European Medicines Agency

London, 17 June 2008
EMEA/197729/2008/EN/FINAL

The European Medicines Agency in 2007

Summary of the thirteenth annual report of the EMEA

This document provides a summary of the EMEA annual report for 2007. The full annual report for 2007 was adopted by the Management Board on 6 March 2008, and is available on the EMEA website:

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MISSION STATEMENT

The mission of the European Medicines Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.

Legal role

The European Medicines Agency is the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

The Agency provides the Member States and the institutions of the EU the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

Principal activities

Working with the Member States and the European Commission as partners in a European medicines network, the European Medicines Agency:

- provides independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to public and animal health that involve medicines;
- applies efficient and transparent evaluation procedures to help bring new medicines to the market by means of a single, EU-wide marketing authorisation granted by the European Commission;
- implements measures for continuously supervising the quality, safety and efficacy of authorised medicines to ensure that their benefits outweigh their risks;
- provides scientific advice and incentives to stimulate the development and improve the availability of innovative new medicines;
- recommends safe limits for residues of veterinary medicines used in food-producing animals, for the establishment of maximum residue limits by the European Commission;
- involves representatives of patients, healthcare professionals and other stakeholders in its work, to facilitate dialogue on issues of common interest;
- publishes impartial and comprehensible information about medicines and their use;
- develops best practice for medicines evaluation and supervision in Europe, and contributes alongside the Member States and the European Commission to the harmonisation of regulatory standards at the international level.

Guiding principles

- We are strongly committed to public and animal health.
- We make independent recommendations based on scientific evidence, using state-of-the-art knowledge and expertise in our field.
- We support research and innovation to stimulate the development of better medicines.
- We value the contribution of our partners and stakeholders to our work.
- We assure continual improvement of our processes and procedures, in accordance with recognised quality standards.
- We adhere to high standards of professional and personal integrity.
- We communicate in an open, transparent manner with all of our partners, stakeholders and colleagues.
- We promote the well-being, motivation and ongoing professional development of every member of the Agency.

FOREWORD BY THE CHAIR OF THE MANAGEMENT BOARD

Pat O'Mahony

I am very pleased to introduce the EMEA annual report for 2007. The summaries of activities presented here reflect the excellent performance of all EMEA staff and national competent authority experts.

My role as Chair of the Management Board commenced in June 2007, following my election by the members. It is a great honour to be appointed to this post and I look forward to working with the members and all partners to advance the important work we undertake on behalf of citizens. I succeeded Professor Hannes Wahlroos, who had so successfully chaired the Management Board for the previous three years. I would like to express my deep gratitude, and that of the entire network, to Hannes for his important contribution, which is greatly appreciated.

The mission of the EMEA is to foster scientific excellence in the evaluation and supervision of medicines for the benefit of public and animal health, and all that we do collectively is focused to that end.

Throughout 2007, the EMEA worked in close cooperation with others in the European medicines network, in particular in the area of risk-management, which is so fundamental to our consumer-protection role. Other areas of cooperation included the development of telematics and discussion on common resource and competence planning.

The EMEA experienced yet another year of increases in all of its areas of activity. The new paediatric legislation was successfully implemented, and a new scientific committee was established to oversee the performance of new tasks for the Agency and for the network.

The Agency made a substantial contribution in the area of research and development through the work of the EMEA/CHMP think-tank on innovative drug development and through the support given to the Innovative Medicines Initiative.

The Agency also contributed to the availability of a number of new medicines on the market, including new chemical entities and similar biological and generic medicines.

I would like to express my gratitude to the Executive Director and all EMEA staff for their commitment and excellent contribution during the year. I would like to thank the members of all the scientific committees and working parties for their hard work, and also to thank the staff of the European Commission for their ongoing support.

I look forward to continued progress and success in 2008.

INTRODUCTION BY THE EXECUTIVE DIRECTOR

Thomas Lönngren

I am pleased to report that the European Medicines Agency once again made a strong contribution to EU-wide efforts in support of making high-quality, safe and effective medicines available for use in human and animal populations.

In this, the thirteenth year of its operation, the EMEA delivered a strong performance in its core activity areas relating to the evaluation and supervision of medicines, while also pursuing with good results its broader mandate to stimulate innovation within the EU and contribute to European and global cooperation on scientific and regulatory practices in the field of medicines.

An important indicator of the EMEA's activity during any year is the number of applications it receives and processes for the initial marketing authorisation of medicines. In 2007, the Agency received 90 such applications relating to medicines for human use and 15 for veterinary medicines. The number for human medicines is higher than in any previous year, and the number of opinions adopted by the Agency's Committee for Medicinal Products for Human Use (CHMP), at 65, was also the highest ever recorded.

The public-health benefit behind these figures is that many new medicines to treat a range of diseases and conditions – from cancers to cardiovascular and neurological disorders – are now available for the treatment of Europe's patients. Similarly, new veterinary prevention and treatment options are now available for Europe's food-producing and companion animals. Notably, given recent attention paid in the media to the risk of a bird-flu pandemic, two vaccines against avian influenza were made available for use in poultry.

Perhaps the most tangible and significant achievement of 2007 was the Agency's successful introduction of new procedures and creation of a new scientific committee dedicated to implementing the EU's Paediatric Regulation, which came into force on 26 January 2007. With the foundation of this new legislative framework and the EMEA's operation of it, children across Europe will begin to benefit from medicines that are developed with their specific needs and best interests at heart.

The Paediatric Committee – the Agency's fifth scientific committee – was launched with great enthusiasm in July of this year, and immediately began to elaborate scientific and procedural arrangements for the assessment of paediatric investigation plans and related regulatory instruments.

This year also saw Bulgaria and Romania welcomed into the EU family of nations, and they were quickly integrated into the work of the EMEA as full members of the European medicines network, while preparatory work to integrate Croatia and Turkey was also conducted in advance of these countries' possible accession to the EU.

Within the existing network, the EMEA worked closely with Member State national competent authorities on activities intended to improve the efficiency of the use of available resources and to secure the long-term availability of appropriate scientific expertise. This latter is particularly necessary given the increasing complexity of evaluation procedures and the advent of advanced therapies and other new technologies in the medical domain.

Activities in the area of supporting innovation and improving access to medicines yielded some very positive results in 2007. The initial success of the EMEA's SME Office seen in 2006 was reconfirmed this year, with Europe's smaller innovative companies demonstrating a keen interest in the dedicated support on offer to them from the EMEA. Interest in the Agency's provision of scientific advice and protocol assistance also continued to be high, with demand increasing for the third year in a row.

Further support for increased availability of medicines was also generated through the Agency's high output in relation to medicines for rare diseases – with more positive opinions being adopted in favour of orphan designation than in any previous year – and through the continuing work of the Agency's Innovation Task Force and Think-tank on innovative drug development, as well as through its support for the European Commission's Pharmaceutical Forum and Innovative Medicines Initiative. Likewise, innovation and availability remained high priorities in the veterinary area, with input being given from

the Agency to the Heads of Medicines Agencies (HMA) action plan to promote the availability of veterinary medicines and to the European Technology Platform for Global Animal Health, as well as to the further development of measures to assist companies seeking to authorise medicines for limited markets. The EMEA also supported the Commission in its work to develop the new Regulation on Advanced Therapies, which was published in December 2007 and which will usher in further new responsibilities for the Agency in 2008.

The EMEA's cooperation with global partner organisations continued apace in 2007, with the Agency playing an active role in the International Conferences on Harmonisation (ICH and VICH); working closely with the World Health Organization, in particular on issues relating to medicines for developing countries; consolidating its information-exchange programme with the US Food and Drug Administration in relation to human and veterinary medicines; and signing confidentiality arrangements to allow closer cooperation between the EMEA, the European Commission and the Japanese authorities on regulatory issues concerning medicines.

Cooperation among EU Agencies was intensive too, with the EMEA engaging in activities with the European Centre for Disease Prevention and Control, in particular in relation to pandemic-influenza preparedness and advanced therapies; with the European Food Safety Authority; with the European Monitoring Centre for Drugs and Drug Addiction; and with the European Directorate for the Quality of Medicines and HealthCare.

On an organisational level, the EMEA conducted elections of chairs and vice-chairs for four of its scientific committees, including the new Paediatric Committee, and of a new chair for its Management Board. The Agency also progressed well with its development and maintenance of information-technology services, as well as with its programme to enhance the participation of patients and healthcare professionals in EMEA activities.

In summary, 2007 was a very productive year with intense activity in many areas, as you will note when you read the detail of this annual report. For their hard work and dedication throughout the year, I express my deep gratitude to all members of the EMEA staff, as well as to all the experts and colleagues of the Member State national competent authorities and our partners at the European Commission and European Parliament who have contributed greatly to another successful year for the EMEA.

1 PRIORITIES IN 2007

1.1 Implementation of the legislation on medicines for children

The Agency received entirely new responsibilities with the entry into force of Regulation (EC) No 1901/2006 on medicinal products for paediatric use (the Paediatric Regulation) on 26 January 2007. With the support of the national competent authorities the Agency succeeded in establishing the Paediatric Committee (PDCO) – the Agency's fifth scientific committee – and putting in place the necessary procedures for the assessment of paediatric investigation plans (PIPs) and waiver applications.

Paediatric Committee fully operational

The PDCO held its first meeting on 4-5 July 2007. Seven meetings were held in total.

Daniel Brasseur, former Chair of the Committee for Medicinal Products for Human Use (CHMP) and of the former Paediatric Working Party, was elected Chair; Gérard Pons was elected Vice-chair.

PIPs and waivers

The EMEA received applications for PIPs and full or partial waivers relating to 202 indications. These corresponded to 85 applications with an average of 2 to 4 indications per application.

Ten opinions on PIPs and waivers were adopted, covering 15 indications. Eight of the 10 opinions adopted were for full waivers and 2 were for PIPs.

The EMEA had adopted a decision on 4 of the 10 opinions by the end of 2007.

The EMEA issued a decision on a 'list of class waivers', which includes conditions that do not affect children and for which the requirement to submit a PIP can therefore be waived.

1.2 Safety of medicines for human and veterinary use

Improving the safety of medicines for human and veterinary use was once again one of the Agency's top priorities. Considerable effort was made, together with the national competent authorities for medicines in the EU Member States, to apply a proactive approach to the safety of medicines, with particular emphasis on the establishment of an intensive drug-monitoring system.

Concept of risk-management plans firmly established

Risk-management plans (RMPs) are submitted as part of a new application or an application involving a significant change in the marketing authorisation. The EMEA reviewed 92% of the risk-management plans submitted as part of new applications. Of these, 90% and 86% related to line-extension and extension-of-indication applications respectively. Reviews were undertaken in the context of a peer-review process within the CHMP.

European risk-management strategy (ERMS) for medicines for human use: further progress made

A new rolling two-year work programme for 2008-2009 was prepared by the EMEA and adopted by the Heads of Medicines Agencies, together with the ERMS status report.

The first phase of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) project was concluded, resulting in the establishment of an inventory.

Safety of medicines included in 7th Framework Programme

Discussions with the European Commission resulted in the inclusion of the topic 'Relative safety of NSAIDs' in the 2007 work programme for the health theme of the 7th Framework Programme. In addition, a list of the top five public-health issues in drug safety was developed by the CHMP/Pharmacovigilance Working Party in view of a reply to subsequent calls for proposals in the context of the 7th Framework Programme.

Strengthening EudraVigilance to support proactive pharmacovigilance in the EU

The number of national competent authorities and pharmaceutical companies reporting electronically to EudraVigilance (the EU database on adverse drug reactions) increased in 2007. However, 100% compliance has still not been achieved.

The Agency prepared a EudraVigilance action plan, which was subsequently adopted by the Heads of Medicines Agencies and the EMEA Management Board, to address implementation problems relating to the quality of submitted data and legal reporting deadlines.

The EudraVigilance Datawarehouse and Analysis System (EVDAS) was rolled out to the national competent authorities on 6 July 2007. This should lead to improved use of the EudraVigilance database in the overall conduct of pharmacovigilance at EU level.

Development of EudraVigilance Veterinary (EVV) delayed in 2007

Development of EVV was delayed for a period of some 6 months during 2007, due to re-prioritisation of resources to further develop the EudraVigilance (human) data warehouse. Following resumption of activity on EVV, the Agency and the Veterinary Joint Implementation Group developed the EudraVigilance Veterinary Action Plan, which was endorsed by the EMEA Management Board and the Heads of Medicines Agencies. This plan now gives the required predictability to future development of EVV that is necessary for national competent authorities to commit the necessary resources to ensure its full and timely implementation.

EudraVigilance Veterinary became the main reporting tool used by national competent authorities. Only a few reports were submitted electronically by marketing-authorisation holders, due to the majority of large veterinary pharmaceutical companies still being in the implementation and testing phase.

Action plan for European Surveillance Strategy

During the year, a refined action plan was established for veterinary medicines under the European Surveillance Strategy, which now includes priorities for promotion of adverse-reaction reporting, implementation of electronic reporting of these reactions, data analysis, and worksharing between Member States. Communication on safety issues between all stakeholders is also considered a high priority.

1.3 Stimulation of innovation

A number of the Agency's core business activities are directly aimed at facilitating innovation and research, and as such, supporting the objectives of the Lisbon agenda.

Activities relating to orphan designation and scientific advice on the rise

The EMEA continued to support the development of medicines for rare diseases and to provide high-quality scientific advice to companies developing medicines. The levels of activity in these areas increased again in 2007 (see chapter 2).

SME Office: supporting innovation among Europe's SMEs

Recognising that micro, small and medium-sized enterprises (SMEs) are often a motor for innovation – particularly in the field of new technologies and emerging therapies – the Agency's SME Office continued to implement the EMEA's policy to support them.

In 2007, 212 companies requested SME status, and 172 requests were approved. This brought the total number of companies with assigned SME status to 246 at the end of 2007. The majority of these companies are developing medicines for human use, 9 are developing medicines for veterinary use, 8 are developing medicines both for human and veterinary use, and 19 are regulatory consultants.

Services provided by the SME Office included processing of requests for fee reduction or deferral, requests for administrative assistance – more than three times the initially forecasted requests were received – and translation support for product information.

The EMEA provided guidance and training for SMEs. The SME User Guide was updated in 2007 to reflect the experience gained during the course of 2006. The first SME workshop was held on 2 February 2007.

Innovation Task Force: supporting development of advanced-therapy medicines

The Innovation Task Force (ITF) – an EMEA multidisciplinary group that includes scientific, regulatory and legal competences – held 18 briefing meetings with companies developing medicines in the area of emerging therapies and new technologies.

Sponsors may request advice on whether their product can be classed as a medicinal product, thus being eligible for EMEA procedures. Thirty-one requests for classification were received.

The CHMP adopted 18 classification reports, drafted by the ITF, describing the scientific and regulatory criteria for the definition of a medicinal product.

Early dialogue with sponsors

Implementation of new procedures to facilitate early dialogue with sponsors resulted in an increased number of requests for regulatory eligibility and briefing meetings.

EMEA/CHMP think-tank on innovative drug development: final report published

The final report, titled 'Innovative Drug Development Approaches', focused on identifying scientific bottlenecks and emerging science in the development of medicines – both in industry's research and development and in the academic environment – and on generating recommendations for future EMEA actions.

Contributing to the Innovative Medicines Initiative

The EMEA actively participated in the preparatory steps of the Innovative Medicines Initiative – a public-private partnership between the pharmaceutical industry and the European Communities, which aims to address bottlenecks in the development of medicines.

European Technology Platform for Global Animal Health

The EMEA was a member of the Steering Committee of the European Technology Platform for Global Animal Health, which aims to accelerate the development of novel animal-health products, for both major and minor markets, within the context of the 7th Framework Programme. The Agency participated in the preparation of the action plan, released in August 2007, for implementation of the Strategic Research Agenda.

1.4 Earlier and improved availability of medicines

Special authorisation procedures in operation

Accelerated assessment, conditional marketing authorisation and marketing authorisation under exceptional circumstances are special marketing-authorisation procedures aimed at bringing medicines of high public and animal-health interest to the market more quickly. These procedures were operated with increasing effectiveness in 2007, resulting in 4 opinions being adopted following accelerated assessment (relating to 2 medicines for human use and 2 for veterinary use), 3 opinions recommending granting of a conditional marketing authorisation (relating to 3 medicines for human use) and 6 opinions recommending granting of a marketing authorisation under exceptional circumstances (relating to 4 medicines for human use and 2 for veterinary use).

Stimulating availability of veterinary medicines for limited markets

The Committee for Medicinal Products for Veterinary Use (CVMP) produced internal reflection papers on the criteria to be used for defining a 'limited market' and on the procedure whereby the Committee formally classifies a medicine as indicated for a limited market.

The CVMP endorsed a set of proposals for measures that could be provided by the EMEA to assist companies with the submission of applications through the centralised procedure relating to limited markets, in line with the requirements of Article 79 of Regulation 726/2004. These proposals require

contributions from both the Agency and national competent authorities. They form part of the overall response of the European regulatory network to the lack of availability of veterinary medicines.

Promoting access to vaccines against major epizootic diseases of domestic livestock

The CVMP adopted a reflection paper on minimum data requirements for authorisation of bluetongue vaccines for emergency use. Bluetongue is an insect-borne disease of domestic ruminants, principally sheep, whose geographical range has now spread to include much of the EU. Vaccination is seen as an important method of control.

Continuing high priority was given to the authorisation of vaccines against avian influenza in chickens, because control of the disease in chickens reduces the likelihood of a pandemic developing through transfer of the virus from birds to man. In this context, the CVMP adopted a positive opinion for an H7 avian-influenza vaccine.

Global Animal Health Conference

In collaboration with IFAH-Global, the EMEA hosted a Global Animal Health Conference on 15-16 November 2007. This conference brought together all major stakeholders in animal health, including industry, academia, international animal-health organisations, and regulators from around the world. The meeting considered the major challenges facing the development of new medicines and the continuing availability of existing ones. A series of conclusions were reached that will assist decision-makers in the relevant organisations.

1.5 Transparency, communication and provision of information

In 2007, the Agency's activities in relation to transparency and communication concentrated on consolidating existing activities.

Good progress on implementing rules on access to documents

The Agency strengthened its internal handling of requests for access to documents.

The EMEA received a total of 92 requests for access to documents – an increase of more than 30% over 2006. Thirty-seven of the 92 requests were refused.

Ninety-five percent of requests for access to documents were processed within the established timelines.

Further improvements in relation to provision of information on medicines

Key activities in this area during 2007 included the systematic publication of assessment reports for withdrawn or refused marketing-authorisation applications, the publication of press releases and question-and-answer documents providing information in cases where there were safety concerns with medicines, and the provision of product-related information in all EU languages.

New guidance available

The guideline on summary of product characteristics was revised in order to introduce new requirements in accordance with the new Paediatric Regulation. A draft was published for a three-month public consultation in December 2007.

Guidance for the assessment of user-testing results by the CHMP was prepared and adopted in agreement with the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMD(h)).

EPAR summaries for the public

Sixty-four summaries of European public assessment reports (EPARs) written in a manner understandable to the public were prepared for new marketing authorisations. In addition, the EMEA systematically updated EPAR summaries relating to major variations.

Information about medicines in all EU languages

Efforts to provide product-related information in all EU languages continued throughout 2007. Compliance by Member States with the translation-checking process was very good overall, in both

pre-authorisation and post-authorisation phases. In addition, feedback from the Member States indicated good quality overall of the translations provided by the pharmaceutical industry.

The EMEA coordinated the post-opinion linguistic review for 76 new applications and line extensions.

Bulgarian, Romanian and (following the expiry of the derogation) Maltese were successfully included in the translations framework.

Further development of interaction with healthcare professionals, patients and consumers

A status report on the progress of the implementation plan for the framework of interaction with patients and consumers was presented to the Patients' and Consumers' Working Party (PCWP) during its December 2007 meeting.

The development of a framework of interaction between the EMEA and healthcare professionals was started in 2007.

The development of recommendations of the EMEA/CHMP Working Group with Healthcare Professionals (HCP WG) started in 2007.

The first joint meeting with patients and healthcare professionals was held on 1 June 2007. Following this meeting, it was concluded that joint meetings would be held at least once a year, and that representatives from each group would attend meetings of the other group.

1.6 The European medicines network

The European medicines network – a partnership of more than 40 medicines regulatory authorities in the European Union (EU) – is the basis of the EMEA's success. The network gives the EMEA access to a pool of more than 4,000 experts, allowing the Agency to source the best-available scientific expertise for regulating medicines in the EU. Experts participate in the work of the EMEA as members of the scientific committees, working parties, scientific advisory groups or related groups.

EU enlargement

Bulgaria and Romania joined the EU on 1 January 2007. The transition from observer status to full participation in the European medicines network and in the work of the Agency was facilitated as a result of careful preparations in the run-up to these countries' accession to the EU.

In view of the possible accession of Croatia and Turkey, the Agency organised a conference in each of these countries to prepare the groundwork for their potential future integration into the European medicines network.

Clinical-trials conference

The Agency organised a highly successful conference with a wide range of stakeholders who examined the operation of the Clinical Trials Directive after three years of practical experience, and published a report on the feedback provided.

Resource planning in the network

Resources in the network are scarce, and work began on developing planning processes for improved use and efficiency of the available resources. The EMEA participated in the planning process at the level of the Heads of Medicines Agencies.

The EMEA started an exercise to improve the organisation of working parties, aimed at achieving more efficient meetings and a better distribution of tasks among members of the scientific committees and their working parties.

Audioconferencing was introduced for some meetings, reducing the need for experts to travel to the EMEA.

Workshops, conferences, training

The Agency held a number of workshops and conferences to address critical scientific areas, involving academia, regulatory authorities and, where appropriate, pharmaceutical industry. Topics covered included first-in-man clinical trials, biosimilar medicinal products, immunogenicity of therapeutic

proteins, adaptive design in confirmatory clinical trials, process-analytical technology for biological medicines, user-testing of package leaflets, and cell- and tissue-engineered medicines.

The Agency also organised a number of training sessions for assessors from national competent authorities. Topics covered included gene-therapy medicines, diagnostics, oncology development, new approaches to quality assessment, and pandemic influenza.

Principles and processes for advanced education exchanges between regulatory authorities, academia and, where appropriate, industry were established. As a result of this, the Agency held regular contacts with relevant learned societies, particularly those involved in the areas of cardiology, diabetes, central nervous system and oncology.

With a view to participating in educational programmes for regulatory scientists, in conjunction with academia and the national competent authorities, the EMEA contributed to the initiative started by Italy for a European school for regulatory assessment of medicines.

Experts from academia and university hospitals on secondment to the EMEA contributed to the work of the European medicines network, ensuring the availability of complementary expertise.

2 MEDICINES FOR HUMAN USE

2.1 Orphan medicines

Increase in applications and opinions

A total of 125 applications were received for the designation of orphan medicines – the fourth consecutive year in which more than one hundred such applications have been submitted. The Committee for Orphan Medicinal Products (COMP) adopted 97 positive opinions on orphan designation – the highest number ever – and 1 negative opinion. The number of withdrawn applications – 19 – was the lowest in the past seven years.

Cancer again the main therapeutic area represented

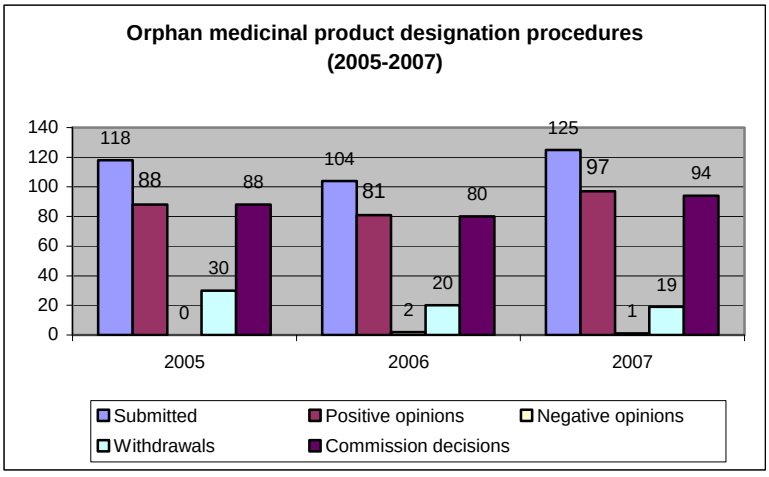
As in previous years, cancer treatment was the most-represented therapeutic area for which the COMP adopted positive orphan-designation opinions.

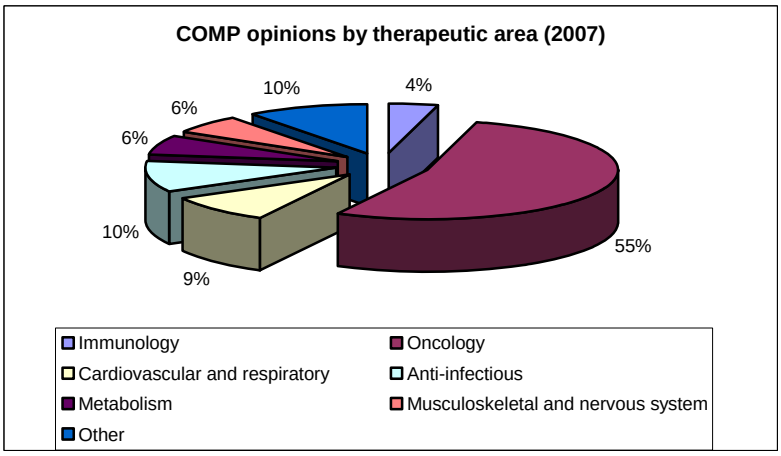
Almost half of orphan-designated medicines for treatment of children

Forty-nine percent of orphan medicines designated in 2007 were for conditions affecting children, including 4% intended exclusively for paediatric use.

Forty-four orphan-designated medicines authorised for use in the EU

By the end of 2007, a total of 44 orphan medicines had been granted a marketing authorisation by the European Commission since the orphan policy entered into force in 2001.

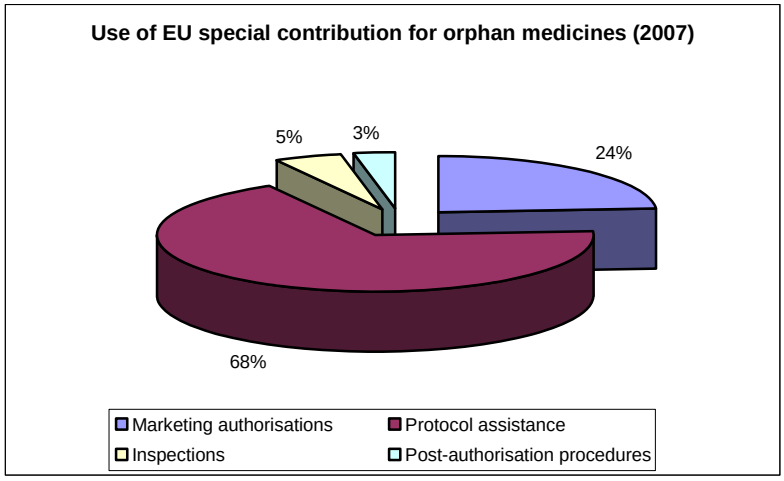




EU special contribution for orphan medicines

A total of €4.89 million from the EU special contribution was used to grant fee reductions for orphan medicines in 2007.

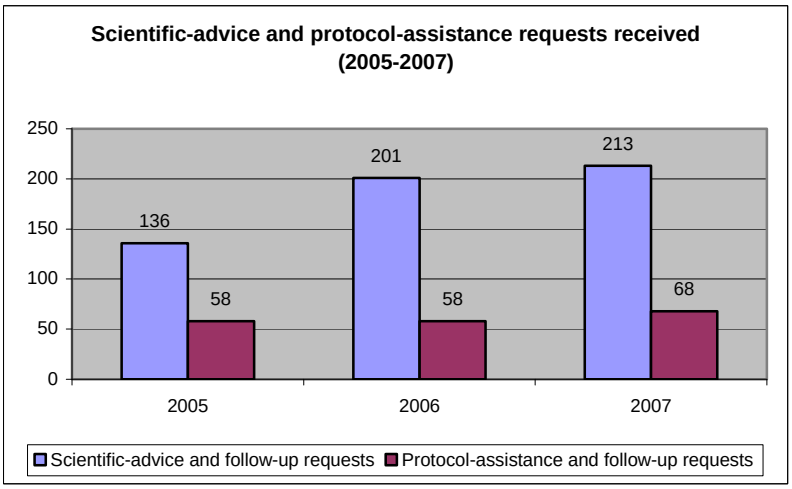
The Agency amended its policy on fee reductions for orphan medicines in 2007 to continue to focus on incentives to support protocol assistance, marketing-authorisation applications and other pre-authorisation activities, and to support SMEs in the first year after granting of a marketing authorisation.



2.2 Scientific advice and protocol assistance

Interest in obtaining scientific advice and protocol assistance remained high

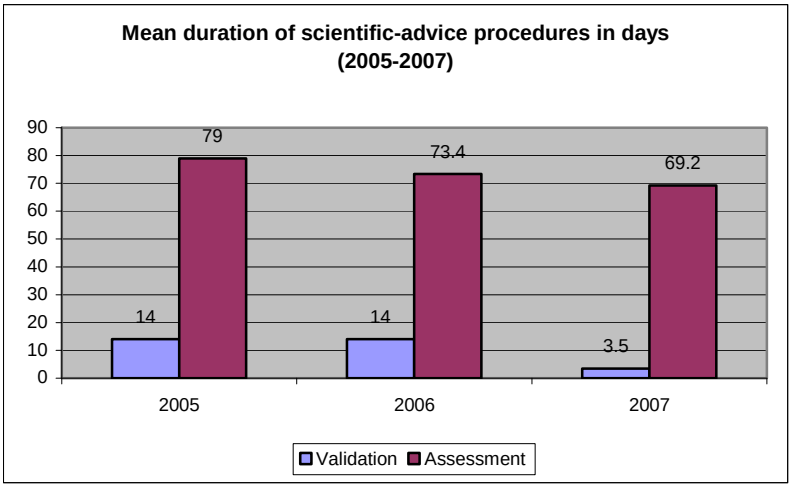
The number of scientific-advice requests was slightly higher than in 2006, with 213 requests received in 2007. A marked increase in the number of requests for protocol assistance was registered, with 17% more requests received than in 2006.



More procedures finalised, in shorter time

A total of 288 scientific-advice, protocol-assistance and follow-up requests were finalised in 2007, compared to 257 in 2006.

As in previous years, the Agency and the Scientific Advice Working Party (SAWP) once again shortened the average time required for the delivery of scientific advice.



2.3 Initial evaluation

New applications in 2007

The total number of new applications – 90 – was higher than in any other year. However, the number of initial applications by active substance, i.e. without double applications, was 19% lower than in 2006.

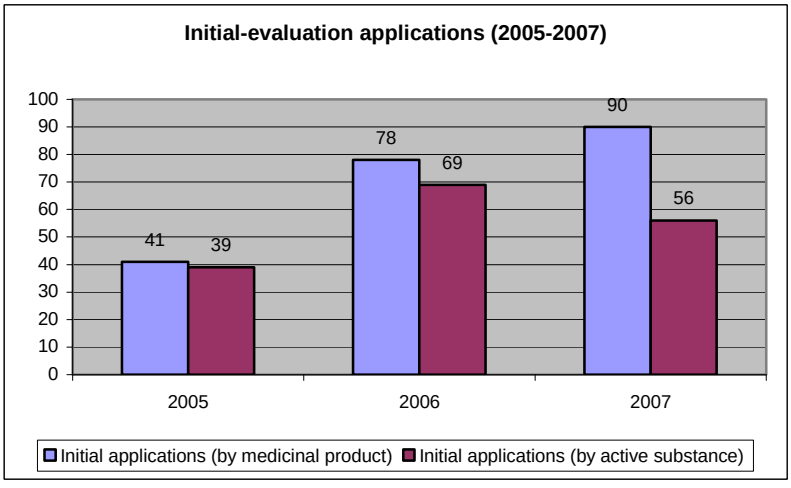
The number of marketing-authorisation applications for orphan-designated medicines was lower than in 2006, but close to the 7-year average since the introduction of orphan legislation.

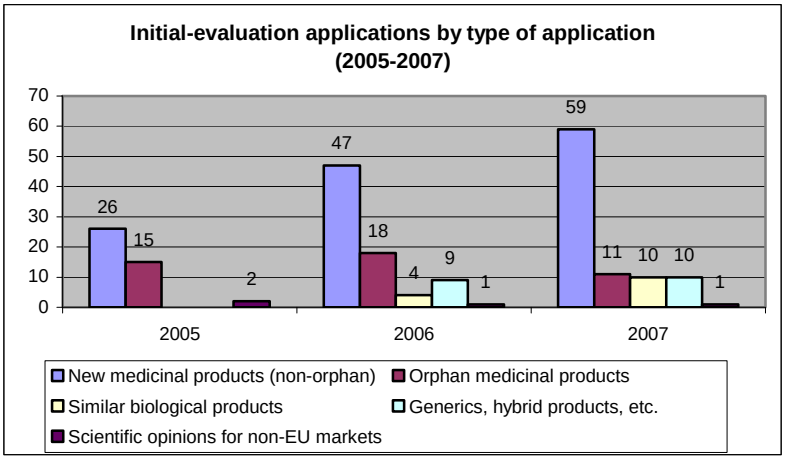
With the legal and regulatory framework for similar biological medicines now firmly established, 10 applications for these were received in 2007.

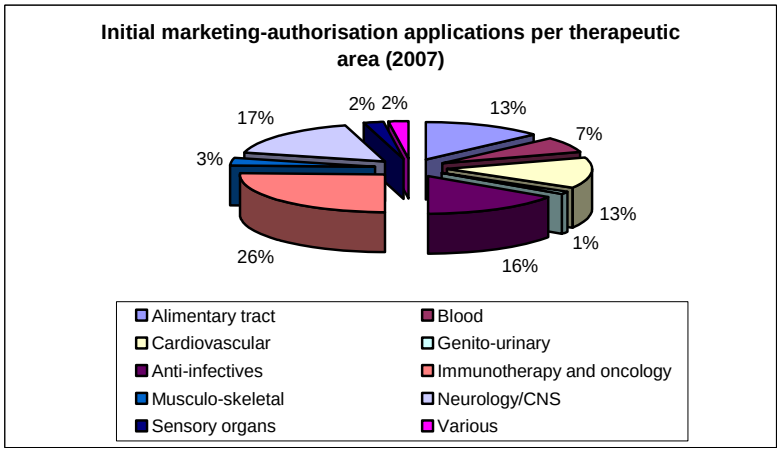
One application was received for a scientific opinion on medicinal products intended for non-EU markets.

Medicines to treat cancer still dominate

Applications for new medicines for use in the treatment of cancer once again represented the highest proportion by therapeutic area in 2007. Neurology and the central nervous system were the next most-represented therapeutic groups, followed by anti-infectives.



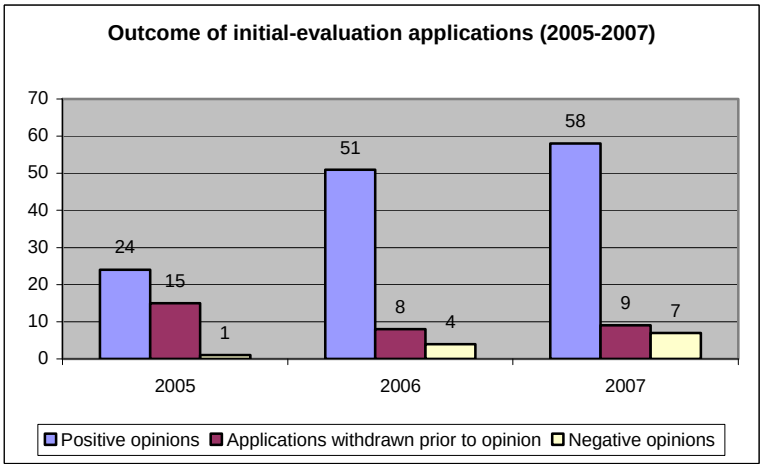




Opinions adopted in 2007

In 2007, the EMEA's Committee for Medicinal Products for Human Use (CHMP) adopted 58 positive opinions on initial-evaluation applications – the highest number ever.

Seven out of the total number of 65 opinions adopted were negative, recommending that the marketing authorisation for these medicines be refused. Nine applications were withdrawn prior to opinion.



Medicines for treatment of cancer the most-represented therapeutic area

The highest number of positive opinions adopted was for cancer medicines, followed by anti-infectives and alimentary-tract medicines.

Use of special authorisation procedures: facilitating availability of medicines

Two positive opinions were adopted for medicines that were reviewed under accelerated assessment (Isentress and Soliris).

Three opinions were adopted recommending granting of a conditional marketing authorisation (Isentress, Vectibix and Tyverb).

Four opinions were adopted recommending granting of a marketing authorisation under exceptional circumstances (Focetria, Increlex, Atriance, Yondelis).

Public-health benefits of medicines recommended for authorisation in 2007

Medicines of notable public-health interest that received a positive opinion from the CHMP in 2007 included:

A designated orphan medicinal product intended to reduce haemolysis (destruction of red blood cells) in patients with paroxysmal nocturnal haemoglobinuria (PNH) – a rare blood disorder in which the red blood cells are destroyed more rapidly than normal, causing the urine to turn dark. This was the first medicine for which an accelerated-assessment procedure was concluded successfully. It was also the first medicine submitted by a company benefiting from incentives for SMEs.

The second vaccine for prophylaxis against high-grade cervical intraepithelial neoplasia (CIN grades 2 and 3) and cervical cancer causally related to human papilloma virus (HPV) types 16 and 18.

A medicine belonging to a new class of antiretrovirals (CCR5 inhibitors). Its benefit – when used in combination with other antiretroviral medicines – is its ability to reduce the amount of HIV in plasma (viral load) and increase the number of T cells (specifically CD4 cells) in treatment-experienced patients with CCR5-tropic HIV-1.

Two mock-up pandemic-influenza vaccines intended for the prevention of influenza during an officially declared pandemic situation. A mock-up pandemic vaccine is not intended for stockpiling, but can be used to speed up the availability of a final vaccine in the event of a pandemic, once the pandemic strain has been identified.

A medicine with a chemical structure resembling that of thalidomide. It is authorised for the treatment of multiple myeloma, where it works by blocking the development of tumour cells and by stimulating some of the specialised cells of the immune system to attack the cancerous cells.

The first two dipeptidyl peptidase 4 (DPP-IV) inhibitors, both indicated for the treatment of type-II diabetes. They work by blocking the breakdown of incretin hormones in the body, thereby stimulating the pancreas to produce insulin when blood-glucose level is high, and also decreasing the levels of the hormone glucagon. They bring about a reduction in blood-glucose levels and help to control type-II diabetes.

The first renin inhibitor indicated for the treatment of hypertension. It blocks the activity of renin, an enzyme which is involved in the production of angiotensin I that is subsequently converted into the hormone angiotensin II, a powerful vasoconstrictor (it narrows blood vessels and consequently raises the blood pressure). By blocking the production of angiotensin I, levels of both angiotensin I and angiotensin II fall. This causes vasodilation (widening of the blood vessels), so that the blood pressure drops and the potential risk of damage caused by high blood pressure can be reduced.

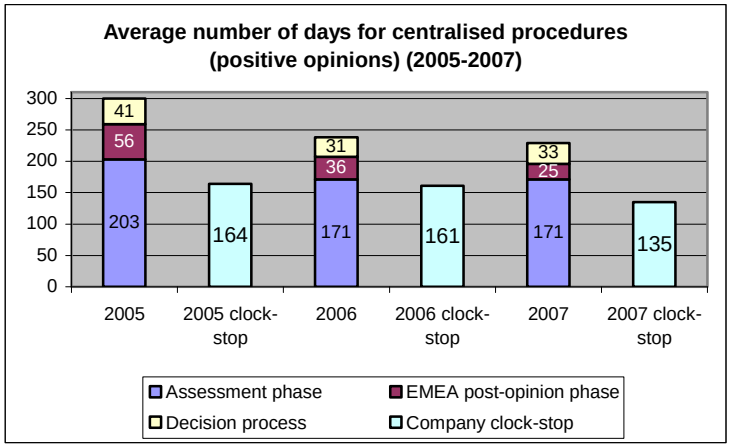
A medicinal product for the treatment of metastatic carcinoma of the colon or rectum, after failure of oxaliplatin- and/or irinotecan-containing chemotherapy regimens.

A medicinal product for the treatment of patients with advanced soft-tissue sarcoma (namely liposarcoma and leiomyosarcoma), after failure of anthracyclines and ifosfamide, or patients who are unsuited to receive these agents.

An antidote medicinal product used for treating cyanide poisoning.

Time required for centralised procedure remains low

The average time required for the assessment, post-opinion and decision phases of the centralised procedure remained approximately at the 2006 level. There was a marked improvement in the average clock-stop time required by applicant companies.

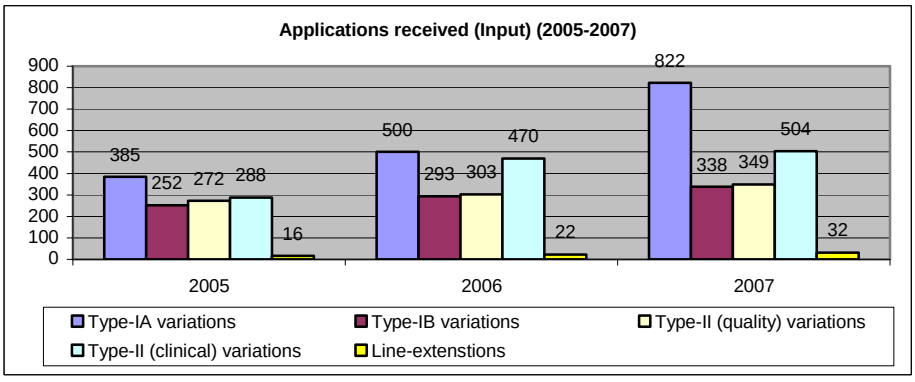


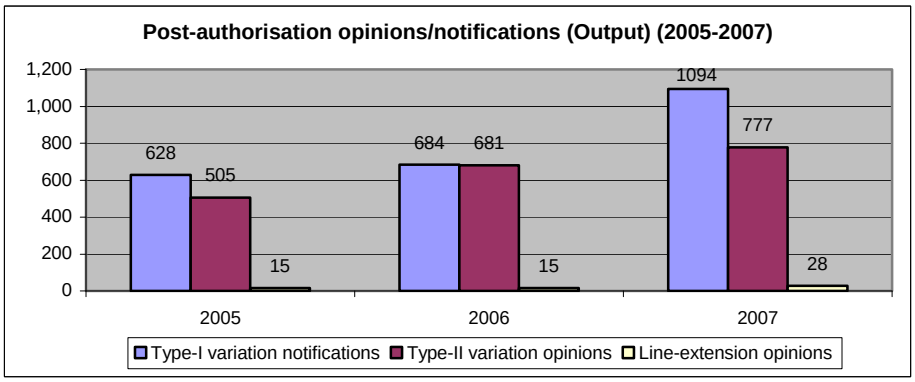
2.4 Post-authorisation activities

Number of variations up by almost 30%

The number of applications for variations and line extensions of marketing authorisations continued to rise. A total of 2,045 applications were received in 2007 – an increase of almost 30% compared to the previous year.

For adopted post-authorisation opinions or notifications, the increase was even more pronounced, with a rise of 37% over the previous year.





Extensions of indications broaden scope of existing medicines

The CHMP adopted 41 opinions for new indications, providing additional treatment options for patients. Two negative opinions were adopted, recommending the refusal of applications for an extension of indication.

Most of the new indications related to medicines approved for the treatment of various forms of cancer, such as hepatocellular carcinoma, locally advanced squamous cell carcinoma, metastatic breast cancer, advanced gastric cancer, advanced or metastatic renal cell cancer, metastatic colorectal cancer, non-small cell lung cancer, relapsed multiple myeloma and B-cell chronic lymphocytic leukaemia, and follicular non-Hodgkin's lymphoma.

Several extensions of indication were granted for the treatment of diabetes, providing more options for the combined use of oral antidiabetics and insulins.

New indications were also approved in the fields of cardiovascular, infectious, rheumatoid and inflammatory-bowel diseases and central-nervous-system disorders.

Six medicines had their use extended to include the treatment of children and adolescents suffering from diseases such as Crohn's disease, anaemia associated with chronic renal failure, or HIV, or to include immunisation against additional infections caused by streptococcus pneumoniae.

Restrictions of indication

The CHMP restricted the indication for a number of medicines for efficacy or safety reasons, including:

Visudyne (verteporfin). The indication in patients with age-related macular degeneration with occult subfoveal choroidal neovascularisation with evidence of recent or ongoing disease progression was deleted as the results of a confirmatory study failed to support the efficacy of the use of Visudyne in these patients;

Ketek (telithromycin). For the treatment of bronchitis, sinusitis and tonsillitis/pharyngitis, Ketek should only be used for infections caused by bacterial strains that are suspected or proven to be resistant to, or cannot be treated with, macrolide or beta-lactam antibiotics. No such restrictions were recommended for the remaining indication, the treatment of community-acquired pneumonia;

epoetins, both centrally authorised (Aranesp, Nespo, Dynepo, Mircera, NeoRecormon, Binokrit, Epoetin Alfa Hexal, Abseamed) and nationally authorised (Eprex). Following review of data from recent clinical trials showing consistent unexplained excess mortality in patients with anaemia associated with cancer who had been treated with epoetins, the indication in the treatment of anaemia was restricted to anaemia associated with symptoms.

Contra-indications, warnings and precautions for use

The CHMP recommended new contra-indications for 20 centrally authorised medicines, and in some instances for the entire classes of centrally authorised medicines (class labelling), including:

Viracept (nelfinavir mesilate): co-administration with omeprazole;

Acomplia (rimonabant): ongoing major depressive illness and/or ongoing antidepressive treatment;

Agenerase, Aptivus, Crixivan, Invirase, Kaletra, Norvir, Prezista, Reyataz, Telzir, Viracept (protease inhibitors): concomitant use with oral midazolam (while further directions concerning co-administration with parenteral midazolam are provided in the SPC) (class labelling);

Pegintron (peginterferon alpha 2b), Viraferonpeg (peginterferon alpha 2b) and Rebetol (ribavirin): initiation of treatment of hepatitis C in patients with hepatitis C and HIV co-infection who have cirrhosis and a Child-Pugh score of 6 or higher.

The CHMP recommended the deletion of contra-indications for 12 centrally authorised medicines, and in some instances for the entire class of centrally authorised medicines (class labelling), including:

pioglitazone- (Actos, Glustin, Competact, Tandemact) and rosiglitazone- (Avandia, Avandamet, Avaglim) containing medicines: deletion of the contra-indication for their combined use with insulins (class labelling);

Stocrin and Sustiva (efavirenz): deletion of the contra-indication for their co-administration with voriconazole.

The CHMP concluded more than 100 type-II variations relating to special warnings and precautions for use, including:

a new safety warning for Tamiflu (oseltamivir phosphate) and the risk of neuropsychiatric adverse events;

a new warning for recombinant factor VIII medicines regarding the possible recurrence of inhibitors after switching from one recombinant factor VIII medicine to another in previously treated patients with more than 100 exposure days who have a history of inhibitor development (class labelling);

a new warning for pioglitazone- and rosiglitazone-containing medicines regarding the increase of bone fractures in women; and for rosiglitazone-containing medicines only regarding a possible risk of ischaemic heart disease;

a new warning with an urgent safety restriction (USR) concerning the rare but serious risk of drug rash with eosinophilia and systemic symptoms (a severe type of allergic reaction) with strontium-ranelate-containing medicines (used to treat osteoporosis in women who have been through menopause).

Safety review of Viracept

The CHMP conducted a review of Viracept (nelfinavir), further to contamination during the manufacturing process of several batches of the active substance with ethyl mesilate, a known genotoxic substance. The CHMP first recommended the suspension of the marketing authorisation and the recall of Viracept from the market. Following the assessment of the corrective and preventive measures put in place by the marketing-authorisation holder and the inspection of the manufacturing site – which provided reassurance that the cause of the contamination had been eliminated and that future production of Viracept would meet the required quality standards – the CHMP subsequently recommended the lifting of the suspension of the marketing authorisation and the re-introduction of the medicine onto the market in the European Union.

2.5 Parallel distribution

The numbers of initial parallel-distribution notifications and notifications of change exceeded the expected numbers, with 1,937 initial notifications (8% more than forecast) and 3,518 notifications of change (45% more than forecast) being received.

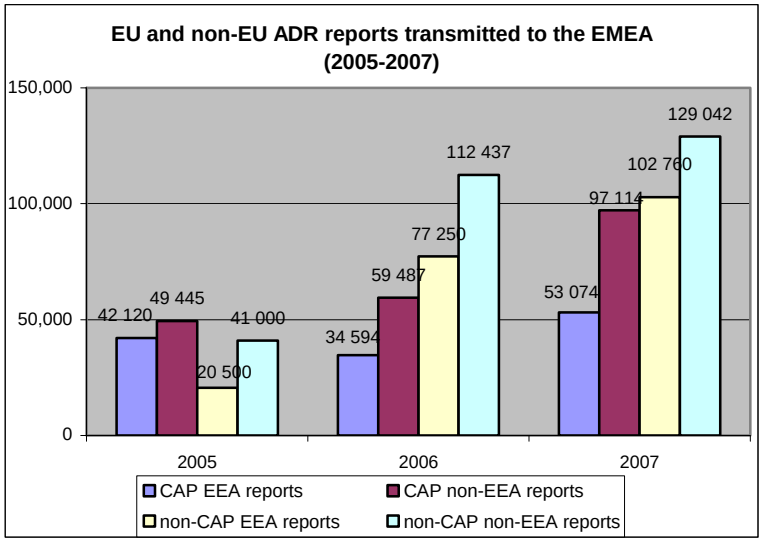
The timelines set out in the procedures were not adhered to, due to the high number of notification requests received, a backlog from previous years and a lack of resources.

2.6 Pharmacovigilance and maintenance activities

The wide range of activities undertaken in the field of pharmacovigilance and maintenance have allowed a more proactive approach to safety of medicines to be taken, thus contributing to the protection of public health.

25% more adverse-drug-reaction reports received in 2007

The EMEA received 381,990 adverse-drug-reaction (ADR) reports in 2007 – an increase of more than 25% compared to the previous year. Forty percent of ADR reports received related to centrally authorised medicines.



The EMEA received 63,393 reports concerning investigational medicines, i.e. adverse drug reactions observed during clinical trials. This is an increase of 18% compared to 2006.

Detection of pharmacovigilance signals

A total of 762 suspected signals concerning 139 intensively monitored medicines, and 349 suspected signals concerning 162 routinely monitored medicines, were identified. Following further investigation, 22% (132) of suspected signals required follow-up for intensively monitored medicines, including involving the rapporteur for 43 signals. About 10% (33) of signals were followed up for routinely monitored medicines, with involvement of the rapporteur in 21 cases.

2.7 Arbitration and Community referrals

Number of referrals submitted to the EMEA continued to rise

A total of 57 referrals were received in 2007: 40% more than in 2006. Thirty-six procedures were finalised.

A new referral procedure – the procedure following Article 107(2) of Directive 2001/83/EC as amended – was used for the first time in 2007. Altogether, 5 referrals were carried out under this procedure.

Nine out of the 36 finalised referral procedures related to safety concerns. In 3 cases, the CHMP recommended withdrawal and in 2 cases temporary suspension of the marketing authorisation.

According to revised EU legislation, Member States can initiate referrals regarding herbal medicines. As of December 2007, however, no referrals regarding herbal medicines had been received.

The CHMP adopted 2 opinions on scientific matters in the context of Article 5(3) procedures: 1 on the adequacy of guidelines on medicines in the context of the elderly, the other on the potential risk of carcinogens, mutagens and substances toxic to reproduction (CMRs) when used as excipients in medicines for human use.

Procedures of high public-health interest finalised in 2007

Review of **mifepristone**-containing medicines, following safety and efficacy concerns regarding the use of the approved 600mg dose of mifepristone, as compared to the use of a 200mg dose, in the medical termination of developing intra-uterine pregnancy in sequential use with prostaglandin analogue. The CHMP concluded that the available data support the effectiveness of a 600mg dose of mifepristone, followed by the use of prostaglandin analogues, for the termination of pregnancy up to 63 days after the onset of amenorrhoea (absence of menstrual periods). In pregnancies up to 63 days, comparative studies between 200mg and 600mg mifepristone in combination with 1mg

gemeprost delivered vaginally suggest that 200mg mifepristone may be as effective as 600mg mifepristone. However, in pregnancies up to 49 days, comparative studies between 200mg and 600mg mifepristone in combination with 400µg misoprostol delivered orally cannot exclude a slightly higher risk of continuing pregnancies with the 200mg dose. Based on the available published data, the benefit/risk profile of mifepristone in combination with oral misoprostol for pregnancy from 50 to up to 63 days is unfavourable due to poor efficacy.

Review of medicines containing **bicalutamide** 150mg, triggered by safety concerns, in particular heart problems, when the medicine is used in the treatment of early prostate cancer. The CHMP concluded that the benefits of these medicines outweigh their risks, but only in those patients who are at high risk of their disease getting worse (Article 31 procedure).

Review of **piroxicam**-containing medicines, triggered by safety concerns over gastrointestinal side effects and serious skin reactions. The CHMP concluded that piroxicam should no longer be used for treatment of short-term painful and inflammatory conditions. Piroxicam can still be prescribed for the symptomatic relief of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. However, it should not be the first choice of non-steroidal anti-inflammatory drug (NSAID) treatment in these conditions (Article 31 procedure).

Review of **veralipride**-containing medicines, following the withdrawal of veralipride form the Spanish market because of reports of serious side effects affecting the nervous system and a number of regulatory actions in other EU Member States where veralipride was authorised. The CHMP concluded that the risks outweigh the benefits and recommended the withdrawal of the marketing authorisation for all veralipride-containing medicines (Article 31 procedure).

Review of systemic formulation of **nimesulide**-containing medicines, following the suspension of the marketing authorisation for these medicines in Ireland due to concerns over serious liver problems. The CHMP concluded that the benefit-risk of nimesulide continues to be positive and recommended the maintenance of the marketing authorisation but with a restricted use (Article 107(2) procedure).

Review of **clobutinol**-containing medicines, following the suspension of the marketing authorisation for these medicines in Germany due to concerns regarding side-effects affecting the heart. The CHMP concluded that the benefits of these medicines do not outweigh their risks and therefore recommended that the marketing authorisations for clobutinol-containing medicines be withdrawn throughout the EU (Article 107(2) procedure).

Review of **carisoprodol**, following the plan to withdraw the marketing authorisation for this medicine in Norway due to risks of intoxication, psychomotor impairment, addiction and misuse due to off-label prescribing. The CHMP concluded the risks of these medicines outweigh their benefits and recommended the suspension of the marketing authorisations (Article 107(2) procedure).

Review of **lumiracoxib**-containing medicines, intended for the treatment of osteoarthritis, further to notification by the UK, which was considering the suspension of the marketing authorisation due to possible increased risk of hepatotoxic adverse events at the 100mg dose. The CHMP recommended the withdrawal of the marketing authorisations for all lumiracoxib-containing medicines because of the risk of serious side effects affecting the liver (Article 107(2) procedure).

Review of **aprotinin**-containing medicines, used to reduce perioperative blood loss and the need for blood transfusion in those patients undergoing cardiopulmonary bypass in the course of coronary-artery-bypass-graft (CABG) surgery. This was further to the decision by Germany to suspend all nationally authorised medicines containing aprotinin for intravenous use due to an increased risk of mortality in the aprotinin arm of the BART study (Article 107(2) procedure).

Review of medicines containing 30µg **ethinyl estradiol** + 2mg **chlormadinone acetate**, because of differences among Member States on whether the indication of these two medicines should be extended to include the treatment of women suffering from moderate acne. The CHMP recommended the refusal of the new indication because the data submitted were considered insufficient to demonstrate efficacy in the applied indication (Article 6(12) procedure).

Review of generic medicines containing **cetirizine,** because of concerns over their bioequivalence. Further to a CHMP review conducted in 2006, the concerned national marketing authorisations

were suspended by the European Commission, because of concerns regarding compliance with good clinical and laboratory practices (GCP/GLP) that impacted on the quality and reliability of bioequivalence studies supporting the marketing authorisations. Due to GCP concerns still identified in a further study, the CHMP recommended the revocation of the marketing authorisations for these generic medicines (Article 36 procedure).

2.8 Herbal medicines

Community herbal monographs

The Agency's Committee on Herbal Medicinal Products (HMPC) released for consultation 16 draft Community herbal monographs for traditional and well-established herbal medicines (birch leaf, butcher's broom, calendula flower, elder flower, eleutherococcus root, European goldenrod, hop strobiles, horsetail herb, melilot, mullein flower, nettle herb, oat fruit, oat herb, peppermint leaf, purple coneflower herb and willow bark).

Thirteen Community herbal monographs for traditional and well-established herbal medicines were finalised (aniseed, anise oil, bitter-fennel fruit, bitter-fennel-fruit oil, cascara, melissa leaf, passion flower, peppermint oil, primula root, primula flower, rhubarb, sweet-fennel fruit and thyme herb).

Community list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products

The HMPC adopted 2 entries to the 'list of herbal substances, preparations and combinations thereof for use in traditional herbal medicines' (bitter-fennel fruit and sweet-fennel fruit). They were transmitted to the European Commission for approval.

Four entries to the list were released for public consultation (aniseed, calendula flower, eleutherococcus root and purple coneflower herb).

Consultation on the experience with the directive on herbal medicines

In August 2007, the HMPC provided comments on the draft communication from the Commission to the Council and the European Parliament released for consultation in May 2007 on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC (introduced by Directive 2004/24/EC) on specific provisions applicable to traditional herbal medicinal products. The HMPC status report on the progress made in relation to the implementation of the Directive since its entry into force, which had been forwarded to the European Commission for the preparation of its draft communication, was published on the EMEA website.

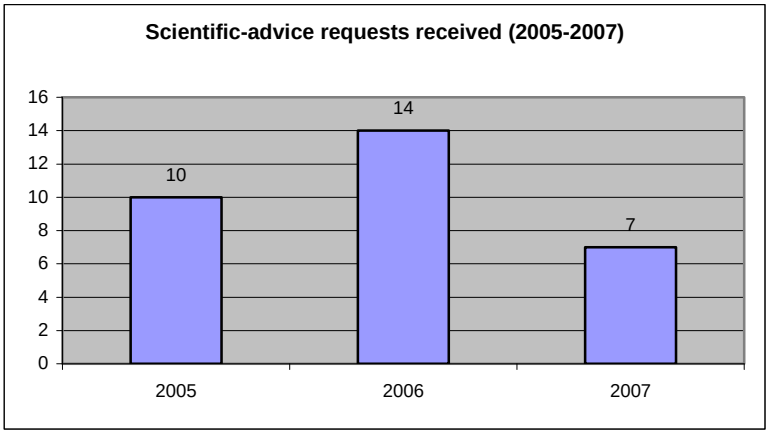
3 MEDICINES FOR VETERINARY USE

3.1 Scientific advice

Level of activity in relation to scientific advice lower than expected

In 2007, the Agency received 7 requests for scientific advice (16 were forecast). At this stage, there is no suggestion that there is a general trend for decreasing activity in this area, but the level of activity will continue to be monitored.

The average time required to finalise procedures for provision of scientific advice in 2007 was 48 days, which is a reduction from the average time of 55 days in 2006.



Two marketing authorisations issued in 2007 for veterinary medicines benefited from having received scientific advice from the Committee for Medicinal Products for Veterinary Use (CVMP): 1 medicine for treatment of congestive heart failure in dogs, and 1 vaccine against porcine circovirus infection in pigs.

Free scientific advice for minor uses and minor species

Free scientific advice was granted for 2 applications in 2007 under the provisions of the programme for minor uses and minor species: 1 related to development of a vaccine for sheep, goats and cattle, and the other concerned a live vaccine for wild rabbits.

3.2 Initial evaluation

Applications received

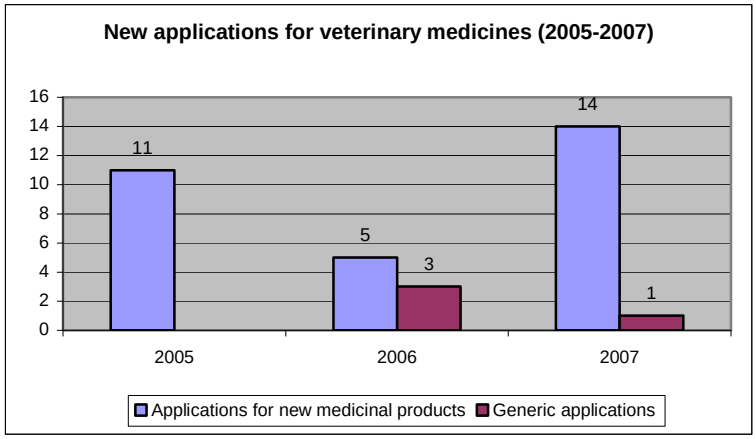
The Agency received a total of 15 initial marketing-authorisation applications for veterinary medicinal products, 8 of which were for pharmaceutical products and 7 for immunologicals.

Of the 8 pharmaceutical applications, 1 was a generic application. Five concerned medicines for companion animals, principally dogs, and the other 3 concerned medicines indicated for pigs, cattle and rabbits.

All 7 immunological applications were indicated for food-producing animals: 2 for poultry, 2 for pigs, 1 for cattle, 1 for both cattle and sheep, and 1 for horses.

Two applications were made for medicines that had received free scientific advice under the programme for minor uses and minor species.

Overall, these figures are consistent with a trend towards the introduction of immunological methods of control for disease problems in food-producing animals and an emphasis on companion-animal medicines in the field of veterinary pharmaceuticals.



Opinions adopted

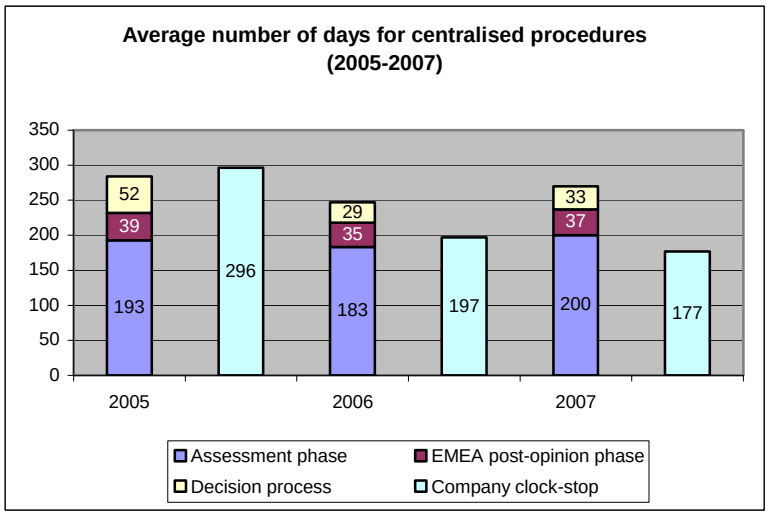
In 2007, the CVMP adopted a total of 9 positive opinions for initial marketing-authorisation applications – 4 fewer than in 2006.

Use of special authorisation procedures

Two opinions were adopted following accelerated assessment of the application.

The CVMP recommended a marketing authorisation under exceptional circumstances for 2 medicines.

Assessment of new applications by the CVMP took an average of 200 days. This increase from 183 days in 2006 arose due to fewer accelerated procedures being completed in 2007.



Animal-health benefits of medicines recommended for authorisation in 2007

Medicines of notable animal-health interest that received a positive opinion from the CVMP in 2007 included:

2 vaccines against avian influenza in poultry, mainly chickens. Applications for these 2 vaccines were evaluated on an accelerated timetable, taking into account the epidemiological situation within the EU and the contribution of the Agency to pandemic preparedness. The vaccines were authorised under exceptional circumstances and are subject to specific obligations and follow-up measures, including enhanced pharmacovigilance measures, to ensure the safe use of the products;

2 vaccines for pigs, against porcine circovirus type 2. Porcine circovirus is involved in the aetiology of porcine multisystemic wasting syndrome (PMWS), which is considered one of the most significant challenges facing the pig industry in the EU, and the authorisation of these products should assist with control of this disease;

other medicines, including 1 to treat heart failure in dogs, 1 to obtain temporary infertility in male dogs, 1 for treatment of overweight and obese dogs, and 1 generic medicine for treating musculoskeletal disorders in dogs.

3.3 Establishment of maximum residue limits

Applications for maximum residue limits (MRLs)

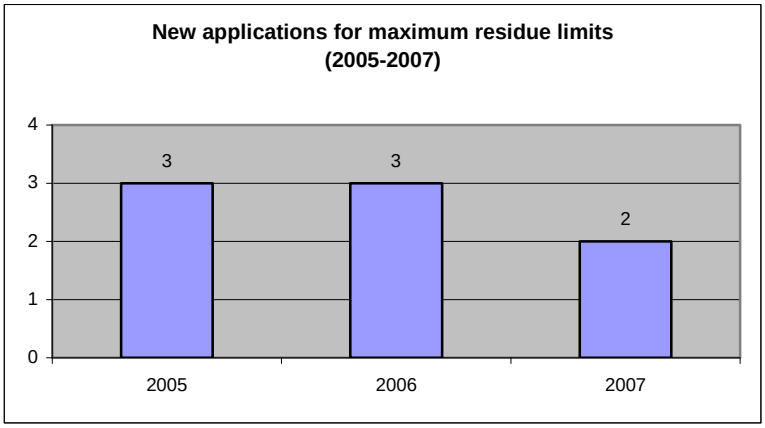
In 2007, the EMEA received and validated 2 new applications for MRLs – 1 fewer than was forecast for the year.

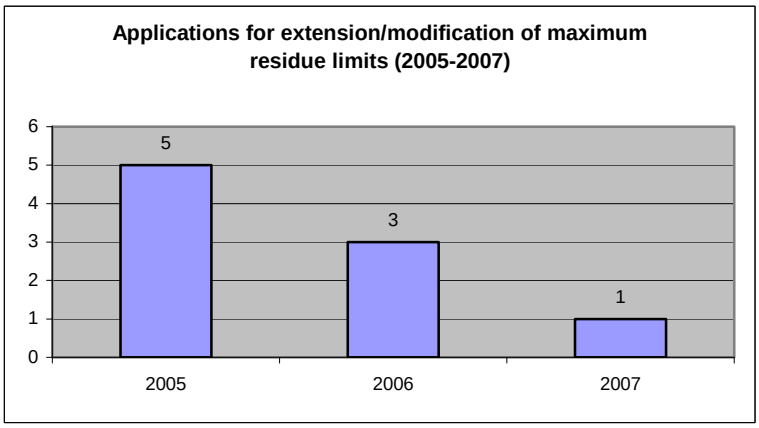
Concerns over small number of new MRL applications

The small number of new MRL applications is of concern as it clearly shows that very few new molecules are being introduced onto the veterinary market for livestock species. The ongoing decrease in MRL applications is consistent with the comparatively greater interest currently seen for the development of new medicines for companion animals rather than for food-producing animals.

There was also a shortfall in the number of applications submitted for extension or modification of MRLs, with only 1 of the forecast 5 being submitted.

The lack of uptake of extension applications is possibly related to the fact that many extensions that are of interest to companies have already been undertaken by the CVMP as free-of-charge extrapolations over recent years, as part of the CVMP's efforts to facilitate authorisation of medicines for minor uses and minor species.





Opinions on maximum residue limits

The CVMP adopted 3 positive opinions for the establishment of new MRLs.

One positive opinion related to the establishment of final MRLs further to previous provisional MRLs for a new substance.

Four positive opinions related to the extension of existing MRLs to other species.

All applications for new MRLs and for extension or modification of MRLs were processed within the 120-day legal timeframe.

3.4 Post-authorisation activities

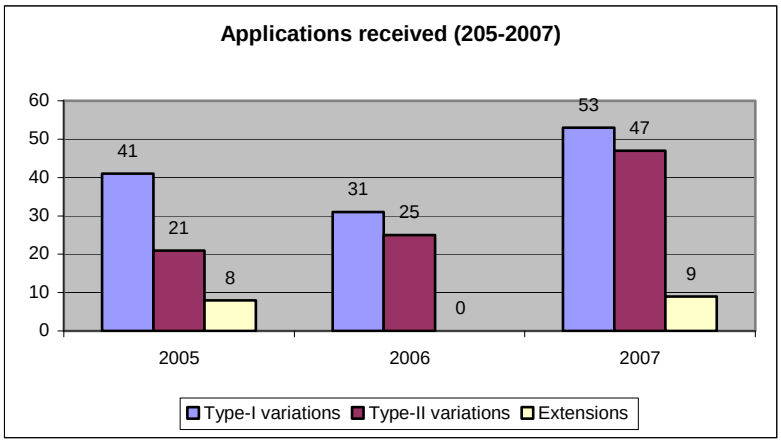
Number of applications for variations to marketing authorisations increases

The overall number of applications for variations to marketing authorisations received in 2007 was significantly higher than in 2006, in part accounted for by the greater number of centrally authorised medicines on the market.

A total of 53 type-I variation applications were received, relating to 29 type-IA and 24 type-IB variations. There were also 47 applications relating to the more complex type-II variations. Of these, 13 concerned pharmaceutical products and 34 concerned immunological products.

There were 9 applications for extension of marketing authorisation. Of these, 5 concerned pharmaceutical products and 4 concerned immunologicals.

All variation applications were evaluated within the regulatory time limits.



3.5 Pharmacovigilance and maintenance activities

Pharmacovigilance in the veterinary sector in the EU continues to undergo changes triggered by the revised pharmaceuticals legislation introduced in 2004. The electronic exchange of pharmacovigilance information within the EU is improving, as are active surveillance, harmonisation and risk management.

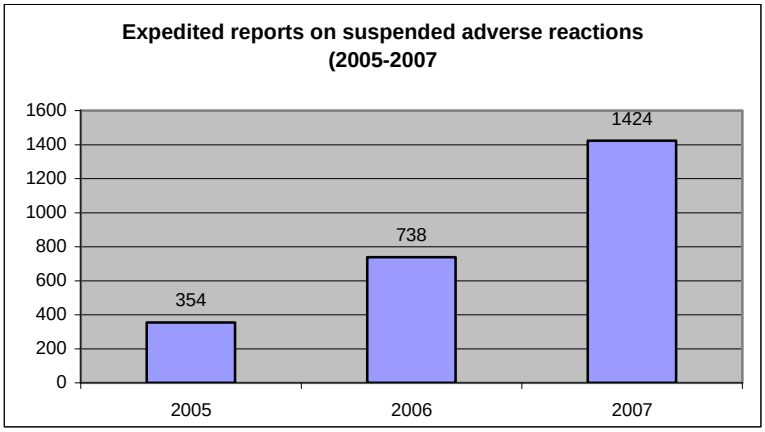
Marked increase in expedited reporting of suspected adverse reactions observed

The number of reports received was almost double the number of reports received in 2006. It is believed this results from, among other factors, the Agency's efforts to promote awareness of expedited reporting.

For centrally authorised veterinary medicines, a total of 1,424 expedited spontaneous reports of suspected adverse reactions were reported within the 15-day legal timeframe in 2007.

Of the 1,424 reports received, 1,212 related to suspected adverse reactions in animals and 213 to reactions in humans following exposure to a veterinary medicinal product.

One hundred and thirty-three reports received related to food-producing animals (mainly cattle, pigs and horses), following treatment of 17,459 animals, of which 4,428 showed suspected adverse reactions.



Periodic safety update reports (PSURs)

Eighty-one PSURs were received in 2007 for centrally authorised medicines.

Following its review of PSURs, the CVMP recommended in 6 cases that variations be submitted for the medicines concerned, mainly for the addition of new adverse-reaction information to the product information.

3.6 Arbitration and Community referrals

Procedures started in 2007

A total of 6 referral procedures relating to veterinary medicines were initiated, of which 1 related to safety concerns for existing medicines.

Three of the referrals were made under Article 33 and 3 were made under Article 35 of Directive 2001/82/EC.

Referral procedures concluded in 2007

The CVMP completed the assessment and issued opinions on 3 of the referral procedures started in 2007 and on 7 of the referral procedures started in 2006.

All referrals were processed within the legal timeframe.

4 INSPECTIONS

4.1 GMP, GCP, pharmacovigilance and GLP inspections

Increased number of inspections

Good manufacturing practice (GMP) inspection numbers – including inspections in the context of plasma master files (PMFs) – showed a 32% increase compared with 2006 (110). This reflects the increasing number of authorised medicines requiring re-inspection, increasing numbers of variations, and some unanticipated PMF inspections.

The number of good clinical practice (GCP) and pharmacovigilance inspections in 2007 was more than twice the number in 2006. This reflects an increase in the number of routine inspection requests, in line with the policy on GCP inspections adopted in 2006, as well as an increasing focus on inspections in countries where there is little European experience.

Two good laboratory practice (GLP) (non-clinical) inspections were carried out.

All inspections were managed within the legislative deadlines.

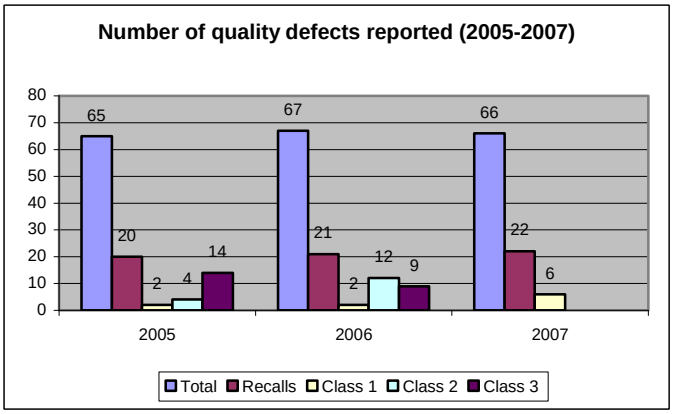
Product defects and deviations

Sixty-six quality defects were successfully coordinated, 22 of which resulted in recalls.

Six of these were class-1 recalls, compared with 2 during all of 2006.

One of the class-1 recalls (Viracept) led to a substantial amount of follow-up activity, to prevent reoccurrence of similar issues (critical GMP failure leading to high-level contamination with genotoxic impurities) with any similar medicines (mesilate and related active substances) in the EU, whether centrally authorised or authorised through mutual-recognition, decentralised or national procedures.

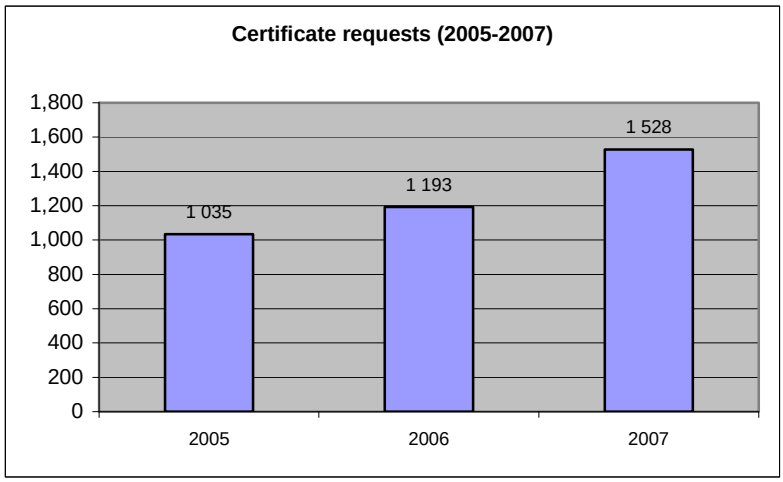
Four out of the 6 class-1 recalls related to counterfeited centrally authorised medicines.



4.2 Certificates of medicinal products

The number of certificate requests increased by 28% relative to 2006, compared with an expected increase of 16%.

Certificates within the framework of cooperation with the World Health Organization and certificates for SMEs also increased.

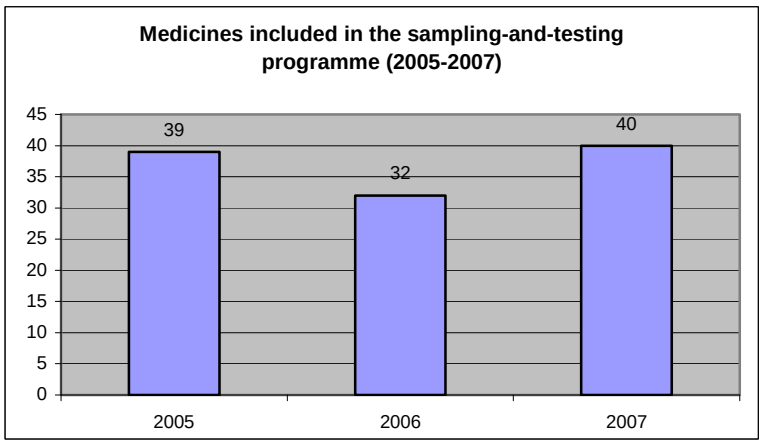


4.3 Sampling and testing

The EMEA, the European Directorate for the Quality of Medicines and HealthCare, and the national authorities in the sampling-and-testing programme continued their close collaboration in 2007, with a view to assuring effective and continued post-marketing surveillance of the quality of medicines.

Forty medicines were tested as part of the 2007 programme.

A new risk-based approach to the selection of medicines and parameters for testing was discussed and agreed by the relevant working parties/groups for medicines for human use. Specific criteria for veterinary medicines require further development.



5 EU TELEMATICS STRATEGY

2007 was the fifth year of implementation of the EU telematics projects by the Agency.

The majority of EU telematics systems were in use at the beginning of 2007. These systems are evolving in line with communicated requirements.

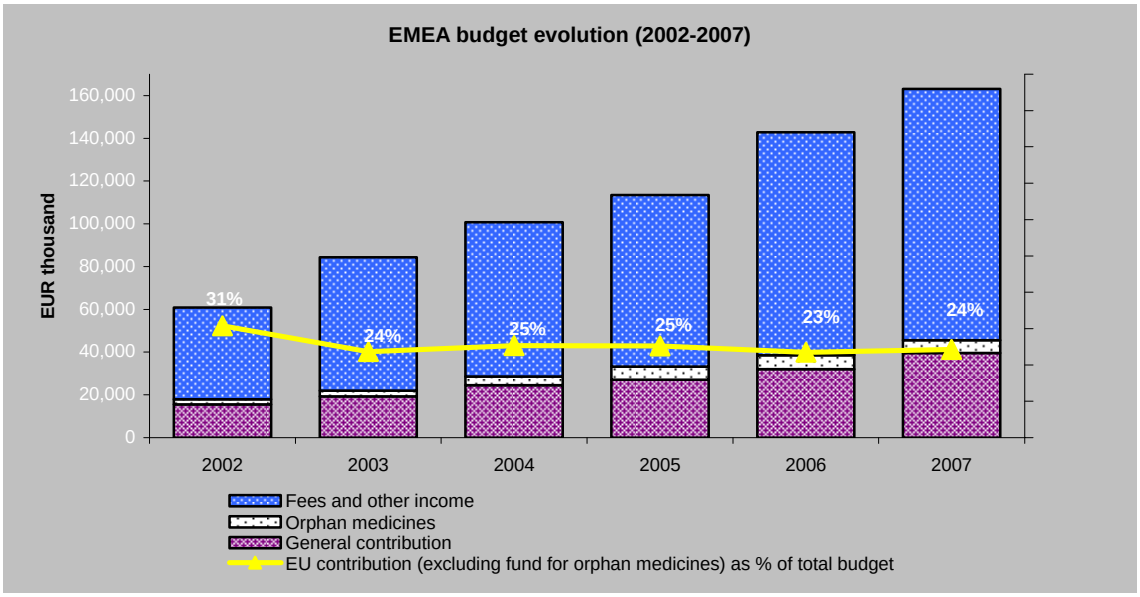
System or process ***(Status in 2006)***	**2007 milestones**
EudraNet *(In production)*	High performance of EudraNet was achieved both in terms of system availability and quality of management, development and operation of EudraNet applications (EudraNet II, EudraLink, ECD, Experts Database, etc.). Inspections agencies that are not part of the national medicines agencies were added into the EudraNet. Further, advanced network-management and performance services were implemented.
EudraPharm *(In production)*	EudraPharm was updated in 2007. The new features include advanced search for product information in a number of EU languages (being tested), a new sitemap offering improved navigation, and the inclusion of maximum residue limit (MRL) information for veterinary medicines.
EudraVigilance *(In production)*	The EudraVigilance DataWarehouse and Analysis System (EVDAS) was rolled out to the national competent authorities on 6 July 2007. It is designed to support signal-detection and the assessment of adverse-drug-reaction reports. Quantitative signal-detection methodologies were included in EVDAS and new functionality facilitating the review of signals was added to EudraVigilance.
Eudra DataWarehouse *(In pre-production)*	Development of the Eudra DataWarehouse was ongoing. However, work on the interim DataWarehouse solution for EudraVigilance Human had severe impact on work in this area. A first version for use by national competent authorities was released in September 2007.
EudraCT *(In production)*	In addition to preliminary specification work for the next major upgrade, technical upgrades were implemented on the system.
EudraCT Paediatrics Database *(At inception)*	Work on this has barely started, as guidelines fundamental to the determination of the scope and functionality of the proposed system are not yet available in final form.
EudraGMP *(In production)*	The first version of EudraGMP was launched in April 2007, and version 1.1 was released into production in December 2007.
European Review System *(Installation)*	The roll-out across the NCAs has resulted in the majority of NCAs having an installation or having opted for a different tool. Work remained to be done in respect of a small number of NCAs.
PIM (Product Information Management) *(In pilot production)*	Pilot activities were undertaken in respect of both new and post-authorisation applications. A decision was taken to extend the pilot phase into 2008.
EU Telematics Controlled Terms *(In pilot production)*	Definition and implementation of EU Telematics controlled terms continued. The first pilot was released in September.

6 EMEA BUDGET AND STAFF

The Agency's total budget in 2007 was €163,113,000 – an increase of approximately 20% compared to 2006.

Sixty-seven percent of the Agency's revenue came from fee income.

The Agency paid a total of €53.6 million to the national competent authorities for the provision of services in the evaluation of medicines for human and veterinary use.



The number of staff employed at the EMEA was 441, in addition to which there were 124 seconded national experts and contract agents.

Twenty-nine internal and external recruitment procedures were carried out.

The EMEA continued to invest in the professional development of staff. The number of training days taken by EMEA staff was up by almost 30% on the previous year, reaching a total of 4,166 days.