, new legislation will be implemented in the latter part of 2005 under which MAs will be renewed after five years and, unless there are pharmacovigilance reasons to request an additional five-year renewal, they will then be valid indefinitely. The five-yearly submission of Periodic Safety Update Reports (PSURs) at the time of renewal will be replaced by a three-yearly PSUR cycle.

As part of the European Risk Management Strategy, the UK has had a major involvement in developing a scheme for sharing the assessment of PSURs throughout Europe. A pilot scheme is under evaluation and, once implemented fully, this scheme will lead to more effective use of PSUR data and avoid duplication of effort on the part of Member States and industry.

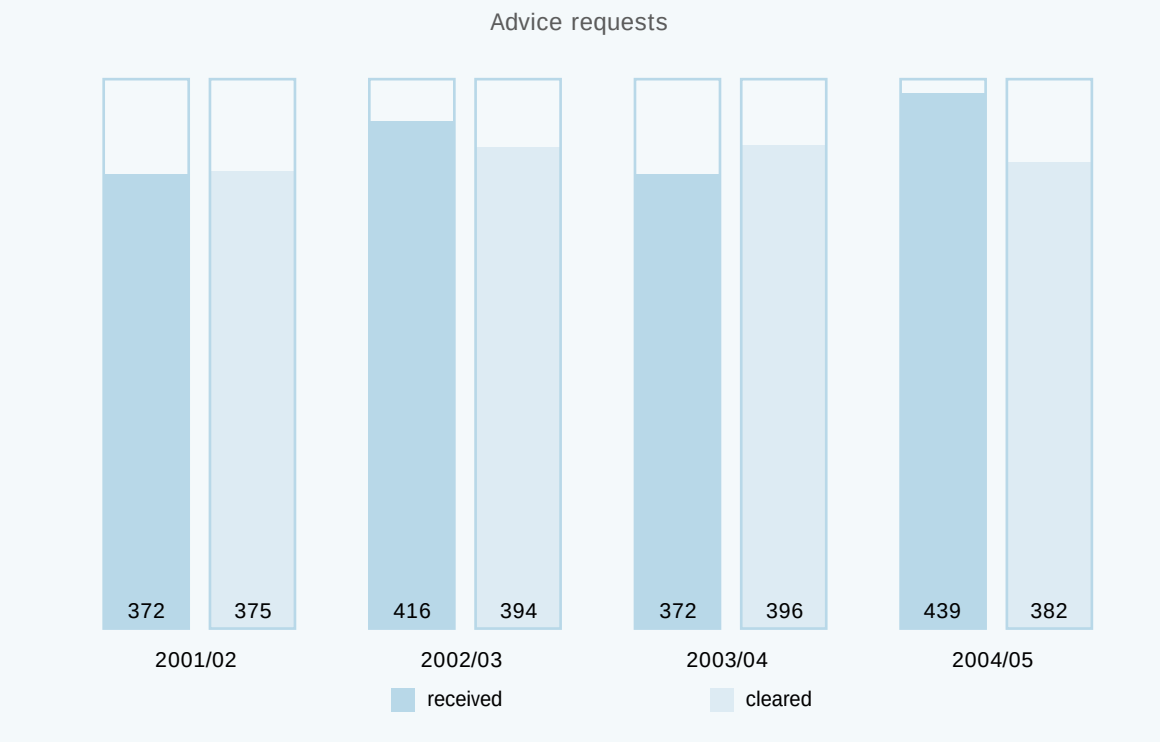
Medicines advertising investigated

	2001/02	2002/03	2003/04	2004/05
Number of complaints received	109	157	157	120
Number of advertisements withdrawn or amended as a result of action on complaints	81	98	102	72
Number of advertisements withdrawn or amended as a result of Agency scrutiny	50	28	28	13
Number of corrective statements published	1	3	9	4
Products for which advertising was reviewed prior to issue	16	15	17	30

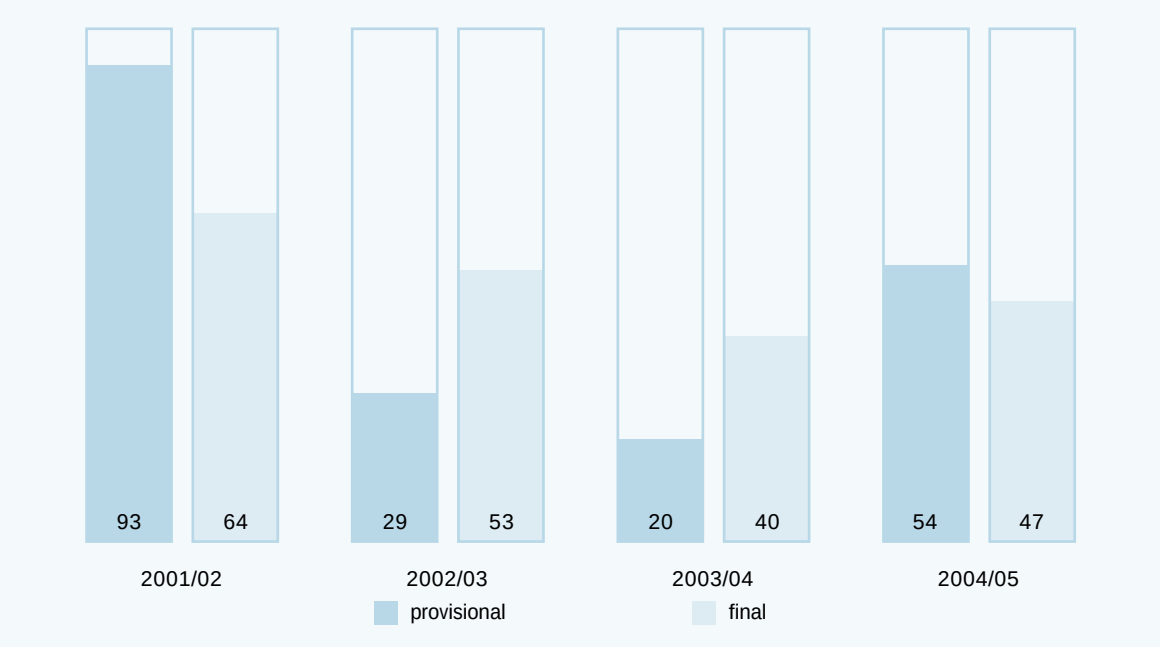
This year's statistics reflect the increased work the Agency has undertaken on targeted review of advertising prior to issue. This has led to lower numbers of published advertisements requiring withdrawal or correction. The Agency has also issued advice by regular *MAIL* articles on advertising issues and by publishing a new edition of *Advertising and Promotion of Medicines in the UK*, or *The Blue Guide*. This was launched at the first MHRA Advertising Seminar in February 2005 for a period of public consultation.

Borderline medicines considered

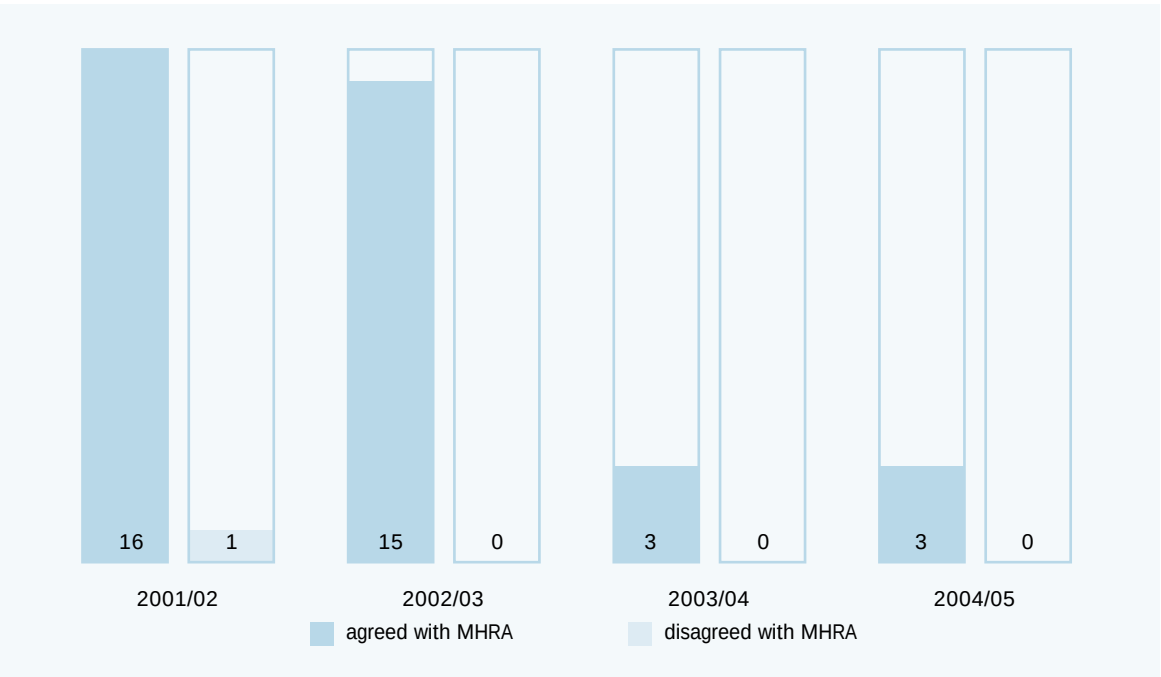
In addition to the regular checks the Agency makes to ensure that licensed medicinal products meet the required quality and safety standards, the medicines Borderline Section examines products that are not licensed as medicines but appear to be presented as such or have therapeutically active ingredients.



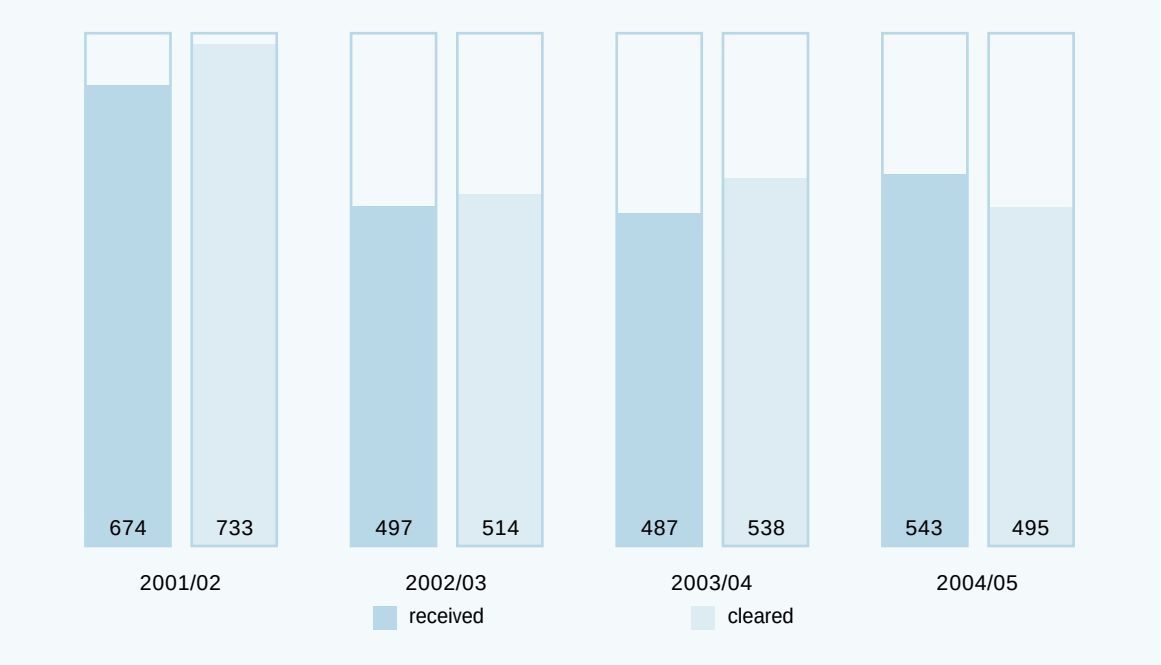
Statutory determinations issued



Independent Review Panel hearings



Complaints of breaches of legislation



Sales of British Pharmacopoeia (BP)/BP Chemical Reference Substances

	2003	2004
Sales of BP	2,795	2,772

	2003/04	2004/05
Sales of BP Chemical Reference Substances	11,275	10,569

Number of written regulatory enquiries handled (including borderline, classification and other regulatory interpretations)

2004/05	1,300
2003/04	1,318
2002/03	994
2001/02	658

Nanotechnology

Nanotechnology is a diverse subject that involves working with matter on an ultra-small scale, where the properties of materials differ significantly and unpredictably from larger-scale structures. Developments in nanotechnology are likely to have a considerable impact on healthcare and to lead to a wide variety of innovative therapies bringing substantial benefits to patients.

The Agency set up an internal working group in 2003 to keep a watching brief on developments in this area and was thus in a good position to respond to the increasing public interest in nanotechnology and, in particular, to the report on the subject by the Royal Society (RS) and the Royal Academy of Engineering (RAE). This report made a number of recommendations to Government, including that DH should review the regulations for new medical devices and medicines to ensure that particle size and chemistry are taken into account in investigating possible adverse side effects.

The Agency is implementing this recommendation and contributed to the Government response to the report. In addition, CSM and CSD considered the implications of developments in nanotechnology. The Agency is organising a one-day international conference on nanotechnology in October 2005, as part of the UK's EU Presidency activities.

Healthcare Industries Task Force (HITF)

Great advances are being made in medical technology. The UK healthcare industry is highly innovative and has the potential to grow into one of our most successful industrial sectors. HITF was set up to gain a better understanding of how government and industry can work together to maximise the benefit to the NHS, patients, industry and the national economy. HITF was jointly chaired by Lord Warner, Under Secretary of State for Health and Sir Christopher O'Donnell, Chief Executive of Smith and Nephew, and brought together government and industry leaders to identify steps to develop and stimulate the growth and performance of the UK healthcare industry, and to maximise the benefit to patients from healthcare products. Its report *Better health through partnership: a programme for action* was published in November 2004 and it sets out a number of measures to improve people's access to useful new medical technologies. The Agency's Chief Executive was a member of the task force representing the regulatory aspects and will continue to represent and promote the MHRA's interests as the outputs are implemented.

Manufacturers' Online Reporting Environment (MORE)

MORE is a secure, Internet-based system that allows medical device manufacturers electronically to submit full details of any medical device-related adverse incident or device recall direct to the MHRA Adverse Incident Centre. The information is then transferred automatically into the Agency's incident tracking database. Throughout the year, activity on MORE has increased steadily. Approximately 10% of the total number of reports received from manufacturers now come via this route. Following the very positive outcome of a 2004 survey of registered MORE users, the Agency developed plans for a number of enhancements. These are scheduled for completion and live implementation by the end of 2005.

Service improvements

Part of the Agency's role in safeguarding public health involves providing an efficient and effective service to its stakeholders, and the MHRA constantly strives to improve the quality of that service. Key improvements this year have included:

- setting up the Agency's own media centre to meet user needs;
- better guidance for device manufacturers on clinical investigations, to help re-submissions and provide information for active devices and for biological safety aspects;
- structure of meetings held with notified bodies and device industry changed to better reflect their needs; and
- speedier and more effective handling of Freedom of Information (FOI) requests.

Scientific advice

In July 2003, the Agency introduced a more formal system of offering scientific and regulatory advice to companies during the development phase of new medicinal products. This replaced a previous, more informal system. Companies can seek advice on quality, regulatory procedures, and pre-clinical and clinical testing. The more formal system needs written questions and briefing documents. Following a face-to-face meeting where these questions are discussed, the Agency provides written answers. Advice letters are reviewed for quality and consistency by a senior group of assessors and managers before being sent to companies. Companies pay a small fee for scientific advice, although no charge is made for regulatory advice.

10% of the reports received from device manufacturers now come via MORE.

In the period from the introduction of the procedures in July 2003 to March 2004, the Agency held 103 meetings with companies; in 2004/05, the Agency held 171 meetings, representing a 25% annual increase.

Review of the advisory committee structure

The UK medicines advisory committees have remained essentially unchanged since their introduction under the Medicines Act of 1968. Since then, European medicines legislation has changed the type and volume of their work significantly. The interests of people serving on committees has also attracted increasing public debate. Because of this, and changes to the EU scientific committees, the Agency decided to review its advisory committee arrangements.

An MHRA group is overseeing all aspects of the review. It undertook public consultations during the year on the overall advisory committee structure and on proposals for declaring and handling interests held by individuals serving on the committees.

The Medicines Commission and CSM will be replaced by a Commission on Human Medicines from October 2005, but Section 4 committees will remain and a range of expert advisory groups will underpin their work. All the committees will in future include lay members. The main regulations needed to make the changes were laid before Parliament in March 2005.

The Agency is revising its code of practice on the interests of individuals serving on committees. Chairmen and members of statutory committees will not hold personal interests in the industry they regulate. All other interests will be declared and managed under the code.

Committee on the Safety of Devices

A new Committee on the Safety of Devices was appointed in April. John Williams CBE was re-appointed as the Chairman for a further four-year term of office. The Committee has 21 specialist and three lay members in addition to the Chairman.

Tissue engineering

Tissue engineering is a developing technology combining various elements of medicines, materials science, biology and engineering. Hitherto, tissue engineering products have typically been developed for use in cartilage repair and for burns and ulcers.

European developments

The European Commission is currently developing proposals for regulation. In April 2005, the Commission consulted on a proposal for a harmonised regulatory framework. Responses indicated broad support for the principle of legislation in order to safeguard public health and to provide a secure legal basis within which the tissue engineering sector can develop. The Commission is expected to adopt formal proposals later in 2005.

The Medicines Commission and the Committee on Safety of Medicines will be **replaced** by a Commission on Human Medicines from October 2005.

MHRA activities

In 2004, in preparation for negotiations on the expected European proposals, the MHRA embarked on a fact-finding programme to establish the views of stakeholders, including the relevant industry trade associations, academic research interests and those involved in tissue engineering activities in hospitals.

Forward look

The MHRA will work with the European Commission, other Member States, industry and other interested parties to develop an appropriate legislative framework which will protect public health, help future innovation and comply with the principles of better regulation.

Did you know?

The MHRA is revising its code of practice on the interests of individuals serving on committees. Chairmen and members of statutory committees will not hold personal interests in the industry they regulate.

From left to right: Kathleen Glazik, Chris Markham, DTS Business Services

Providing authoritative and accessible information

The MHRA has exhibited at a wide range of conferences, seminars and workshops – providing a unique opportunity to showcase our work.

Conferences and seminars

The Conference and Education Function is responsible for organising branded meetings on topics related to the control of medicines and devices. It also operates as a central contact point for other providers of conference and training seminars wanting Agency speakers. The Agency has a commitment to provide professional, value-driven events that inform and promote discussion on a diverse range of topics. Some of the areas covered during the year include:

- pharmacovigilance;
- the Traditional Herbal Medicines Directive;
- GCP inspections;
- variations to marketing authorisations;
- advertising: *The Blue Guide*;

Above, from left to right: Claire O'Brien, Susanne Kirlew, Sara Coakley, Press Office

- the Clinical Trials Directive: a year after implementation;
- the role of the qualified person;
- infusion pumps study day;
- Medical Device Liaison Officer conference; and
- getting the best from the MHRA.

The Agency has exhibited at a wide range of conferences, seminars and workshops throughout the year. The exhibitions provide a unique opportunity to showcase the work of the Agency. These included:

- the British Pharmaceutical Conference;
- the Drug Information Association (DIA) Conference and Exhibition in Portugal and Washington;
- the Health Protection Agency (HPA) Conference and Exhibition;
- the National Institute for Health and Clinical Excellence (NICE) Conference;
- the Nursing in Practice Exhibition; and
- the Diabetes UK Conference and Exhibition.

These are all important initiatives in developing and maintaining links with key stakeholders in the area of healthcare while also promoting the key work of the Agency. These events have provided up-to-date information in an open and interactive manner to key stakeholders and have recorded very high levels of customer satisfaction.

Website

The website is a prime communication channel for the Agency. It must explain the Agency's role and provide rapid, widely accessible and tailored access to the Agency's knowledge, with a hierarchy of detail so that users can access information at levels appropriate to them. A major project is under way to redevelop an integrated website (covering medicines and devices), due to be launched in September 2005. Its content will reflect the views of stakeholders and will incorporate new features such as e-mail alerts to help users get targeted information appropriate to their needs. It will be accessible to users with disabilities and will adopt best practices in both design and accessibility, complying with e-government minimum requirements for websites.

Central Enquiry Point (CEP)

The CEP is the first point of contact for public enquiries to the Agency. It receives over 600 telephone calls, 250 e-mails and 50 letters every week. The highly trained CEP team either answer queries themselves or transfer them to the appropriate Agency expert. The target is to reply to 90% of written requests within seven working days; this was achieved this year. The CEP also provides an important central Agency briefing point for the public on topics that have attracted media attention. Issues dealt with during the year included:

- changes in the names of medicines (BANs to rINNs);
- atypical antipsychotics;
- SSRI antidepressant drugs;
- COX-2 anti-inflammatory drugs; and
- withdrawal of co-proxamol from the market.

The Agency met its ministerial correspondence target of answering 90% within 20 days.

Publications

Medicines

MAIL (Medicines Act Information Letter) is the MHRA's bi-monthly newsletter for medicines, available in print by subscription, and free of charge on the Agency website. It is a key source of information for all those involved in the licensing and manufacturing of medicines. This year it continued the high standard readers have come to expect from the *MAIL* editorial team and has provided a range of articles giving in-depth coverage of the key topics of current concern. *MAIL* now has an e-mail alerting service to inform readers when it is published on the Agency's website. This is available for a small subscription and has proved very popular.

> The website provides rapid, widely accessible and tailored **access** to the MHRA's knowledge.

Did you know?

The MHRA receives over 600 telephone calls, 250 e-mails and 50 letters every week. Our target is to reply to 90% of written requests within seven working days and we achieved this goal.

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

- statins and cytochrome P450 interactions;
- reminder: paroxetine prescribing advice;
- Cisapride: licences cancelled;
- Tolcapone: return to market;
- review of the evidence regarding long-term safety of HRT;
- combined oral contraceptives: VTE;
- reminder: thiazolidinediones (glitazones) contraindications;
- risk:benefit of co-proxamol;
- SSI BCG vaccine and local reactions;
- changes in the names of certain medicines;
- reminder: flucloxacillin and serious hepatic disorders;
- interaction between warfarin and cranberry juice: new advice;
- black cohosh (Cimicifuga racemosa) and hepatotoxicity;
- reminder: safety of traditional Chinese medicines and herbal remedies; and
- dose adjustment and monitoring of low molecular weight heparins.

Devices

The devices sector has produced a wide range of publications over the past year. These have included three *Device Bulletins* covering:

- guidance for healthcare professionals and liaison officers on reporting adverse incidents and dissemination of MDAs;
- an analysis of adverse incident reports received and investigated in 2004/05; and
- guidance for users, carers, healthcare professionals and manufacturers on the stability of wheelchairs.

The investigation of adverse incidents is important in maintaining both patient and user safety. In order to promote this reporting by all healthcare professionals, the Agency has also produced a leaflet setting out guidance on how to report adverse events, with a pocket-sized mini-leaflet for instant access and ease of use.

The Agency has also published nine editions of *One Liners*, a single-page publication aimed at highlighting user and practice issues associated with medical devices. These continue to be popular and have included a specially produced edition for the British Pharmaceutical Conference and one for the Health Protection Agency Conference.

Increasingly, medical conditions are being diagnosed and monitored by point-of-care test kits. These have the advantage of not requiring laboratory analysis, with results being immediately available. For this reason, the Agency has also produced a leaflet entitled *Point-of-Care Testing: Top Ten Tips*, providing good practice guidance for users of these devices. The Agency produced a further leaflet setting out guidance on safe use and choice of device, following difficulties encountered in the use of implantable vascular access ports.

The Agency also continues to be responsible for, and to support the work of, the Microbiology Advisory Committee. This year, this group has rewritten part of its manual, covering protocols for the sterilisation, disinfecting and cleaning of medical equipment.

Device Safety Alert Broadcast System

The Safety Alert Broadcast System (SABS) is a key means of communicating important safety information to the NHS. Its aim is to bring different types of safety alerts together into one electronic system so that they are delivered to the NHS in a streamlined, efficient and consistent way.

The Agency uses SABS to e-mail MDAs directly to SABS contacts, many of whom also function as Medical Device Liaison Officers. This has reduced production and postage costs and increased the speed of distribution of MDAs.

Device Liaison Officers Focus Group and national conference

This group comprises a cross-section of officers drawn from NHS trusts, primary care trusts (PCTs) and social services departments. It provides support for officers and a forum for sharing problems, exchanging ideas and commenting on MHRA issues and proposals. It also gives officers an opportunity to provide feedback to the MHRA. Another role of the group is to allow officers to contribute to the best practice guidance for disseminating safety warnings and reporting adverse incidents, and to develop rapid and efficient methods to disseminate safety warnings within their organisations.

The Agency hosted two Liaison Officer Focus Group meetings during the year. In January 2005, a PCT-specific meeting discussed independent contractor issues, including GPs, and other related issues. This meeting involved 35 PCTs providing the Agency with an opportunity to support its Liaison Officers on very practical issues affecting them. In March, the Agency held its annual Liaison Officer Focus Group meeting attended by representatives from all NHS trust areas and social service sectors. Discussions centred on the SABS and the continuing challenges of MDA distribution, with group work sharing experiences and best practice.

The annual national Medical Device Liaison Officer conference was held in York in November 2004, helping and encouraging the Agency's Liaison Officers, particularly those in the north of England. Over 200 delegates attended the event, described as the best yet. In his keynote speech, the Chief Executive highlighted the importance of the conference and the vital role of the Medical Device Liaison Officers.

Press Office

The MHRA Press Office, created as part of the new Communications Directorate, went live in March 2005. All press functions were taken in-house from DH, who previously had responsibility for Agency press relations.

There are now two Press Officers and a Media Relations Manager running the office. Its focus is to open up the Agency's policies, procedures and information to a much wider audience, both within the healthcare sector and to the broader public and patients. The new Press Office, therefore, aims to be more proactive and is focusing on fostering relations with those who can assist the Agency in getting across key messages.

The MHRA is keen to raise its profile with the wider public in order to assure them that it is protecting and enhancing consumer choice through its regulatory function. The Press Office has already successfully managed to increase media coverage on key issues, using a variety of forums such as broadcasting, health journals, national newspapers and lifestyle magazines. It will continue to target key media sources over the coming year as part of the overall communications strategy, and to engage with the public and key stakeholders.

Communications strategy development

Last year was an important year in the development of a new approach to communications within the Agency. During the first part of the year, an external consultancy undertook a wide-ranging review of the organisation's communication activity to identify strengths and weaknesses and to make recommendations for action.

Interviews were carried out with a wide range of the Agency's stakeholders and staff, and a detailed survey of patient groups was undertaken. A report summarising the feedback and making recommendations was presented to the Agency Board in summer 2004.

The report identifies some areas of strength on which the Agency needs to build. For example, the quality of its scientific advice is widely recognised among healthcare professionals, and the volume of information that the organisation now places on its website is welcomed. However, there are a number of areas where the Agency needs to take significant steps forward if it is to build a genuine communications culture. These include:

- initiatives to encourage greater public engagement. The Agency must do more to involve the lay perspective in its work, providing real opportunities for patients and the public to contribute to its decisions and policies. This will in part be achieved by building the organisation's media relations function, using the media as a key channel of communication with the general public, but it will also include more direct interaction with the public through involvement in expert groups, patient forums and focus groups;
- greater consideration of the impact of regulatory decisions on front-line staff. The Agency needs to work with partner organisations to make it easier for front-line healthcare staff to act on its regulatory decisions. This may include the production of more detailed briefing and, in some cases, education and training materials;
- further initiatives to increase openness and transparency. The introduction during 2004/05 of patient reporting of suspected ADRs though Yellow Cards, the opening to public scrutiny of the Yellow Card database of suspected reactions, and the publication of the evidence base behind

From left to right: Susan Soanes, Keith Pryor, Emma Heeley, GPRD

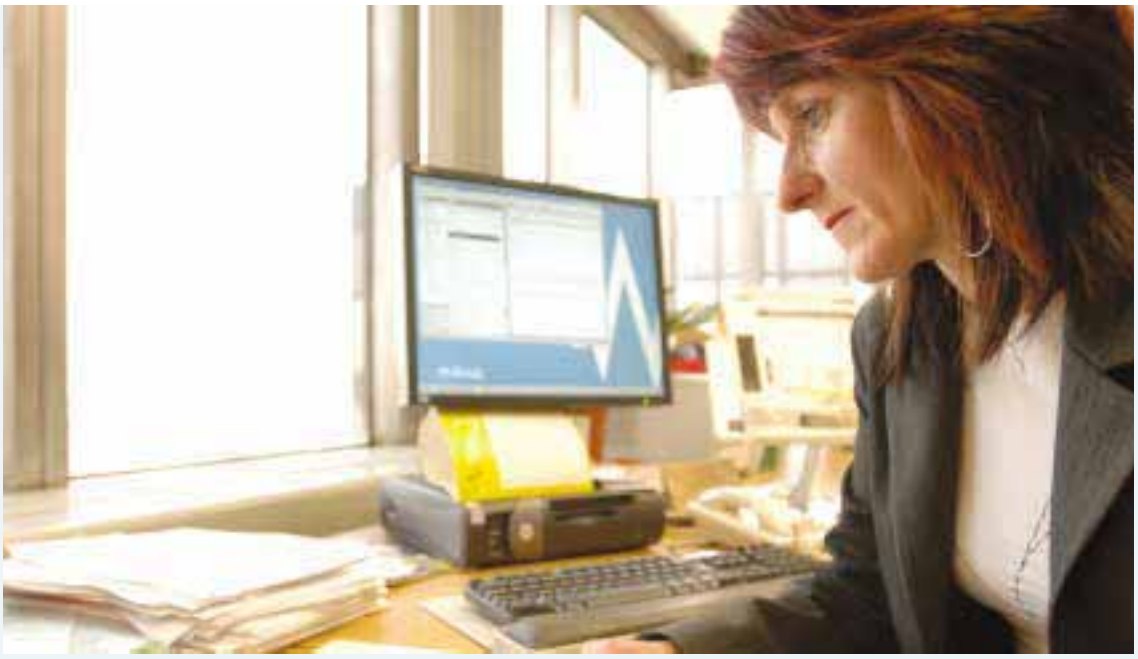
the recommendations of the Expert Group built on these foundations to deliver a sustained programme of work in this area; and

- underpinning all these recommendations was the need for the Agency to establish a dedicated communications function. A Communications Director took up post at the end of January 2005. In mid-March, the Agency took on its media relations function from DH and the Communications Division itself came into being on 1 April 2005.

These initiatives create a firm base on which further activity can be built next year, including the Agency's first communications strategy scheduled for July 2005.

Freedom of information

The Freedom of Information Act 2000 was fully implemented in January 2005 and the Agency, in common with many other public bodies, became subject to the provisions of the Act. The Agency undertook a series of training sessions to ensure that all staff were aware of the Act and of their responsibilities under the legislation. Those training sessions have been followed up by internal updates, aiming to help staff develop a body of expertise as more requests for information are received and handled under the Act. The Agency already makes a great deal of information available via the Publication Scheme required under the Act, and additional information also appears on the Agency's website. A register of the type of requests received under the Act, and the information disclosed as a result of those requests, will also be published on the website.



Lynda Scammell, Enforcement and Intelligence

Influencing European and international integration

In March 2005, the MHRA launched a public consultation to ensure that the revised EU legislation is successfully implemented.

2001 Review implementation

Following detailed negotiations, Member States and the European Parliament agreed revised legislation, which the *Official Journal* published on 30 April 2004, relating to medicines for human use. Member States have until October 2005 to transpose the new provisions into national law. The legislation sets out revised procedures for regulating medicines in the EU, and changes cover the full range of marketing authorisation, post-licensing plus inspection and enforcement activities. The agreed legislation meets the Government's objective for the Review, of further guaranteeing public health protection in the UK through effective regulation of medicines.

Above, from left to right: Matilda Vallender, Adrian Evans, Wayne Jeffries, Maria Barrett, Patience Holland, Warner Payne, Rosemary Pask-Hughes, British Pharmacopoeia

During the year, Member States prepared for implementation, with the UK taking a leading role in discussions on matters of interpretation. Following a full public consultation, Ministers decided to introduce three provisions in advance of the final date of transposition as they offered clear public health benefits. In March 2005, the Agency launched a public consultation on the remaining provisions, to ensure that the revised legislation is successfully implemented by the final date of transposition.

Benchmarking of EU medicines agencies (BEMA)

The aim of the BEMA exercise is to help develop a world-class pharmaceutical regulatory system based on a network of agencies operating to best practice standards within the EU. Since early 2004, the MHRA has led development of a series of key performance indicators for use in the benchmarking exercise. The planning stage is now nearing completion, and agencies, including the MHRA, will shortly begin a process of self-assessment using the performance indicators. A peer-review visit by representatives from other agencies will follow, with the eventual sharing of best practices between Member States. They will complete the first benchmarking cycle by April 2006 and then develop proposals for the second cycle.

Twinning

Twinning enables the Agency to build alliances with other Member States and to extend its influence across the EU. Through twinning, established Member States are able to provide technical assistance to new and prospective Member States through the provision of training in key areas.

In partnership with the Irish Medicines Board, the MHRA successfully completed a twinning project with the Medicines Regulatory Unit of Malta in October 2004. In February 2005, it successfully bid to take part in a twinning project with the State Pharmaceutical Inspection (SPI) service in Latvia. The specific objective is to strengthen the professional capacity of the SPI regulatory supervision of medicinal products in accordance with EU legislation. The project will also cover legislation relating to marketing authorisation and post-licensing activities.

Other aspects of EU relations

Overall, the MHRA continues to play a leading role in the EU medicines regulatory system, through the attendance at a range of EU committees of both staff and outside experts with relevant expertise.

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

The MHRA supports the work of the EDQM OMCL network, providing representatives to its two advisory groups on the general network and on the EU network, and participating in the sampling and testing programme for centrally authorised products. The Agency analysed 17 products as part of the programme. The MHRA also participated in the collaborative programme of work-sharing and result-sharing of analyses of Mutual Recognition products. In February 2005, the MHRA laboratory was audited under the EDQM mutual joint audit programme.

Working with the FDA

The USA, being one of the largest healthcare markets in the world, is home to many leading companies producing new, and innovative, medicines and medical devices. The MHRA has a long-standing and valuable relationship with the USA, at both FDA and company levels. The Agency recognises the importance of these links, in terms of protecting public health and supporting its role as UK regulator, and continues to develop them. In particular, the MHRA and FDA have continued their close co-operation to share information in relation to medical devices and in ensuring the safety, quality and efficacy of medicines.

The MHRA continues to play a **leading role** in the EU medicines regulatory system.

Devices regulation

This was another busy, but successful and productive, year for the devices sector in Europe. In particular, following the largely UK-inspired 2002 review of the medical devices directives, work started on producing a Commission amending directive. The UK has helped with this, along with industry and notified bodies. The Commission is now finalising its proposals, and negotiations on the amending directive are expected to begin later this year.

Agreement was achieved on a Commission directive to reclassify hip, knee and shoulder total joint replacements as class III medical devices. This means they are subject to the most stringent controls allowed for before being placed on the market. The agreement, against fierce opposition from industry, was started by the UK a number of years ago. Work to transpose the directive into national law is now under way.

The Agency again chaired the Notified Body Operations Group, aiming to improve the performance of notified bodies. The Group has prepared various guidance documents and supplied training for new Member States. In addition, it started work on creating a system of peer-review for the work of designating authorities, and reviewed a range of documents prepared by the European Notified Bodies Group. The Agency is also a leading member of the Clinical Evaluation Task Force, which is working to improve the quality of clinical data used by manufacturers to justify performance claims for their devices. The work of the Market Surveillance Operations Group, which aims to improve the effectiveness of post-market surveillance activities, also increased. The Agency chaired an ad hoc working group set up to produce guidance on Member States' expectations of how authorised representatives should operate.

Hip, knee and shoulder joint replacements are now re-classed as **class III** medical devices.

The Agency helped on various Commission initiatives to help new Member States understand the requirements of the medical devices directives. This included sharing experiences, as well as actively participating in two workshops in Tallinn, Estonia and in Malta.

British Pharmacopoeia (BP)

The BP 2004 was published in August 2004. It incorporated supplements 4.6, 4.7 and 4.8 of the *European Pharmacopoeia* (EP) and included five new monographs of national origin and 60 new EP monographs. A BP 2004 Addendum was published in February 2005, incorporating all of the fifth edition of the EP.

Membership of the expert groups and working party of the EP Commission was reviewed during the year. The UK provides members to all of the EP expert groups and chairs two of the chemical groups.

The BP represents the MHRA on the World Health Organization Committee on International Non-proprietary Names (rINNs) and on the EMEA brand-naming review group, which provides comments on proposals for rINNs and on proposed trade names. Some 193 proposals for rINNs were considered during the year, of which 179 were agreed.

Due to the closure of the Canons Park site, the BP laboratory relocated and is now co-located with the MHRA laboratory at the Laboratory of the Government Chemist in Teddington.

The MHRA has participated in **workshops** in Estonia and Malta – to help new EU Member States understand the requirements of the medical devices directives.

Did you know?

The MHRA plays a major role in European and international affairs. We have ensured that the 2001 Review of medicines legislation was implemented on time and we provide more scientific advice to the Committee for Medicinal Products for Human Use (CHMP) than any other regulatory authority.

Paediatric medicines

There is a continuing need for new paediatric medicines, and medicines that are currently used in children but outside the licensing framework, to be properly evaluated and formulated. Good progress is being made on a European regulation on medicines for paediatric use, which will make necessary changes to the regulatory structure. It is still on target for finalisation by the end of 2006 and will be a priority when the UK takes over Presidency of the EU in July 2005. In the meantime, the Agency, together with DH, has developed 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. Fee waivers were introduced from 2005 to encourage paediatric applications.

In response to a request, companies have submitted all completed paediatric clinical trial data to the MHRA. Assessment is under way, and information on use in children is being introduced into the product literature. Assessment reports are published on the MHRA website in the interests of increasing the information available to prescribers. Other areas where the Agency has been working with the pharmaceutical industry include discontinued medicines, imported medicines and the development of new paediatric formulations.

From left to right: Morell David, Sarah Wark, Pharmacovigilance

Operating a successful and fully integrated business

A MORI staff survey showed that 75% of MHRA staff speak highly of the Agency's work to people outside the organisation.

Human Resources (HR) strategy

The HR strategy was developed during the year in consultation with Agency managers and staff, and was approved by the Executive Board in December 2004 and by the Agency Board in January 2005.

HR Division

HR staff from the former medicines and devices sectors are now fully integrated and co-located to form a single division. The structure was designed to help a business-partnering approach providing professional services and support to the organisation. The Agency recognised the importance of HR issues with the creation of a separate division and the appointment of the Director of Human Resources to the Executive Board from April 2004.

Above, from left to right: Crystal Waters, Jemma Jaques, Alberto Rossi, Human Resources

Policy

The aim of the policy function is to ensure that all Agency staff are provided with an HR policy framework that is clear, up to date and accessible. The Agency made considerable progress on the harmonisation of terms and conditions of employment, together with HR policy and procedure, to provide a single set of arrangements. These were regularly reviewed to reflect changes in employment legislation and business requirements. Staff turnover and retention was reviewed, and exit interviews improved, to provide more detailed analysis to help improve staff retention. Best practice guides for managers were produced in core HR policies. As a result of the expertise within the HR team, DH invited the Agency to join a number of its working groups to help policy development. Support was provided to the Arm's-Length Body Review undertaken by DH. One of the outcomes was the transfer of the Device Evaluation Service to the Purchasing and Supply Agency (PASA).

Operations

The aim of the operations function is to provide accurate, consistent advice and support regarding HR policies and procedures within a reasonable time. The average number of staff employed during the year was 781. Recruitment was a major and successful activity, with some 101 internal and 96 external recruitment campaigns during the year, and the Agency achieved a high level of positive feedback from candidates. The Sentinel IT HR computer system was developed further to maximise the services available. Work started on adding the devices staff to the database, which will enable self-service access for all Agency staff later in the year. Professional and proactive support to managers dealing with grievances led to a 73% reduction in formal grievance and employment tribunal cases, with the number of cases now minimal.

Learning and development

As part of the HR strategy, the Agency approved a strategy for learning and development which provides commitment to continuous learning and development.

Organisational development

This provides the framework and support to enable effective leadership and improvement in the overall performance of the Agency. Individual training needs were identified during the annual performance review process, while at the organisational level training was established by consulting with directors and managers. These needs were brought together in the Agency training plan. The management and leadership development programme was a major success, with 54 managers joining the programme in the year. The Agency introduced a new initiative to provide facilitated team-building workshops away from the office. These were seen as very successful in introducing the culture of teamworking and in raising awareness of the value of individual contributions.

People development

Developing people to be committed and to have the right skills to achieve the Agency's objectives and enjoy shared success is another key part of the strategy. A comprehensive programme of training was delivered, with courses in IT, time management and presentation skills. The Agency reviewed its induction process, and improvements were made for new staff with a three-level induction programme culminating in a joint session with the Chief Executive and the Executive Board. Continuing Professional Development in all relevant professions was actively encouraged and supported.

Did you know?

The MHRA employs nearly 800 staff. But we are not resting on our laurels: last year, we conducted 101 internal and 96 external recruitment campaigns to ensure we keep getting the brightest and best working for us.

Continuing Professional Development (CPD)

Revalidation of doctors

The focus on revalidation of doctors in the UK has changed since the publication of the final report of the Shipman Inquiry earlier this year. The inquiry Chairperson, Dame Janet Smith, recommended that the current plans for revalidation, which were due to start in August 2005, be put on hold. She has asked the Chief Medical Officer (CMO) to set up a working party to determine the best way forward. The CMO has issued a consultation document, and MHRA medical staff are encouraged to reply to it. An official Agency response will also follow.

Although the final process of revalidation is unknown, it is fairly certain that it will embrace the protection of patients and an emphasis on doctors' responsibility to keep up to date in their chosen speciality.

With that in mind, the Agency is encouraging its physicians to continue to collect evidence of good practice and to undertake CPD.

CPD for government pharmacists

All practising pharmacists in the UK have to understand, undertake and prove they are doing CPD from the beginning of 2005. The Agency has worked with the statutory body for pharmacists, the Royal Pharmaceutical Society of Great Britain, to develop competencies specifically tailored to the needs of pharmacists working within government. The Agency has run facilitated workshops and coaching opportunities for its pharmacists so that they are fully prepared for this statutory requirement. This is to continue, particularly when revalidation is introduced.

Equality and diversity

The Agency extended its Valuing Diversity Advisory Group to include staff from the former medicines and devices sectors. Work started on developing values, behaviour and working practices that recognise and value the differences between people, help them to realise their potential, enhance their performance and enable them to deliver improved service. This work culminated in the Executive Board approving the use of the Diversity Excellence Model. This model will provide a framework for implementing and measuring diversity in the Agency, and the detailed assessment will be carried out later in the year.

Industrial and employee relations

The Agency held regular meetings with trade union and staff representatives. The previous good and constructive relations were maintained over the year, enabling the Agency to introduce significant change within the spirit of partnership. The MHRA Industrial Relations Council was introduced, and the Chief Executive and Agency directors met senior and local representatives of the trade unions to discuss issues of joint interest.

The Diversity Excellence Model will provide a framework for implementing and measuring diversity in the MHRA.

Staff attitude survey

The Agency asked MORI to run its first staff survey in the summer of 2004. Two-thirds of staff responded through a comprehensive online questionnaire. The response rate compared favourably with MORI's public sector experience, as did the answers to most of the questions for which comparisons were available. The survey demonstrated outstanding levels of commitment to the Agency's objectives (88% of staff) and willingness to speak highly of the Agency's work to people outside (75%). Staff had a lot of pride in working for the Agency. Line managers were viewed relatively favourably, as were several aspects of internal communications. Some 91% acknowledged that they had friendly colleagues.

Staff also gave some less comfortable messages. The Executive Board reviewed all the responses and chose a number of themes for further investigation and action. Several of them were offered for discussion among staff. Those who volunteered for discussion groups added insights to flesh out the bald statistics of the survey. They also made some recommendations for action which the Executive Board considered at the turn of the year. Eight themes will be taken forward during 2005/06, each with Board leadership. Most relate to areas where survey responses gave cause for concern, but a couple are in areas where the Agency wants to see improvements even if it already compares favourably with other organisations. The themes are:

- effective management of change;
- effective internal communications;
- improving physical workplace conditions;
- the Executive Board's visibility, profile and leadership;
- reducing stress and adjusting work–life balances;
- addressing bullying, harassment and discrimination effectively;
- rewarding good performance and valuing and recognising people; and
- focusing on customers.

The first three have targets for improvement in the Business Plan for 2005/06. The Agency hopes to measure improvements at the end of that year or shortly thereafter.

Co-location of Agency staff

The decision to merge the Medical Devices Agency and the Medicines Control Agency raised issues relating to both location and organisation. From the outset, the physical co-location of the majority of staff on one site was seen as an essential prerequisite to creating a single cohesive unit. Investigation of the options available in terms of accommodation took some time, but during the latter part of 2004 it was clear that the use of additional floors within Market Towers was a viable proposition, and a project was initiated to manage the move.

A three-phase approach was adopted to moving the Devices IT infrastructure:

- Phase 1: relocate while maintaining access to current systems delivered through the DH office information system;
- Phase 2: embark upon a programme of technical integration immediately subsequent to the move, migrating Devices staff to the core applications delivered under Sentinel about six months after relocation; and
- Phase 3: integrate business applications under Sentinel.

The target set for the completion of co-location was 31 March 2005. However, problems with the installation of external data links caused a delay and co-location eventually took place a month later. In all other respects the project went well and Devices staff were able to work effectively from their first day in the new office.

Sentinel

During the past year, the Agency has continued to implement its Information Management Strategy which commenced in January 2003. The programme, Sentinel, delivers electronic working both internally within the Agency and externally with its stakeholders.

The Agency implemented four base applications, including document management, which went live together with the business support application for clinical trials in September 2004. The business support application for export certificates went live in January 2005. During the year, the Agency designed and largely built two substantial business support applications for product licensing and process licensing. It also completed the design for the third large component, pharmacovigilance. Product licensing will become operational in the summer of 2005 and will impact on the daily work of nearly 500 staff in the Agency. Process licensing will become operational in the autumn of 2005. Additionally, the external portal will become operational in the autumn and enable companies to send applications to the MHRA electronically via a secure link. The finance component, which was implemented in the previous year, was used from April 2004. As Sentinel becomes operational, new ways of working are needed and the Agency will be undergoing significant change as a result. The Agency rolled out the document management system to all staff and, in preparation for electronic working, some 25 million pages of data and documents were digitised and loaded into the system.

To provide appropriate desktop hardware to enhance electronic working, the Agency rolled out a new desktop to all staff who will be using Sentinel, together with larger, flat screens.

Implementation of Sentinel will assist the Agency's stakeholders by providing effective and efficient electronic means of communication that will enable the MHRA 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.

From left to right: Sean Jones, Licensing, Joanna Barrett, Sentinel, Keith Pugh, Post-Licensing

Working with Government – relations with other government departments

The Agency is responsible for the development of policy relating to the regulation of medicines and devices, and it maintains close links with DH. In particular, it meets three to four times a year with key DH staff in a Medicines Regulatory Policy Forum to review progress on specific policy issues. It maintains close links with the Veterinary Medicines Directorate which regulates veterinary medicines in the UK. It also has regular dealings on specific regulatory issues with a wide range of other government departments, such as Department of Trade and Industry, Home Office, Treasury and Cabinet Office, as well as other regulatory agencies in the UK.

House of Commons Health Select Committee: Report on the Influence of the Pharmaceutical Industry

In June 2004, the Health Select Committee of the House of Commons announced that it planned to hold an inquiry into the pharmaceutical industry. As part of its inquiry, the Committee examined the regulation of medicines in some detail, taking written and oral evidence from senior officials in the Agency.

The report was published in April 2005. It was a wide-ranging report, with recommendations being addressed to different parts of Government and the pharmaceutical industry itself. It raised a number of issues of direct relevance to the regulatory process. They include the need to work with industry on the design of clinical trials, the regulation of advertising and promotion, and the need to introduce new medicines more safely. It also examined the regulatory histories of a small number of high-profile medicines in some detail.

The Agency is already addressing many of the issues raised in the report, such as increasing the patient voice in the regulatory process, the introduction of greater transparency into the regulatory process, and action to protect public health. However, in a time of continuing change, the Agency recognises that the report will have an important influence on the future direction of the Agency and its relationships with patients, prescribers and industry.

From left to right: Katrina Ekberg, Shona Johnson, Fiona Taylor-Smith, Shaezar Karim, Facilities and Estates

Performance against key targets 2004/05

TARGET	OUTCOME
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: 100% within three working days 90% within one working day Serious: 100% within seven working days 95% within three working days	Achieved; all targets met or exceeded (see page 24)
Develop better or additional measures and procedures for assuring and assessing the quality and effectiveness of the Agency's decision making.	Achieved; with development of a Quality Management System for the Agency and benchmarking among EU Member States (see page 46)

Above, from left to right: Cliff Double, Charles Apps, Valerie Field, Imaging and Acute Care

TARGET	OUTCOME
Agree by the end of June 2004 an outline communications strategy for 2004/05 and the actions and resources that are needed to implement that strategy, including the establishment of a dedicated communications function. Implement agreed actions during the year.	Not achieved; there were 45 agreed actions of which 35 were implemented (see page 44)
Issue timely drug alerts and MDAs which identify clear and appropriate action which recipients can achieve within realistic timescales, and review the effectiveness of these alerts.	Achieved; targets met or exceeded (see page 21)
Provide draft replies to 90% of correspondence received by Ministers within 20 days.	Achieved (see page 41)
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.	Achieved; resulting in the development of a European Risk Management Strategy (see page 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.	Achieved; so far as lay within the power of the Agency; the Commission's proposals were delayed (see page 38)
Review the Agency's contacts with and forums for discussion with industry, and establish, with industry, effective and transparent structures and lines of communication.	Achieved; with a range of regular meetings both formal and informal (see page 37)
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 services to its customers.	Achieved; through the development of the Quality Management System and through forthcoming surveys of public perceptions and those of GPs (see page 18)
Develop and implement by the end of July 2004 an organisational structure and decision-making forums to suit the needs of the merged Agency.	Achieved; through a unified Executive Board and a number of sub-committees (see page 11)
Subject to approval of the business case, co-locate all London-based staff in a single building and achieve this with the minimum of disruption to services and staff (an average of no more than three days' loss of productive working time for staff whose locations change, excluding those supervising the move).	Not achieved; co-location took place on 3 May 2005 (see page 53)
Ensure that the Agency achieves its agreed budgeted surplus.	Achieved (see page 60)

Performance against these key targets has been verified by independent auditors.

Looking forward

"None of the Agency's achievements would be possible without an outstanding contribution from its staff. I would like to thank them and look forward to working together with them over the coming year."

Professor Kent Woods, Chief Executive Officer

Key targets for 2005/06

1. Implement proposals for a new medicines advisory body structure, and introduce revised codes of practice on the interests in the pharmaceutical industry of committee members and staff by October 2005.

2. Promote and demonstrate wider use of the GPRD and Yellow Card database in the interests of medicines safety and reduced medication error, with measured increased usage in both databases.

3. Capture more promptly the reports of ADRs and device adverse incidents, initiating timely and appropriate action to protect public health, particularly for those reports in which medication error is suspected.

Above, from left to right: Tom Clutton-Brock, Jonathan Plumb, Michael Peel, Susanne Ludgate, Devices Clinical

Maximum number of working days between receipt of reports and making them available for evaluation and analysis:

- three for fatal and serious device adverse incidents;
- three for fatal ADRs and five for serious reactions; and
- seven for identification and transmission of suspected medication errors to the National Patient Safety Agency.

4. Provide health professionals with greater knowledge about the regulation and safe usage of medicines and devices, produce and pilot at least two new postgraduate-level education programmes or tools for assessment which are acceptable to relevant professional bodies and, at undergraduate level, secure agreement for the introduction in 2006/07 of examination questions relating to medicinal products in at least four medical school curricula.

5. Engage proactively with the public and healthcare professionals, in particular promoting understanding of risk and drawing attention to the dangers of Internet sales, positioning this work in the development and agreement by July 2005 of a wider two-year communications strategy containing actions that will be completed by March 2006.

6. Improve the transparency of decision making within the Agency, and accountability to the public, by publishing UK Public Assessment Reports for medicinal products licensed from October 2005, by providing summaries of the evidence supporting major safety decisions, and by ensuring that all requests under the Freedom of Information Act are replied to within 20 working days, with internal reviews showing 90% of them complying with the principles contained in the Act and guidance issued by the Department for Constitutional Affairs and the Information Commissioner.

7. Implement the new UK legislation for improving patient information leaflets (PILs), including through 'user testing' with target patient groups. By 30 October 2005, issue practical guidance for company-initiated applications as developed through Europe. Arrange for user testing of PILs for ten priority medicines, taking into account medication error, other safety concerns, specific target populations such as children, and/or widespread usage.

8. Within one month of receiving the European Commission's expected legislative proposals on the regulation of tissue-engineered products, and of its expected draft amending directive on medical devices, agree timetabled plans for the launch and conduct of negotiations during the UK Presidency; and fulfil those plans.

9. Assessment of clinical trial authorisations for medicines:

   - *Phase I (normal volunteer) trials:*
     100% in 21 calendar days
     with an average of 14 calendar days or less

   - *All other trials*
     100% in 30 calendar days

   - Assessment of clinical investigation notifications for medical devices:
     100% in 60 days
     with an average of 54 days or less

10. Increase the number of appropriately labelled medicines for children, including in at least two new therapeutic classes, and ensure relevant and up-to-date advice for paediatric medicines is available for health professionals and patients.

Medicines and Healthcare products Regulatory Agency

Accounts
2004/05

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 2005. 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 and the Medical Devices Agency. 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.

Main activities

The aim of the MHRA is 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
- 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 2004/05 together with information on future developments.

Results

The results for the year are set out on page 73. There was an operating surplus of £1.030 million (2003/04 £8.324 million). Income for the year was £72.420 million (2003/04 £67.032 million) and expenditure was £71.390 million (2003/04 £58.708 million). Interest receivable was £1.039 million (2003/04 £0.790 million) and interest payable was £0.200 million (2003/04 £0.199 million). The dividend payable on public dividend capital (PDC) was £0.300 million (2003/04 £0.246 million).

After the inclusion of interest and dividends, the retained surplus for the year was £1.569 million (2003/04 £8.669 million). The retained surplus carried forward is £14.138 million (2003/04 £12.569 million).

The overall increase in income of £5.388 million is due to an increase in Department of Health funding of £0.158 million and an increase of £5.230 million arising from an improved trading performance in licensing and inspections, service fees, BP, GPRD and other income sources. The Department of Health funding increase comprises an increase of £1.481 million for medical devices work and £1.227 million towards relocation costs partly offset by the non-recurrence of a £2.600 million subsidy paid by the Department of Health in 2003/04.

The increase in expenditure of £12.682 million comprises an increase in staff costs of £2.976 million and an increase in other operating costs of £8.879 million. The increase in other operating costs arises mainly from computing costs connected with the Sentinel programme, accommodation costs largely for new space, and the cost of relocating London-based staff into one building. Depreciation costs increased by £0.827 million.

Fees for the MHRA's medicine regulation activities were increased by 3.7% from April 2004. For 2005/06 there is no general increase in fees. Some new fees have been introduced and some are planned for later in the year (following appropriate consultation) to fund changes arising mainly from the 2001 review of medicines regulations and the directive for traditional herbal medicines. 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. The Agency is on target to achieve this return. The dividend payable on PDC is £0.300 million (2003/04 £0.246 million). The amount of dividend payable is agreed each year in advance with the Department of Health.

MHRA management carried out an impairment review of the information management assets for GPRD and the Sentinel programme. The intention of the review, which has been carried out in compliance with Financial Reporting Standard (FRS) 11 'Impairment of Tangible Fixed Assets and Goodwill', was to establish whether the current cash flow projections for those assets supported the carrying value of the assets recognised in the Agency's balance sheet.

The realisable savings and opportunities to develop further income streams support the carrying value of the Sentinel assets. Current projections show that the net present value of future cash flows arising from operating the GPRD asset is £7.710 million. The carrying value of the asset has therefore been written down to this value, an impairment of £2.500 million. This impairment charge has been deducted from the revaluation reserve.

Before the impairment charge and indexation, the assets increased in value by £6.291 million. The major part of this expenditure is related to the Sentinel programme.

The auditor of the MHRA is the Comptroller and Auditor General and the costs of the audit were £0.085 million (2003/04 £0.103 million). No non-audit work was undertaken by the Comptroller and Auditor General.

Details of the post-balance sheet events affecting the Agency are set out in Note 24.

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 2004 and March 2005, 77% of invoices by number (2003/04 98%) were paid in accordance with these terms.

MHRA senior management

During the year, the senior management arrangements included the Agency Board and an Executive Board (established on 1 April 2004).

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

Professor Sir Alasdair Breckenridge	Chairman
Professor Kent Woods	Chief Executive
Ms Lisa Arnold	Non-Executive Director
Miss Shelley Dolan	Non-Executive Director
Mr Michael Fox	Non-Executive Director
Mr Charles Kernahan	Non-Executive Director
Professor Angus Mackay	Non-Executive Director
Mr Garry Watts	Non-Executive Director

The members of the Executive Board during the year were:

Mr R K Alder	
Mr C Bray	
Mr S Gregor	joined 31 January 2005
Mr G Heddell	joined 4 January 2005
Miss D Hepburn	
Dr I Hudson	
Mr G Le Fevre	
Dr S Ludgate	
Dr G Munro	left 31 May 2004
Dr J M Raine	
Mr S Rogers	
Mr G Savage	
Mr J Taylor	June 2004 – December 2004
Dr L Wood	left 31 December 2004
Professor K Woods	

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, 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.

Professor Kent Woods
Chief Executive and Accounting Officer
23 November 2005

Statement of the Agency's and Chief Executive's responsibilities

Under Section 4(6) of the Government Trading Funds Act 1973, the Treasury has directed the Medicines and Healthcare products Regulatory Agency (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 for the year ended 31 March 2005

1 Scope of responsibility

As Accounting Officer, I have responsibility for maintaining a sound system of internal control that supports the achievement of the Medicines and Healthcare products Regulatory Agency's (MHRA's) policies, aims and objectives while safeguarding the public funds and assets for which I am personally responsible in accordance with the responsibilities assigned to me in *Government Accounting*.

The MHRA came into existence on 1 April 2003 on the merger of the Medicines Control Agency and the Medical Devices Agency. I have been the Chief Executive and Accounting Officer throughout the year to 31 March 2005.

To support me in my role as Accounting Officer, there is an Agency Board, an Executive Board and a Risk and Audit Committee. The Agency's risk management system, based on guidance produced by the Department of Health, National Audit Office and Treasury, has operated independently of the Department of Health but the Department has been kept informed through its representative on the Agency's Risk and Audit Committee. The National Audit Office is the Agency's external auditor. Bentley Jennison was reappointed as the Agency's internal auditor for three years commencing 1 April 2005, following a re-tendering exercise for the internal audit service, on the cessation of the previous contract.

2 The purpose of the system of internal control

The Agency's system of internal control is designed to manage risk to a reasonable level rather than to eliminate all risk of failure to achieve policies, aims and objectives; it can therefore only provide reasonable and not absolute assurance of effectiveness. The system of internal control is based on an ongoing process designed to identify and prioritise the risks to the achievement of the Agency's policies, aims and objectives, to evaluate the likelihood of those risks being realised and the impact should they be realised, and to manage them efficiently, effectively and economically. The Agency's system of internal control has been in place for the year to 31 March 2005 and up to the date of approval of the annual report and accounts, and accords with Treasury guidance.

3 Capacity to handle risk

A risk management framework, standard operating procedure and an Agency guide to risk management have been in place and updated as appropriate. Information about corporate governance and risk management has been incorporated into the induction procedure. All these documents have been placed on the MHRA Intranet and were available to all staff. A dedicated risk management unit was set up with a risk management co-ordinator available to facilitate risk management training and to provide risk management support. A risk management seminar to foster risk awareness was held during the year, to which all staff were invited.

The systems of internal control and risk management have been endorsed by the Agency Board, the Executive Board and the Risk and Audit Committee, and were in existence throughout the year.

The Executive Board is responsible for the identification and monitoring of the Agency's high-level risks. The Executive Board reviews the Agency's high-level risk register on a quarterly basis and maintains corporate responsibility for the operation of the risk management system.

The Agency is committed to continuous improvement of its risk management system and has consequently agreed to an annual review by the internal auditor to highlight examples of best practice that could be considered for adoption by the Agency. One such observation was that the interests of stakeholders be specifically recognised in the Agency's standard operating procedure on risk management and associated guidance.

4 The risk and control framework

The most practical means of undertaking risk assessments has been through round table discussions. Identification of the context of risk has 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 government.

A single risk management and corporate governance system has been in place throughout the year. All high-level risks are owned and monitored by specific members of senior management.

An Agency high-level risk register was created following an Executive Board workshop in July 2004. This document was approved by the Executive Board in September 2004 and subsequently reviewed and updated in December 2004 and March 2005. The identification and management of risks is integrated into the Agency's planning system. Regular reports are submitted to the Risk and Audit Committee, where the high-level risk register is also discussed.

Divisional risk registers are maintained at operational level and record the risks identified and the action taken to mitigate these risks. These are dynamic working documents that are updated regularly in order to ensure that the risk registers reflect the most up-to-date position.

To strengthen the Agency's risk management system, a cross-Agency Risk and Audit Liaison Group was formed. Its main purpose is to create a forum where divisional risk and audit issues can be discussed and monitored by senior representatives from all divisions of the Agency, and, if appropriate, make recommendations to the Executive Board.

In compliance with their stewardship responsibilities, each divisional head is required to complete an annual statement of accountability, confirming that systems of effective internal control have been in place, within their areas of responsibility, throughout the period under review.

The internal audit service adopts a risk-based approach in its regular cycle of internal audits of the Agency's operations. An annual statement of assurance is prepared by the Internal Auditor for the Agency's Accounting Officer.

5 Significant internal control issues

During the year ended 31 March 2005, the finance function underwent a significant change in personnel. In addition, the Agency's plan to implement an upgraded suite of operating systems required the introduction of a new accounting system. This combination, exacerbated by some significant weaknesses in the internal financial control environment which became more critical during the year, has required extensive manual interventions in the preparation of the year end financial statements. As set out below, both the internal and external auditors have drawn attention to these internal financial control weaknesses, and pointed out their potentially serious nature. Specifically in relation to the audit of the 2004/05 financial statements, the National Audit Office, in an interim report, identified a number of significant weaknesses in internal financial control, which, if left unresolved, could have serious consequences.

The internal financial control weaknesses during the year, their cause, the auditors' comments thereon and the preparation of the year end financial statements have been discussed and reviewed by the Agency's Risk and Audit Committee, together with all other audit reports. As soon as the Risk and Audit Committee became aware of the problems in June 2005, the Committee Chairman requested a firm programme of action from the Agency describing what would be done to resolve the issue. Additional resources, and the manner in which these resources would be deployed, were also discussed. Since then the Agency's finance section has been examining the various control accounts to reconcile them to the underlying records. I have held regular meetings with the Committee Chairman, the National Audit Office and the finance section to ensure the completion of the financial statements in a form which was suitable of receiving a clear audit opinion. In relation to internal financial control weaknesses, I have arranged for regular reports from the finance section to provide an assurance that adequate financial controls are in operation.

In addition to the routine internal audit of these, I am also exploring the commissioning of an external review of the Agency's financial controls. The Committee has assured me that, provided the identified internal financial control weaknesses are addressed, the necessary amendments to the new accounting system are made, and the financial control systems are regularly monitored, then the identified risks to the Agency's objectives will have been managed to a reasonable level.

6 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 is informed by the work of the internal auditor and the divisional heads within the Agency who have responsibility for the development and maintenance of the internal control framework, and comments made by the external auditor in his management letter and other reports. I have been advised on the implications of the result of my review of the effectiveness of the systems of internal control by the Agency Board, the Executive Board, and the Risk and Audit Committee.

Corporate governance management structure

The Agency Board, consisting of a Chairman, six Non-Executive Directors and the Chief Executive of the Agency, was in place throughout the year to 31 March 2005. The Agency Board has met monthly to discuss the Agency's plans and strategic direction and to take action as appropriate. As a civil servant, the Chief Executive is answerable to the Civil Service Code of Conduct. A register of interests is maintained for Agency and Executive Board members and all staff.

The Executive Board, consisting of divisional heads, has also convened monthly to formally discuss the Agency's plans and to take executive responsibility for the operational management of the Agency. As part of this agenda, the Agency's risk management strategy and high-level risks have been reviewed on a regular basis.

Quarterly reports were sent to me and to the Executive Board, setting out the Agency's key performance targets and monitoring their progress. In addition, the reports brought to our attention any control issues through the early warning processes embedded within the Agency's business operations.

The Agency's risk management and corporate governance systems were each subject to an internal audit review during the year and received substantial assurances. The review confirmed that robust risk management and corporate governance arrangements had been established in the Agency.

The Risk and Audit Committee

The Risk and Audit Committee is an important part of the Agency's risk management system. The Committee has met four times during the year to 31 March 2005. It reviewed the Agency's annual report and accounts for 2003/04, the effectiveness of the Agency's risk management system, the external audit plans for the 2004/05 audit of the financial statements and the 2005/06 internal audit plan. The Committee discussed and considered audit reports from the internal auditor and the management letter on internal control from the National Audit Office, reviewed the 2003/04 annual assurance statement from the internal auditor and gave advice to the Chief Executive on the level of assurance provided by the internal and external audit reports.

Internal audit

The role of the internal audit service is to provide management with an objective assessment of whether systems and controls are working properly. It is a key part of the Agency's internal control system because it measures and evaluates the adequacy and effectiveness of other controls. The Agency's internal audit service throughout the year was provided by Bentley Jennison, who operated to the standards defined in the *Government Internal Audit Manual*. Bentley Jennison was reappointed as the Agency's internal auditor for a period of three years from 1 April 2005, following a re-tendering exercise.

The partner in charge of the Agency's internal audit service performed the role of Head of Internal Audit. He has produced regular reports on the adequacy and effectiveness of the systems of internal control in various operational areas, together with recommendations for improvement.

The audit programme for 2004/05 was based on the risks identified within the Agency. The internal audit team completed 15 audits, which supported the annual assurance statement. Ten of these audits, including those of risk management and corporate governance, received substantial assurances and three received adequate assurances. In addition, there were two specialist audits. There were no limited assurance opinions and no fundamental recommendations made during the year.

Various action plans, to address the recommendations in the internal audit reports, were agreed by operational management and co-ordinated by the Agency's risk management team. The implementation of recommendations made in a number of previous reports was subject to a 'follow-up' audit carried out during the year. Where the implementation of recommendations was not achieved by 31 March 2005, the action plans were carried forward into 2005/06.

The Head of Internal Audit has also provided an independent opinion and an overall assessment of the Agency's system of internal control, in an annual end of year report. The report concluded that, subject to the comments on internal financial control, in his opinion the Agency had adequate and effective risk management, control and governance processes in place to manage the achievement of the organisation's objectives. In relation to internal control in particular, the report also confirmed that adequate and effective control processes were in place to manage the achievement of the Agency's objectives, except in areas of financial control, where certain follow-up work identified that a number of the key control account reconciliations recommended as part of the 2003/04 work had still to be implemented. Unless addressed, these would have an impact on the Agency's financial control framework, particularly the integrity of the financial management information.

Accounting Officer's comment

Internal financial control weaknesses have been identified and are being addressed. The issues were more complicated than originally considered and consequently took longer to resolve. Steps are also being taken to manage the new accounting systems appropriately. The internal financial control systems are to be the subject of regular monitoring through the year by the internal auditor and the Risk and Audit Committee, to give me an assurance that the remedial action has been fully effective.

Professor Kent Woods
Chief Executive and Accounting Officer
23 November 2005

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 73 to 96 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 77 to 79.

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

As described on page 65, 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 guided by the Auditing Practices Board and the auditing profession's ethical guidance.

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 66 to 70 reflects the Agency's compliance with Treasury's guidance *Corporate governance: 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.

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 2005 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
13 December 2005

Income and expenditure account for the year ended 31 March 2005

Notes		2004/05 £'000	2003/04 £'000
3	Trading income	72,420	64,432
	Department of Health subsidy	–	2,600
		72,420	67,032
5	Staff costs	33,988	31,012
7	Other operating costs	33,719	24,840
9	Depreciation	3,683	2,856
		71,390	58,708
	OPERATING SURPLUS	1,030	8,324
8	Interest receivable	1,039	790
	Interest payable	(200)	(199)
	SURPLUS FOR THE YEAR	1,869	8,915
	Dividend payable on public dividend capital	(300)	(246)
14	RETAINED SURPLUS FOR THE YEAR	1,569	8,669
	Opening retained surplus	12,569	3,900
	RETAINED SURPLUS CARRIED FORWARD	14,138	12,569

NOTE: There were no acquired or discontinued operations during the year.
The notes on pages 77 to 96 form part of these Accounts.

Statement of recognised gains and losses for the year ended 31 March 2005

Notes		2004/05 £'000	2003/04 £'000
	Retained surplus for the year excluding dividend payment	1,869	8,915
14	GPRD impairment	(2,500)	(7,500)
14	Department of Health loans	–	3,400
14	Unrealised surplus on revaluation	68	53
	TOTAL RECOGNISED (LOSSES)/GAINS	(563)	4,868

The notes on pages 77 to 96 form part of these Accounts.

Balance sheet as at 31 March 2005

Notes		31 March 2005 £'000	31 March 2004 £'000
	FIXED ASSETS		
9	Tangible fixed assets	30,527	26,668
	CURRENT ASSETS		
10	Debtors	17,131	6,142
17	Cash at bank and in hand	9,987	22,276
		27,118	28,418
11	Creditors: amounts falling due within one year	(14,517)	(10,882)
	Net current assets	12,601	17,536
	TOTAL ASSETS LESS CURRENT LIABILITIES	43,128	44,204
11	Creditors: amounts falling due after more than one year	(4,728)	(4,728)
12	Provisions for liabilities and charges	(846)	(998)
13	Deferred revenue	(16,785)	(16,846)
	TOTAL NET ASSETS	20,769	21,632
	FINANCED BY:		
14	CAPITAL AND RESERVES		
	Public dividend capital	1,329	1,329
	Revaluation reserve	4,708	7,734
	Retained surplus	14,732	12,569
	TOTAL CAPITAL EMPLOYED	20,769	21,632

The notes on pages 77 to 96 form part of these Accounts.

Professor Kent Woods
Chief Executive and Accounting Officer
23 November 2005

Cash flow statement for the year ended 31 March 2005

Notes		2004/05 £'000	2003/04 £'000
15	NET CASH (OUTFLOW)/INFLOW TO OPERATING ACTIVITIES	(3,783)	12,497
	RETURNS ON INVESTMENTS AND SERVICING OF FINANCE		
	Interest received	1,062	759
	Interest paid	(132)	(142)
	Dividend paid on public dividend capital	–	–
	NET CASH INFLOW FROM RETURNS ON INVESTMENTS AND SERVICING OF FINANCE	930	617
	CAPITAL EXPENDITURE		
	Payments to acquire fixed assets	(9,436)	(6,968)
	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
17	(DECREASE)/INCREASE IN CASH FOR THE YEAR	(12,289)	9,546

The notes on pages 77 to 96 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 2004/05. 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 other than assets under the course of construction, at their value to the business by reference to their current costs.

b 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
Sentinel architecture costs	7 years
Office refurbishment costs	10 years
GPRD data	20 years

c 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.

d 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.

e 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 Executive Board, 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.

f 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.

g 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 97. 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 that 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 those provided out of government funds, namely from public dividend capital (PDC), medium-term loans and the revaluation reserve, excluding values in respect of GPRD data. The actual operating surplus for the year was £1.030 million (2003/04 £8.324 million). The dividend payable on PDC is £0.300 million (2003/04 £0.246 million). The amount of dividend payable is agreed each year in advance with the Department of Health.

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.

3 Income

	2004/05 £'000	2003/04 £'000
Licences and inspections income invoiced during the year	31,817	31,489
Service fee income invoiced during the year	18,940	17,632
	50,757	49,121
Add: income deferred from previous periods (see Note 13)	16,433	12,264
Less: income deferred to future periods (see Note 13)	(16,122)	(16,433)
Income relating to work done in the year	51,068	44,952
Income from miscellaneous activities	6,611	7,497
Department of Health funding	14,741	11,983
	72,420	64,432

	£'000	2004/05 £'000	2003/04 £'000
Licences and inspections			
Applications	18,102		
Clinical trials	853		
EMEA	2,375		
Inspection	3,144		
Renewals	87		
Variations	6,891		
Other	676	32,128	27,320
Service fees		18,940	17,632
Miscellaneous income			
British Pharmacopoeia	1,744		1,767
GPRD	2,902		2,741
Remote Access to marketing Authorisations	564		784
Seminar and twinning	752		547
Other	649	6,611	1,658
Department of Health funding		14,741	11,983
		72,420	64,432

The miscellaneous income for the year is shown net of £0.663 million deferred to future periods (31 March 2004 £0.413 million).

4 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. Department of Health funding in relation to devices activities is also intended to cover the costs of providing this specific service.

	2004/05		2003/04	
	Devices £'000	Medicines £'000	Devices £'000	Medicines £'000
Trading income	415	57,264	584	51,865
Department of Health funding	14,741	–	11,983	–
Department of Health subsidy	–	–	600	2,000
	15,156	57,264	13,167	53,865
Operating costs	(14,673)	(56,717)	(12,167)	(46,541)
Operating surplus	483	547	1,000	7,324

Department of Health funding of £14.741 million includes £1.227 million in respect of the co-location project (see Note 7).

Following the implementation of a time-recording system during 2004/05, the Agency is currently developing a more sophisticated overhead costing model that will enable it to provide more easily information regarding its segmental activities in future years.

5 Staff costs

	2004/05 £'000	2003/04 £'000
Salaries and wages	26,222	24,249
Social security costs	2,340	2,130
Pension contributions	3,874	3,532
	32,436	29,911
Agency and other staff costs	1,499	1,058
Early retirement and redundancy costs	53	43
	33,988	31,012

Pension

The employees of the MHRA, excluding the Chief Executive, are covered by the provisions of the Principal Civil Service Pension Scheme (PCSPS). The PCSPS is an unfunded, multi-employer, defined benefit scheme. The benefit expenditure of the PCSPS is met as it falls due on a pay-as-you-go basis and there is no separate fund of assets to pay the retirement benefits. Employer contributions are based on the costs of pension rights being accrued by employees. For 2004/05, normal employer contributions of £3.874 million were payable to the PCSPS (2003/04 £3.532 million) at rates in the range 12.0% to 18.5% of pensionable pay. The employer's contribution rates are set periodically following an actuarial valuation. The scheme actuary carried out a valuation as at 31 March 2003. As a result, new contribution rates have been set and are being staged over two years. The rates applicable from 1 April 2005 are in the range 16.2% to 24.6% and from 1 April 2006 are in the range 17.1% to 25.5%. The next scheme valuation is due as at 31 March 2007.

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 ten 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 ten 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 to 25% of the fund as a lump sum.

6 Employee details

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

	2004/05	2003/04
Senior management	12	14
Civil service staff	693	664
Secondees	1	2
Short-term contracts	75	67
	781	747

The Chairman's total remuneration for the year, excluding pension contribution, was £75,250. The Chief Executive, who is on secondment to the Agency, received £160,000. 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:

	£
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

Salaries and pension entitlements of the Executive Board

	Salary (as defined below) £'000	Real increase in annual pension and related lump sum at age 60 £'000	Total accrued annual pension and related lump sum at age 60 at 31 March 2005 £'000	CETV at 31 March 2004 £'000	CETV at 31 March 2005 £'000	Real increase in CETV £'000
Mr Roy Alder – Executive Support Director	105–110	5.0–7.5	195–200	845	908	23
Mr Simon Gregor – Director of Communications	10–15	0.0–2.5	0–5	–	2	1
Mr Gerald Heddell – Director of Inspection and Standards Division	20–25	0.0–2.5	0–5	–	5	2
Mr Geoff Le Fevre – Director of Human Resources	85–90	2.5–5.0	10–15	33	53	18
Mr Graham Savage – Director of Finance	100–105	2.5–5.0	78–80	308	343	19

Mr Simon Gregor joined the Agency on 31 January 2005.

Mr Gerald Heddell joined the Agency on 4 January 2005.

Salary

Salary includes gross salary, performance pay or bonuses, overtime, reserved rights to London weighting or London allowances, recruitment and retention allowances, private office allowances and any other allowance to the extent that it is subject to UK taxation.

Pension

The pension arrangements are as described in Note 5 above.

Benefits in kind

None of the above received benefits in kind during 2004/05.

Cash equivalent transfer values

Columns 5 and 6 of the table above show the member's cash equivalent transfer value (CETV) accrued at the beginning and the end of the reporting period. Column 7 reflects the increase in CETV effectively funded by the employer. It takes account of the increase in accrued pension due to inflation, contributions paid by the employee (including the value of any benefits transferred from another pension scheme or arrangement) and uses common market valuation factors for the start and end of the period.

A CETV is the actuarially-assessed, capitalised value of the pension scheme benefits accrued by a member at a particular point in time. The benefits valued are the member's accrued benefits and any contingent spouse's

pension payable from the scheme. A CETV is a payment made by a pension scheme or arrangement to secure pensions benefits in another pension scheme or arrangement when the member leaves a scheme and chooses to transfer the benefits accrued in their former scheme. The pension figures shown relate to the benefits that the individual has accrued as a consequence of their total membership of the pension scheme, not just their service in a senior capacity to which disclosure applies.

The CETV figures include the value of any pension benefit in another scheme or arrangement that the individual has transferred to the civil service pension arrangements and for which the Civil Superannuation Vote has received a transfer payment commensurate to the additional pension liabilities being assumed. They also include any additional pension benefit accrued to the member as a result of their purchasing additional years of pension service in the scheme at their own cost. CETVs are calculated within the guidelines and framework prescribed by the Institute and Faculty of Actuaries.

The following members of the Executive Board have exercised their rights not to disclose salary and pension rights and such information is not included in the table above: Mr C Bray, Miss D Hepburn, Dr I Hudson, Dr S Ludgate, Dr G Munro, Dr J M Raine, Mr S Rogers, Mr J Taylor and Dr L Wood.

The emoluments for the year of the members of the Executive Board fell within the following ranges:

	Number of employees	
	2004/05	2003/04
£0–£9,999	–	1
£10,000–£19,999	1	1
£20,000–£29,999	1	1
£30,000–£39,999	–	–
£40,000–£49,999	–	1
£50,000–£59,999	–	–
£60,000–£69,999	–	1
£70,000–£79,999	–	1
£80,000–£89,999	3	3
£90,000–£99,999	1	1
£100,000–£109,999	2	2
£110,000–£119,999	1	4
£120,000–£129,999	1	–

During 2004/05, no payment was made to any member of the Executive 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).

7 Other operating costs

	2004/05 £'000	2003/04 £'000
Accommodation	7,254	5,848
Audit fee	85	103
Charge for permanent impairment in value of fixed assets	–	221
Clinical assessment	25	18
Committee costs	498	425
Computing	9,347	6,497
Consultancy	785	615
Contracted-out administration services	744	664
Contracted-out personnel and payroll services	615	392
Increase in debt provision	1,270	321
Debt written off	3	50
Device evaluation services	3,033	3,507
Foreign exchange (gain)	(25)	(100)
Irrecoverable VAT	600	–
Legal services	866	877
Loss on disposal	–	3
Marketing	126	145
Medicines testing and laboratory expenses	1,105	751
Other administration costs	859	794
Pharmacovigilance database and other costs	492	347
Printing, stationery and distribution	1,472	1,323
Relocation costs	1,227	–
Telecommunication costs	903	489
Training	1,010	572
Travel and subsistence	1,425	978
	33,719	24,840

a Relocation costs of £1.227 million were incurred by the Agency during 2004/05 as part of its commitment to accommodate all of its employees at Market Towers. These costs can be analysed as follows:

	2004/05 £'000	2003/04 £'000
Computing	45	–
Computing equipment	236	–
Consultancy	342	–
Miscellaneous costs	(7)	–
Printing, stationery and distribution	1	–
Telecommunication costs	70	–
Training	22	–
Utilities	518	–
	1,227	–

b 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.

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

	2004/05 £'000	2003/04 £'000
Rent	3,883	3,141
Catering equipment	31	29
Photocopiers	24	11
IT equipment	455	1
	4,393	3,182

8 Interest receivable

	2004/05 £'000	2003/04 £'000
Bank accounts	1,039	790
	1,039	790

Funds held in the Paymaster General's account earn interest at the rate payable on 'ways and means' advances.

9 Tangible fixed assets

	Total	Computer and telecom equipment	Computer systems and software	Laboratory equipment	Fittings, furniture and office equipment	Assets under construction	GPRD data
	£'000	£'000	£'000	£'000	£'000	£'000	£'000
Cost or valuation							
At 1 April 2004	52,931	3,497	17,384	888	7,126	8,623	15,413
Additions	9,974	430	2,189	47	–	6,597	711
Disposals	–	–	–	–	–	–	–
Indexation	173	–	–	19	154	–	–
Other revaluation	(2,500)	–	–	–	–	–	(2,500)
Transfers	–	511	5,557	–	–	(6,068)	–
At 31 March 2005	60,578	4,438	25,130	954	7,280	9,152	13,624
Depreciation							
At 1 April 2004	26,263	2,286	13,777	466	4,414	–	5,320
Disposals	–	–	–	–	–	–	–
Indexation	105	–	–	10	95	–	–
Other revaluation	–	–	–	–	–	–	–
Charge for the year	3,683	306	2,150	129	504	–	594
At 31 March 2005	30,051	2,592	15,927	605	5,013	–	5,914
Net Book Value							
At 1 April 2004	26,668	1,211	3,607	422	2,712	8,623	10,093
At 31 March 2005	30,527	1,846	9,203	349	2,267	9,152	7,710

The GPRD data asset was valued at 31 March 2005 by consultants from the Agency's internal auditor, Bentley Jennison (Chartered Accountants and Registered Auditors), on the basis of value in use. This has resulted in an impairment of £2.500 million which has been charged against the balance held in the revaluation reserve. The discount rate used was 3.5%, which is the Treasury discount rate.

10 Debtors

	31 March 2005 £'000	31 March 2004 £'000
Trade debtors	13,635	2,866
Prepayments	470	238
Other debtors	1,416	1,482
Accrued income	1,610	1,556
	17,131	6,142

Trade debtors are shown net of a provision for irrecoverable debts of £2.135 million (31 March 2004 £0.864 million) and of a provision for credit notes of £1.914 million (31 March 2004 £2.116 million).

Debtors includes £3.795 million due to the MHRA by the Department of Health as follows:

	31 March 2005 £'000
Trade debtors	1,769
Other debtors	1,425
Accrued income	601
	3,795

11 Creditors

	31 March 2005 £'000	31 March 2004 £'000
Amounts falling due within one year		
Accrued expenses	6,852	6,650
Other creditors	51	1,688
Payments received on account	6,274	2,127
Taxation and social security	822	104
Trade creditors	518	313
	14,517	10,882

Creditors includes £0.822 million due to the Department of Health in respect of taxation and social security.

	31 March 2005 £'000	31 March 2004 £'000
Amounts falling due after more than one year		
Due to Department of Health	4,728	4,728

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

	Total £'000	Between one and two years £'000	Between two and three years £'000	Between three and five years £'000	2003/04 £'000
Fixed interest rate					
4.00%	1,000	1,000	–	–	1,000
4.15%	1,000	–	1,000	–	1,000
4.30%	1,000	–	–	1,000	1,000
4.35%	1,728	–	–	1,728	1,728
At 31 March 2005	4,728	1,000	1,000	2,728	
At 31 March 2004	4,728	1,000	1,000	2,728	4,728

There are no repayments of the loan due within one year.

12 Provision for liabilities and charges

	31 March 2005 £'000	31 March 2004 £'000
Early retirement voluntary severance		
Opening position	527	617
Utilised during year	(127)	(125)
Provided in year	136	128
Reversed unused	(161)	(93)
	375	527
Other provisions		
Opening position	471	929
Utilised during year	–	(438)
Provided in year	–	(20)
Reversed unused	–	–
	471	471
Total provisions	846	998

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.

Other provisions

During 2003/04, a provision was established for the anticipated costs of asbestos safety work within the Agency's Market Towers head office. Further information regarding this work is set out in Note 19.

13 Deferred revenue

	31 March 2004 £'000	Movement £'000	31 March 2005 £'000
Licence fees (applications and variations)	16,433	(311)	16,122
Other fees	413	250	663
	16,846	(61)	16,785

The net movement in deferred revenue is £0.061 million. Revenue deferred at 31 March represents the value of outstanding applications received prior to that date.

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.

14 Capital and reserves

	Government funds		Reserves	
	Total £'000	Public dividend capital £'000	Revaluation reserve £'000	Retained surplus £'000
Balance at 1 April 2004	21,632	1,329	7,734	12,569
Movements 2004/05				
Further borrowings	–	–	–	–
Revaluation of data assets	(2,500)	–	(2,500)	–
Indexation	68	–	68	–
Retained surplus for year	1,569	–	–	1,569
	20,769	1,329	5,302	14,138
Realised depreciation	–	–	(594)	594
Balance at 31 March 2005	20,769	1,329	4,708	14,732

The realised depreciation offsets the charge for the year shown in Note 9.

15 Reconciliation of surplus to net cash inflow from operating activities

	2004/05 £'000	2003/04 £'000
Operating surplus	1,030	8,324
Depreciation	3,683	2,856
Revenue deferred to future periods (Note 13)	16,785	16,846
Revenue deferred from past periods (Note 13)	(16,846)	(12,899)
Increase in debtors	(11,012)	(1,415)
Increase/(decrease) in creditors	2,729	(961)
(Decrease) in provisions	(152)	(548)
Other non-cash items	–	294
Net cash (outflow)/inflow from operating activities	(3,783)	12,497

16 Reconciliation of net cash flow to movement in net funds

	2004/05 £'000	2003/04 £'000
(Decrease)/increase in cash for year	(12,289)	9,546
Cash released from liquid resources	–	–
Repayment of PDC and loans	–	–
New loans granted	–	3,400
Creation of PDC and loans	–	2,657
Movement in net funds	(12,289)	15,603
Net funds at end of previous year	28,333	12,730
Net funds at end of year	16,044	28,333

17 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 loan £'000
Balance at 1 April 2004	28,333	22,276	1,329	4,728
Movements 2004/05				
Loans	–	–	–	–
PDC	–	–	–	–
Decrease in cash at bank	(12,289)	(12,289)	–	–
Balance at 31 March 2005	16,044	9,987	1,329	4,728

18 Capital commitments

	31 March 2005 £'000	31 March 2004 £'000
Contracted	2,634	6,220
Authorised by the Management Board but not contracted	3,420	1,749

The above capital commitments represent capital expenditure commitments for the MHRA as at 31 March 2004 and 31 March 2005.

19 Contingent liabilities

During 2003/04, a provision was established for the anticipated costs of asbestos safety work within the Agency's Market Towers head office. This work was due to be completed during 2004/05; however, before it can be completed, it is necessary to carry out a further risk assessment. Since the original provision was set up on the basis that the asbestos could be dealt with by encapsulation, there may be a contingent liability for unspecified costs if the risk assessment recommends extensive remediation work.

The Department of Health has indemnified the Agency in respect of any claims it may receive as a result of the licensing activities it undertakes on the Department's behalf. Consequently, the Agency does not have any contingent liability in this regard.

20 Related party transactions

As the MHRA is a Trading Fund of the Department of Health, the Department is regarded as a related party within the definition of FRS 8. During 2004/05, the MHRA has had a significant number of material transactions with the Department. Details of the amounts due to/from the Department of Health are set out in Notes 10 and 11.

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, NHS Trusts and local authorities. The balances outstanding at the end of the year are set out below:

	Trade debtor £'000	Trade creditor £'000
Department for Work and Pensions	–	33
Veterinary Medicines Directorate of the Department for Environment, Food and Rural Affairs	51	–
Other central government bodies	28	–
Various NHS Trusts	111	166
Various local authorities	–	22
	190	221

During 2004/05, none of the Board members, members of the key management staff or other related parties has undertaken any material transactions with the MHRA.

21 Losses and special payments

There were no material losses or special payments during the year.

22 Financial commitments

The MHRA has the following financial commitments:

	2004/05 £'000	2003/04 £'000
Land and buildings		
Leases that expire after 5 years	3,609	2,982
Leases expiring within 5 years	703	856
Other	945	277

23 Financial instruments

FRS 13 'Derivatives and Other Financial Instruments' requires disclosure of the role 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 the MHRA's 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 FRS 13, debtors and creditors that 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 £10.0 million. 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.

	2004/05 £'000	Interest rate*	2003/04 £'000	Interest rate*
Account				
Paymaster	9,431	4.09%	22,169	3.10%
Commercial	556	0.50%	107	0.25%
	9,987		22,276	

* 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 £4.728 million. This resulted in interest payable of £0.200 million out of total expenditure in excess of £71.390 million.

Currency risk

The level of currency risk is determined by the level of income generated by activity undertaken on behalf of the EMEA. For 2004/05 this was £2.374 million (3.400 million euros). This represents 3.3% 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.

24 Post-balance sheet events

In October 2003, the Secretary of State for Health announced his intention to review the Department of Health's arm's-length bodies, of which, as an Executive Agency, the MHRA is one. In May 2004, the Secretary of State outlined the first stage of this review and this was followed by a further report in July 2005.

The review reported that the Agency will continue to ensure that all medicines, medical devices and equipment on the UK market meet appropriate standards of safety, quality and performance. The Agency runs a Device Evaluation Service (DES), which reviews equipment and advises NHS providers and purchasers on the best choice of device for particular purposes. A study was commissioned into the need for a DES and the options for its future home and funding.

The review was taken forward by the Healthcare Industry Task Force, which subsequently reported that DES should move under the management of the NHS Purchasing and Supply Agency (PASA). Parliamentary approval was given to amend the MHRA's Trading Fund Order and DES moved to PASA with effect from 1 September 2005.

The MHRA Trading Fund Order is also being amended to enable the MHRA to take on the role of UK competent authority for the safety of blood and blood components under an EU Directive, which the UK must implement from November 2005.

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:

- consists principally of receipts in respect of goods or services provided in the course of the funded operations; and
- 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.

Glossary

ADR	Adverse drug reaction
API	Active pharmaceutical ingredient
BANs	British Approved Names
BEMA	Benchmarking of EU medicines agencies
BP	British Pharmacopoeia
CSM	Committee on Safety of Medicines
CEP	Central Enquiry Point
CHMP	Committee for Medicinal Products for Human Use
CPS	Crown Prosecution Service
CSD	Committee on the Safety of Devices
DIA	Drug Information Association
DMRC	Defective Medicines Report Centre
DH	Department of Health
EDQM	European Directorate for the Quality of Medicines
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
GSL	General Sales List
HITF	Healthcare Industries Task Force
HPA	Health Protection Agency
HR	Human Resources
IMPs	Investigational medicinal products
IVDs	In vitro diagnostic medical devices
MAIL	Medicines Act Information Letter
MAs	Marketing authorisations
MCA	Medicines Control Agency
MDA	Medical Device Agency
MDAs	Medical Device Alerts
MHRA	Medicines and Healthcare products Regulatory Agency
MORE	Manufacturers' On-line Reporting Environment
NICE	National Institute for Health and Clinical Excellence
NHS	National Health Service
OMCL	Official Medicines Control Laboratory
P	Pharmacy only
PASA	Purchasing and Supply Agency
PCTs	Primary care trusts
Pharmacovigilance	Post-marketing surveillance of medicines
PIL	Patient Information Leaflet
POM	Prescription only medicine
PSUR	Periodic Safety Update Reports
rINNs	International Non-proprietary Names
SABS	Safety Alert Broadcast System
SPI	State Pharmaceutical Inspection (Latvia)
SSRIs	Selective serotonin reuptake inhibitors
TSE	Transmissible spongiform encephalopathy
UK	United Kingdom

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