European Medicines Agency

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Annual report of the European Medicines Agency 2006

Adopted by the Management Board on 8 March 2007

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The annual report for 2006 is presented to the Management Board by the Executive Director in accordance with Article 64(3) of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. It is forwarded to the European Parliament, Council, Commission and Member States. A 'Summary of the annual report of the European Medicines Agency 2006' will be made available in the official EU languages.

In accordance with the EMEA Financial Regulation, the Agency is required to publish an analysis and assessment of the authorising officer's annual activity report together with its annual report. The Agency will publish the required analysis and assessment for 2006 on its website once it has been adopted by the Management Board.

Previous annual reports and other reference documents are available from the EMEA website:

www.emea.europa.eu

This report covers activities of the EMEA in 2006. Chapter 1 sets out the activities of the EMEA within the European system. It includes the work of the Agency's Management Board, its partnership with national competent authorities and European institutions, and other general aspects of the EMEA, including transparency and the Agency's international activities.

The operational and technical work of the EMEA is reported in Chapter 2 on medicines for human use, Chapter 3 on veterinary medicines and Chapter 4 on inspection activities. Implementation of the EU telematics strategy, administration and other support activities are described in Chapters 5 and 6.

The report also summarises the operation of the decentralised (mutual recognition) procedure in accordance with Article 38(1) of Council Directive 2001/83/EC on the Community code relating to medicinal products for human use as amended by Directive 2004/27/EC and Article 42(1) of Council Directive 2001/82/EC as amended by Directive 2004/28/EC.

CONTENTS

CONTENTS ---- 3

EMEA MISSION STATEMENT ---- 5

FOREWORD BY THE CHAIRMAN OF THE MANAGEMENT BOARD ---- 6

INTRODUCTION BY THE EXECUTIVE DIRECTOR ---- 7

1. EMEA IN THE EUROPEAN SYSTEM ---- 8
1.1 Management Board ---- 8
1.2 European medicines network ---- 8
1.3 Information and communication ---- 9
1.4 Integrated management ---- 11
1.5 Small and medium-sized enterprises ---- 11
1.6 European public-health activities ---- 12
1.7 Preparation for enlargement ---- 15
1.8 International cooperation ---- 15

2. MEDICINES FOR HUMAN USE ---- 18
2.1 Orphan medicines ---- 18
2.2 Scientific advice and protocol assistance ---- 20
2.3 Initial evaluation ---- 23
2.4 Post-authorisation activities ---- 28
2.5 Safety of medicines ---- 31
2.6 Arbitration, Community referrals and opinions on scientific matters ---- 34
2.7 Herbal medicines ---- 36
2.8 Management and organisation of EMEA scientific committees for human medicines ---- 37
2.9 Parallel distribution ---- 38
2.10 Coordination Group for Mutual Recognition and Decentralised Procedures–Human ---- 39

3. VETERINARY MEDICINES ---- 42
3.1 Scientific advice ---- 42
3.2 Initial evaluation ---- 42
3.3 Availability of veterinary medicines ---- 44
3.4 Maximum residue limits ---- 45
3.5 Post-authorisation activities ---- 46
3.6 Safety of medicines ---- 47
3.7 Arbitration and Community referrals ---- 49
3.8 Management and organisation of the Committee for Medicinal Products for Veterinary Use ---- 50
3.9 Coordination Group for Mutual Recognition and Decentralised Procedures–Veterinary ---- 50

4. INSPECTIONS ---- 52
4.1 GMP, GCP, pharmacovigilance and GLP inspections ---- 52
4.2 Mutual recognition agreements ---- 54
4.3 Sampling and testing ---- 55
4.4 Certificates of a medicinal product ---- 56
4.5 Implementation of the Clinical Trials Directive ---- 57

5. EU TELEMATICS STRATEGY ---------- 58

6. SUPPORT SERVICES ---------- 60
6.1 Personnel and budget ----------60
6.2 Accounts ----------61
6.3 Verification service ----------62
6.4 Infrastructure services ----------62
6.5 Meetings and conferences at the EMEA ----------63
6.6 EMEA document management and publishing ----------64
6.7 Information technology ----------65

ANNEXES---------- 67
Annex 1 Members of the Management Board----------68
Annex 2 Members of the Committee for Medicinal Products for Human Use ----------70
Annex 3 Members of the Committee for Medicinal Products for Veterinary Use ----------73
Annex 4 Members of the Committee on Orphan Medicinal Products ----------75
Annex 5 Members of the Committee on Herbal Medicinal Products ----------77
Annex 6 National competent authority partners ----------79
Annex 7 EMEA budget summaries 2005–2007----------93
Annex 8 EMEA Establishment Plan----------94
Annex 9 CHMP opinions in 2006 on medicinal products for human use ----------95
Annex 10 CVMP opinions in 2006 on medicinal products for veterinary use ---------- 106
Annex 11 COMP opinions in 2006 on designation of orphan medicinal products ---------- 109
Annex 12A HMPC Community herbal monographs ---------- 118
Annex 12B Entry to 'List of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products' ---------- 119
Annex 13 Guidelines and working documents in 2006---------- 120
Annex 14 Arbitration and Community referrals overview 2006 ---------- 130
Annex 15 EMEA contact points ---------- 133

EMEA MISSION STATEMENT

The EMEA's mission is, in the context of a continuing globalisation, to protect and promote public and animal health by:

- developing efficient and transparent procedures to allow rapid access by users to safe and effective innovative medicines and to generic and non-prescription medicines through a single European marketing authorisation,
- controlling the safety of medicines for humans and animals, in particular through a pharmacovigilance network and the establishment of safe limits for residues in food-producing animals,
- facilitating innovation and stimulating research, hence contributing to the competitiveness of EU-based pharmaceutical industry, and
- mobilising and coordinating scientific resources from throughout the EU to provide high-quality evaluation of medicinal products, to advise on research and development programmes, to perform inspections for ensuring fundamental GxP[1] provisions are consistently achieved, and to provide useful and clear information to users and healthcare professionals.

Routes for authorisation of medicinal products in the European system:

- The centralised procedure is compulsory for all medicinal products for human and animal use derived from biotechnology processes. The same applies to all human medicines intended for the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative disorders and for all designated orphan medicines intended for the treatment of rare diseases. Similarly, all veterinary medicines intended for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals have to go through the centralised procedure. For medicinal products that do not fall under any of the above-mentioned categories companies can submit an application for a centralised marketing authorisation to the EMEA, provided the medicinal product constitutes a significant therapeutic, scientific or technical innovation or the product is in any other respect in the interest of patient or animal health.

  Applications are submitted directly to the EMEA. At the conclusion of the scientific evaluation, undertaken in 210 days within the Agency, the opinion of the scientific committee is transmitted to the European Commission to be transformed into a single market authorisation valid throughout the whole European Union.
- The decentralised procedure and the mutual recognition procedure apply to the majority of conventional medicinal products. Both procedures are based upon the principle of recognition of national authorisations. They provides for the extension of marketing authorisations granted by one Member State to one or more other Member States identified by the applicant. Where the original national authorisation cannot be recognised, the points in dispute are submitted to the EMEA for arbitration. The opinion of the scientific committee is transmitted to the European Commission.

The European Commission adopts its decision with the assistance of a standing committee composed of representatives of the Member States.

[1] GXP means 'good clinical practice' (GCP), 'good manufacturing practice' (GMP) and 'good laboratory practice' (GLP) collectively.

FOREWORD BY THE CHAIRMAN OF THE MANAGEMENT BOARD

Professor Hannes Wahlroos

I would like to begin by congratulating the Executive Director, his staff, the scientific committees and all working parties for their outstanding performance in 2006. The results presented in the annual report 2006 document that the Agency's preparatory work to implement the new legal provisions has fully paid off: the Agency has demonstrated that it adapted successfully to the new regulatory framework and was able to run new and existing procedures successfully and efficiently. This success has been recognised by all of the Agency's stakeholders.

2006 was also the first full year in which the Management Board operated in its full composition. The presence of representatives from patients', doctors' and veterinarians' organisations, who joined the Board in September 2005, has added a new dimension to how the Board operates, and their experience and expertise has made an invaluable contribution to the Board's functioning. By saying this I would also like to take this opportunity to thank all the Board members for their contributions to the work of the Board.

The changes brought about by the revised pharmaceutical legislation had a fundamental impact on the structure and organisation of the Management Board. The members have therefore started to look at new ways to improve the Board's involvement in the work of the Agency and its strategic decision-taking. As part of this, an ad hoc working group was created to re-define the Management Board's role and responsibilities.

The Board has been closely following the Agency's achievements in 2006. The EMEA has made considerable efforts to increase its outreach to patients and healthcare professionals by providing them more and better information about medicines, most notably with the launch of the EudraPharm database, and by encouraging their participation the Agency's work. I am convinced that the efforts made will help to secure and build up public confidence in the Agency's actions in relation to medicinal products.

The Agency has continued its contribution to the promotion of research and development in Europe. The scientific advice procedure has been improved and is used increasingly by sponsors of medicinal products. In addition, the Agency made a successful start with the SME Office, which provides assistance to small and medium-sized enterprises involved in the development of medicines in Europe. Finally, the EMEA was an important contributor for the development of strategic research agendas for both human and veterinary medicinal products within the 7th Framework Programme, the EU's chief instrument for funding scientific research and technological development over the period 2007 to 2013.

Continuing its preparedness efforts for pandemic influenza, the Agency has achieved several milestones in 2006 related to both human and animal health. The Board encourages the Agency to continue its good work and to remain alert in view of the threat levels.

At the end of 2006, new European legislation aimed at promoting the development of medicines for children was adopted. The EMEA has worked hard in 2006 to prepare the ground for ensuring the smooth implementation of this new piece of legislation.

Before I come to the end, I would like to commemorate our dear friend and Management Board colleague, Professor Gianmartino Benzi, who passed away in November 2006. His spirit, his enthusiasm and his contributions to the work of the European Medicines Agency are greatly missed.

INTRODUCTION BY THE EXECUTIVE DIRECTOR

Thomas Lönngren

It is once again my pleasure to introduce to you our report on the activities and achievements of the European Medicines Agency in the past year. And 2006 was indeed a year with plenty to report on.

This was the first full year of operation of the new pharmaceutical legislation introduced in the European Union in November 2005, under which the EMEA assumed new responsibilities and saw the scope of its tasks greatly extended.

Despite the operational challenges and increased workload this entailed, the Agency was able to achieve all the main objectives it had set itself for the year, and once more delivered good performance results across the entire spectrum of its activities.

To pick out just a few notable achievements in core business areas:

- There were more positive opinions in favour of new medicines for human use than in any previous year, contributing to the availability of 51 new medicines, 11 of which are intended for the treatment of rare diseases.
- The CVMP adopted positive opinions on the authorisation of 13 new veterinary medicines for treatment of a number of conditions in chickens, cats and dogs.
- The Agency managed record numbers of initial marketing-authorisation applications and post-authorisation variation applications, and of requests for scientific advice, parallel-distribution notifications and certificates.
- The scientific committees were able to speed up the average assessment time for several key procedures, including initial evaluations, orphan designations and scientific advice, thus helping to accelerate the development and availability of new medicines.

In addition to the good performance in core operational areas, the EMEA also made a strong contribution to a number of important European public-health initiatives, such as pandemic-influenza preparedness, the European paediatric initiative, the European risk-management strategy, provision of better information for patients, and tackling antimicrobial resistance to veterinary medicines in food-producing animals.

We also contributed towards stimulating research and development of new medicines through our involvement in the Innovative Medicines Initiative and the European Technology Platform for Global Animal Health, but in particular through the dedicated support provided to small and medium-sized companies by our SME Office, which, in its first year of operation, generated even greater interest than had been expected.

Further progress was made in other areas too, notably our transparency, information and communication initiatives, preparations for the accession to the EU of Bulgaria and Romania, arrangements for the participation of Croatia and Turkey in EMEA activities, and international cooperation with our scientific and regulatory partners at the European and global levels.

As always, I am grateful to the national competent authorities for the scientific resources they have made available to the EMEA. I am also grateful the European Commission and the European Parliament for their continuous support to the EMEA and its mission for public and animal health over the past year. The successes we were able to achieve were due to the smooth operation of the European network as a whole, and in particular to the outstanding work of our scientific committees, working parties and secretariat personnel.

1. EMEA IN THE EUROPEAN SYSTEM

1.1 Management Board

The EMEA Management Board met four times in 2006, under chairman Hannes Wahlroos, from Finnland, and vice-chairman Jytte Lyngvig, from Denmark. The full composition is provided in Annex 1.

Highlights of the Management Board's work in 2006 included:

- Adoption of several proposals for greater transparency, including: revised rules on access to documents; publication of information concerning the withdrawal by a company of its marketing-authorisation application after the Agency's opinion but before the Commission's decision on marketing authorisation; publication of information on withdrawal by applicants, and on refusal by the Agency, of applications concerning new indications for approved medicines; publication of the names of companies that have been assigned SME status by the Agency; extension of the policy on handling of conflicts of interests to include the Members of the Management Board.
- In the veterinary medicines field, extension of the pilot programme offering free scientific advice in respect of medicines for minor uses and minor species (MUMS) for another year, with a view to stimulating development of medicines for limited markets.
- Constitution of a working group on roles and responsibilities of the Management Board, following calls for more involvement of Board members in the work of the Agency.
- Adoption of the Agency's work programme, establishment plan and budget for 2007.

1.2 European medicines network

The EMEA operates in partnership with the national competent authorities for human and veterinary medicinal products in the Member States and the EEA-EFTA countries Iceland, Liechtenstein and Norway. The authorities make scientific resources available in the form of a network of more than 3,500 European experts who assist the Agency in performing its scientific tasks.

Strengthening the European medicines network was one of the priorities for 2006. Actions carried out by the EMEA and the national competent authorities focused on improving the safety of medicines, increasing the availability of new medicines, and enhancing scientific competence within the network.

European Risk-Management Strategy (ERMS) for medicines for human use

The EMEA and national competent authorities further progressed the European Risk-Management Strategy for human medicines. Major initiatives in 2006 included:

- Monitoring the new legislative tools for risk-management, particularly risk-management plans.
- Speeding up electronic reporting by all involved parties and discussing ways to improve the quality of the data submitted.
- Preparing for the establishment of the European Network of Centres of Pharmacoepidemiology and Pharmacovigilance (ENCePP) – a network of academic centres for intensive drug monitoring.
- Reinforcing the scientific expertise of the Pharmacovigiliance Working Party by co-opting 8 specialised experts.
- Preparing guidance on paediatric pharmacovigilance.
- Preparing guidance on pharmacovigilance for vaccines.

EudraVigilance Veterinary and European Surveillance Strategy (ESS) for medicines for veterinary use

Procedures for reporting suspected adverse reactions into EudraVigilance Veterinary by national competent authorities and marketing authorisation holders were considerably enhanced during the year.

The ESS group made good progress on developing an action plan aimed at improving harmonisation and work-sharing between the authorities. The mandate of the Pharmacovigilance Working Party–Veterinary was revised, making it the core scientific group for monitoring pharmacovigilance matters relating to all veterinary medicinal products authorised in the EU.

Conferences, workshops, training sessions

The EMEA organised a number of conferences, workshops and training sessions for assessors and inspectors, designed to share competencies and strengthen cooperation among the network of European experts. Areas covered concerning medicines for human use included: use of biomarkers in medicines-development; slowing progression of neurodegenerative diseases; investigation of medicinal products in neonates and children; obesity in children.

Training sessions relevant to veterinary scientific and therapeutic areas included: establishment of acceptable daily intakes (ADIs) for the purpose of setting maximum residue limits and withdrawal periods; efficacy of veterinary medicinal products.

Payment for scientific services

The EMEA made payments to national competent authorities of the EU Member States and EEA-EFTA countries totalling EUR 49,827,000, representing some 36% of the Agency's total budget in 2006. These payments are made in return for scientific services provided under contract to the EMEA.

1.3 Information and communication

A number of activities were carried out in 2006 in an area of increasing importance to the Agency: the provision of high-quality information to patients and healthcare professionals.

First stage of EudraPharm information-database launched

As part of its responsibility for providing comprehensive and up-to-date information about the medicines it assesses, and in line with requirements of the new pharmaceutical legislation, the EMEA launched a first version of the EudraPharm database, on 6 December 2006. Ultimately, EudraPharm will provide public access to multilingual information about all medicines authorised in the EU.

Reaching out to the public through EPAR summaries

In February 2006, the Agency began publishing summaries of European public assessment reports (EPARs) that are specially written to be understandable by patients and members of the general public. These 'EPAR summary for the public' documents are now written for all newly authorised medicines, and a project has been running in parallel to prepare EPAR summaries for products approved prior to 2006. By the end of the year, a total of 160 EPAR summaries had been published.

Informing about issues of major topical interest

The Agency systematically provided comprehensive information – in the form of press releases and question-and-answer documents – to explain scientific opinions given in areas relating to the safety of medicines, new types of applications and new technological advances, among other areas.

General question-and-answer documents were also prepared to help with communication on subjects such as compassionate use, generic and biosimilar medicines, and evaluation of mock-up vaccines for pandemic influenza.

Efforts to improve transparency of regulatory activity

After consulting its stakeholders, the EMEA put in place procedures to publish information on the withdrawal of applications prior to opinion and on the refusal of marketing authorisations. Question-and-answer documents are now systematically published to give relevant information at the time of withdrawal or refusal of applications. In 2006, information on 14 withdrawals and 7 refusals was published.

Efforts to improve interaction with patients

Building on its framework for interaction with patients and consumers, the EMEA establsihed a new group – the EMEA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) –to provide recommendations to the Agency and its scientific committees on all matters of interest to patients. The PCWP will build on work already undertaken by the former EMEA/CHMP Working Group with Patients' and Consumers' Organisations.

Patients' and consumers' organisations express keen interest for involvement in the EMEA's work

Almost 40 organisations answered the EMEA's call for expressions of interest for involvement in EMEA activities. Following assessment for eligibility criteria of this first wave of applicants, a list of 16 patients' and consumers' organisations meeting the criteria was drawn up. The list will be updated as more organisations qualify to join.

In order to streamline their involvement, the EMEA published, in June, rules for the involvement of members of patients' and/or consumers' organisations in the Agency's committee-related activities.

A satisfaction questionnaire was prepared and will be used in 2007 as a performance indicator for EMEA interaction with patients' and consumers' organisations.

Efforts to improve interaction with healthcare professionals

In December 2006, the EMEA/CHMP Working Group with Healthcare Professionals' Organisations' was created to make recommendations and proposals in view of the development of a framework for interaction with healthcare professionals organisations.

The creation of the working group followed a workshop with healthcare professionals organised by the EMEA on 28 March 2006. Formalising the Agency's interaction with healthcare professionals, the participants of the workshop identified areas for action and recommended to further develop EMEA interaction with healthcare professionals following the same model as the interaction with patients' and consumers' organisations.

Information and communication on veterinary topics

In the veterinary sphere, the EMEA held a very successful Infoday with IFAH-Europe, in November, at which topics including risk-benefit assessment, user-safety guidelines and environmental-risk assessment were addressed in detail.

A focus group meeting was held with CVMP members, industry and national competent authorities to agree on the implementation of practical measures to promote the prudent use of fluoroquinolones in food-producing animals, following detailed consideration of the issue by the CVMP.

Translation of product information

The Agency revised the organisation of translation-checking of product-related information. The revised procedure foresees in-service contracts with the national competent authorities for the checking of translations, and reinforced cooperation with the Translation Centre in Luxembourg for the translation of certain categories of document. The revised procedure was set up following a decision taken by the EMEA Management Board in September 2005, and will comply with the new legal timeframes for review of translations of product information.

Although the first experience with the implementation of the new system was positive, room for improvement was identified, in particular in the field of post-authorisation procedures.

1.4 Integrated management

Management and internal control systems are part of EMEA corporate governance and are consolidated in an integrated quality-management system at the EMEA.

Highlights for 2006 in the area of management and control:

- The Agency's internal audit service carried out audits covering 8 key processes.
- In the framework of the benchmarking of European medicines agencies (BEMA) a second self-assessment exercise was conducted using the BEMA questionnaire.
- The EMEA ensured the logistics, training and anonymous-data storage and analysis throughout the first cycle of BEMA in 2006, and contributed to the peer-review visits to partners in the European network.
- Results from audits by external and internal auditors' groups – from self-assessments, staff-motivation surveys and risk-analyses, as well as feedback from stakeholders – were reviewed as part of the annual management review and considered for the setting of planning directives for 2007.
- The Audit Advisory Committee (AAC) started its second term, with new members selected following 2 procurement exercises conducted in 2005 as well as with 2 new members following an internal selection exercise. In 2006, one tender procedure was conducted to establish a reserve list of AAC members and to select the fourth external member. The AAC held 3 meetings.

1.5 Small and medium-sized enterprises

On 15 December 2005, the EMEA launched an SME Office to provide financial and administrative assistance to micro, small and medium-sized enterprises (SMEs), with the aim of promoting innovation and the development of new human and veterinary medicinal products by these smaller companies.

Enterprises with less than 250 employees and an annual turnover of not more than €50 million or an annual balance-sheet total of not more than €43 million are eligible for assistance from the SME Office.

High interest in SME status

Companies' interest in the SME initiative in 2006, its first year of operation, exceeded expectations. More than 145 companies, including 6 veterinary companies, submitted declarations on their qualification as SMEs to the Agency. Of these, 117 companies from 17 different countries across the EU were assigned SME status. These included a substantial number of micro-enterprises (24%), with many start-up companies originating from university research projects.

Supporting innovation in Europe

The SME Office provided regulatory assistance to 14 companies. Twenty-three SME companies requested scientific advice and a total of €1.4 million in SME fee reductions were processed for scientific advice. Eight SMEs submitted marketing-authorisation applications. Payment of fees totalling €1 million for marketing-authorisation applications and inspections were deferred under the new initiative.

A detailed 'User Guide for SMEs' was published in December 2006 for consultation, covering administrative and procedural aspects of pharmaceutical legislation that are of particular relevance to smaller companies.

1.6 European public-health activities

Better medicines for children

The EMEA contributed actively to the preparation of Regulation (EC) No 1901/2006 on medicinal products for paediatric use, which subsequently entered into force in January 2007. The EMEA and the European Commission (Directorate-General for Enterprise) published a joint Priority Action Plan in July 2006. A dedicated task-force was set up to establish and implement the action plan.

Preparing for a strategy for the establishment of a paediatric research network, the EMEA met with existing networks in the EU. Meetings were also held with the Directorate-General for Research at the European Commission to prepare the funding of research on off-patent medicines.

Other initiatives included the Agency's contribution to recommendations on the ethics of clinical trials in children and a workshop on medicines for neonates, which allowed the Agency to meet with representatives of patients' organisations and learned societies.

Innovation and emerging therapies

The EMEA strengthened its relationship with the European Commission Directorates-General for Enterprise, for Research and for Health and Consumer Protection, as well as with the European Food Safety Authority, in a number of areas relating to emerging therapies and technologies, including nanotechnology and borderline medicinal products.

EMEA involvement in the Innovative Medicines Initiative

The EMEA contributed to the preparatory steps of the Innovative Medicines Initiative through participation in workshops and through frequent dialogue with the Directorate-General for Research. In addition, the Agency made proposals for topics of public-health interest to be included in the project, such as pharmacovigilance. As a complementary action, the CHMP established a think-tank on innovation. This group met with pharmaceutical companies and academic groups during 2006, and will report on the outcome in 2007.

EMEA involvement in the European Technology Platform for Global Animal Health

The Agency is part of the Steering Council of the European Technology Platform for Global Animal Health, and assisted in finalising its Strategic Research Agenda aimed at promoting access to the market for innovative products for animal health, including those for limited markets. The Agency subsequently accepted a place in the coordination group set up to convert those parts of the agenda dealing with regulatory issues into an action plan.

Pandemic-influenza preparedness

The EMEA continued its activities in the area of pandemic-influenza preparedness for vaccines and antivirals. The EMEA Pandemic Influenza Crisis Management Plan was developed and the Joint EMEA-Industry Task Force met in March 2006. Contacts were strengthened with the Directorate-General for Health and Consumer Protection and with the European Centre for Disease Prevention and Control, and regular communication with the US Food and Drug Administration was held to discuss issues of common interest. The EMEA (in collaboration with regulatory authorities in other geographical regions) contributed to the development of the WHO Guidelines on Regulatory Preparedness For Human Pandemic Influenza Vaccines.

Pandemic-influenza 'mock-up' vaccine receives positive opinion

The Agency adopted the first positive opinion for a pandemic-influenza 'mock-up' vaccine in December 2006. A mock-up vaccine is not intended for use outside a declared pandemic-influenza situation, 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.

Pharmacovigilance activities

Following a workshop on risk-management plans for pandemic-influenza vaccines – with representatives from the European Commission, the EMEA, the European Vaccine Manufacturers' Association, the European Centre for Disease Prevention and Control, and Member States – recommendations for a core pharmacovigilance plan for pandemic-influenza vaccines were developed and approved. These recommendations are to be included in the risk-management plans of all pandemic-influenza vaccines.

The EMEA worked on the development of a pharmacovigilance strategy for antivirals in case of pandemic influenza, taking into account the initiatives taken at industry level. As part of this activity, the Agency contributed to a discussion under the responsibility of the Directorate-General for Health and Consumer Protection involving the Health Security Committee and the National Influenza Pandemic Coordinators on the release of recommendations on stockpiling.

Avian-influenza preparedness

Two avian influenza vaccines approved in 2006

The Agency issued positive opinions for authorisation under exceptional circumstances of two avian-influenza vaccines for birds, following accelerated assessment by the CVMP. This prompt action, together with accelerated decision-making procedures of the European Commission, enabled authorised vaccines of high quality to be available for use across the European Union at a time of increased risk during the autumn of 2006.

Other activities included the participation in several international forums on how best to control avian influenza in birds as a means of reducing the potential spread to man. In addition, the EMEA participated in a WHO consultation on the possible use of veterinary vaccine-manufacturing facilities for the manufacture of human pandemic-influenza vaccines.

Antimicrobial resistance

One of the main policy issues tackled by the CVMP during 2006 was measures to limit the development of antimicrobial resistance through the use of veterinary medicinal products. The Committee for Medicinal Products for Veterinary Use (CVMP), based on a proposal from its Scientific Advisory Group on Antimicrobials (SAGAM), adopted a new strategy on antimicrobials for the years ahead.

The CVMP also adopted a reflection paper on the use of quinolones and fluoroquinolones in the EU, critically reviewing recent data on their use and the potential impact on human and animal health. Based on the scientific considerations of the SAGAM, the CVMP proposed risk-management actions, including a recommendation for harmonized prudent-use guidance in the product literature of all (fluoro)quinolone-containing veterinary medicines for food-producing animals. This proposal is now being implemented through cooperation with authorities throughout the European medicines system.

EMEA involvement in the Pharmaceutical Forum

The EMEA contributed to the work of the Pharmaceutical Forum organised by the European Commission, in particular on issues relating to information for patients and to relative effectiveness. As a member of the Information to Patients Working Group, the EMEA prepared and published the

report ‘Statutory Information on Medicines’, which will also be taken into account in the context of the Commission’s report to the European Parliament and the Council following the entry into force of Directive 2001/83/EC as amended.

Scientific activities relating to clinical trials

Following the severe adverse reactions to TGN 1412 (a monoclonal antibody) during a first-in-man clinical trial in the UK, the EMEA established a task-force to prepare a guideline on such trials involving investigational medicinal products considered to be of potentially high risk.

At the request of the European Commission, the EMEA carried out a review of the adequacy of guidance relating to elderly patients’ participation in clinical trials. This report led to initial recommendations for the updating of the CHMP Assessment Report and the Summary of Product Characteristics templates, and a proposal was made to open a phase of reflection on the ICH E7 overarching guideline.

Other European public-health initiatives

- The EMEA responded to the Directorate-General for Health and Consumer Protection’s request for comments on the Scientific Committee on Emerging and Newly Identified Health Risks’ (SCENIHR) scientific opinion on the safety of human-derived products with regard to variant Creutzfeldt-Jakob disease.
- Contacts were maintained with the Directorate-General for Health and Consumer Protection in the areas of quality and safety of blood components, human tissues and cells, because of the relevance of Commission directives on plasma-derived medicinal products and cell-based medicinal products.
- At the request of the European Commission, the EMEA organised a workshop on homeopathic medicinal products, in October 2006. The aim of the workshop was to provide a forum for discussion among all stakeholders on the current legislative framework for homeopathic medicines.
- Cooperation with the European Pharmacopoeia and European Directorate for the Quality of Medicines and Healthcare continued to be an important activity in view of the complementarity of their activities to those of the EMEA in relation to the quality of medicines.
- In the area of anti-infectives, the CHMP established a working relationship with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) to address harmonising the setting of breakpoints for resistance to new antibiotics.
- The EMEA established collaboration with leading European professional societies and cancer-research institutions (ESMO, EORTC) to increase communication and broaden the network of experts.
- The Agency participated actively in the ongoing debate on the EU programme to reduce animal testing and develop other modern approaches to safety assessment.
- The Agency continued its successful collaboration with the European Food Safety Authority (EFSA) in the areas of setting maximum residue limits for feed additives and surveillance for resistance to veterinary antimicrobials in food-producing species. New areas of cooperation were initiated in terms of the role of vaccination in the control of infectious diseases of livestock that are of importance to the EU, such as rabies, Newcastle Disease, avian influenza and bluetongue. The EMEA assisted EFSA in regulatory and procedural aspects relating to the authorisation and use of vaccines.

1.7 Preparation for enlargement

Preparations for the accession of Bulgaria and Romania

Several initiatives were put in place to allow for a smooth transition to EU membership by Bulgaria and Romania.

Representatives of Bulgaria and Romania participated as observers in the work of the EMEA Management Board, its scientific committees and working parties. They also participated in workshops organised by the EMEA in relation to both human and veterinary medicines.

Pre-accession linguistic check

The EMEA, together with the Bulgarian and Romanian competent authorities, set up a pre-accession linguistic-check process (PALC II), to ensure a good standard of quality for Bulgarian and Romanian translations of product information for over 300 centrally authorised products ahead of accession.

Between January and December 2006, a total of 264 human and 59 veterinary centrally authorised products were submitted in Bulgarian and Romanian for a linguistic check by the respective national competent authorities (NCAs). The main stakeholders (industry, NCAs and the EMEA) managed to complete successfully the checking process for 98.5% of all centrally approved products.

The EMEA regularly exchanged information with the medicines regulatory authorities in Bulgaria, Croatia and Romania under the terms of the (n)CADREAC simplified procedure. This relates to opinions on safety-variations, extensions, annual re-assessments and renewal applications adopted by the CHMP for centrally authorised products listed in the EMEA simplified-procedure database, as well as to opinions on any provisional changes to the product information introduced in the context of urgent-safety-restriction procedures.

Participation of Croatia and Turkey in EMEA activities

A multibeneficiary programme on participation of Croatia and Turkey in EMEA activities during 2006 and 2007 was launched in May 2006. An initial meeting was hosted by the EMEA with Croatia and Turkey to review a range of issues relating to authorisation of human and veterinary medicines in preparation for the possible accession of these countries to the EU. National competent authorities of both countries were encouraged to send representatives as passive observers of EMEA meetings, training sessions and workshops.

1.8 International cooperation

The EMEA cooperates closely with other scientific and regulatory institutions and agencies in the public-health arena at EU level.

ICH

An important part of the Agency's cooperation with the US Food and Drug Administration and the Japanese Ministry of Health takes place under the umbrella of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), which also involves Canadian and Swiss health authorities and the World Health Organization (WHO). Six-monthly Steering Committee meetings and several interim meetings were held in 2006. The EMEA proposed that training and attendance at CHMP working-party meetings be opened up to non-ICH countries that are members of the Global Cooperation Group (GCG).

Important initiatives in 2006 included:

- Preparation of global technical guidelines in the field of pharmagenomics.

- In the area of pharmacovigilance, development-safety-update reports (DSURs), adopted as a new topic (ICH E2F) to be addressed at ICH level.
- Input to the development of a concept paper and business plan in relation to risk-communication.
- Launch of a new topic on pharmaceutical quality systems.
- Development of more specific guidance on pharmaceutical development.
- Continuing work in the area of ICH E2B(R): 'Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports', as well as the ICH M5 topic 'Data Elements and Standards for Drug Dictionaries'.
- Continuing work by the ICH Terminology Maintenance Implementation Working Group to develop business requirements.

VICH

The EMEA continued to play an active role in the framework of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH). The EMEA filled the role of EU coordinator for the nine-monthly Steering Committee meetings and provided input into the VICH expert working groups, as well as assisting the implementation of the new phase-II strategy for VICH 2006-2010.

Cooperation with the FDA

Further to the extension in 2005 for five more years of the European Union/Food and Drug Administration confidentiality arrangements, the EMEA and the FDA strengthened their collaboration in various fields, most notably: scientific advice, applications for marketing authorisation, emerging safety issues for medicines; GMP and GCP inspections. There was also interaction on the development of guidelines. Finally, a staff-exchange programme between the two authorities was operated.

Information relating to the safety of medicines was frequently exchanged between the EMEA and FDA during 2006 due to the worldwide review of several high-profile medicines/classes of medicines. This exchange proved to be valuable, both in terms of availability of information important to the decision-making process and in terms of communicating coherent information to healthcare professionals and patients.

Pilot phase for parallel scientific advice continued

The pilot phase for parallel scientific advice between the EMEA and FDA continued during 2006. It is mainly aimed at important (e.g. orphan or paediatric products) or breakthrough medicinal products that have been accorded 'fast track' status in the US.

Other EMEA and FDA initiatives included:

- Extension of clusters of in-depth collaboration in the fields of paediatrics and influenza vaccines.
- Cooperation on oncology matters, including monthly teleconferences to discuss ongoing applications, pending regulatory actions, mutual participation in advisory-committee meetings and joint participation in specialised international conferences.
- Cooperation in the assessment of applications for anti-infective medicines.
- Consolidation of the joint Voluntary Genomic Data Submission (VGDS) briefing-meeting process, paving the way for more in-depth scientific discussions in the area of pharmacogenomics.

The EMEA has also taken up an important role in the FDA's Critical Path initiative that seeks to modernise the scientific process through which a potential human medicinal product is transformed from a discovery into a medicinal product. The EMEA is represented as an observer on the management committee and in expert groups of the consortium focusing on the validation of toxicity-predictive biomarkers.

World Health Organization (WHO)

Cooperation with the WHO covered a wide range of topics, including medicinal products intended for markets outside the EU, pharmacovigilance, anti-infective medicines, microbiocides, pandemic influenza, good manufacturing practice and quality issues, good clinical practice, international non-proprietary names, and a number of areas relating to biological products including vaccines. With regard to combating counterfeit medicines, the EMEA was involved directly in the WHO IMPACT initiative and indirectly through its work with the European Medicines Enforcement Officers (EMEO) group.

Codex Alimentarius and the World Organisation for Animal Health (OIE)

The Agency also participated in international activities of the Codex Alimentarius and the World Organisation for Animal Health (OIE) on matters including: residues of veterinary drugs in food; international policies on minimising the development of antimicrobial resistance; authorisation of vaccines against highly antigencially variable viruses, such as foot-and-mouth disease, avian influenza and bluetongue.

Other international activities

- Together with experts from the US, Canadian and Japanese health authorities, the International Society of Thrombosis and Hemostasis (ISTH), WHO, patients' organisations and industry, the EMEA discussed international standardisation and harmonisation of clinical studies investigating Factor-VIII inhibitor development.
- An EMEA expert meeting on revision of the core summary of product characteristics and note for guidance for human normal immunoglobulin for intravenous administration reviewed the current clinical use of these products. Participants included experts in this field and representatives from the FDA, patients' organisations and industry.
- In order to consolidate knowledge on novel aspects of pharmaceutical development, the EMEA, the International Pharmaceutical Federation (FIP) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) organised a workshop on regulatory aspects of the 'design space' concept, in May 2006.
- A think-tank and joint workshops with academia and industry on development models for disease-modifying medicines in the area of neurodegenerative diseases were organised during 2006.
- In the context of their respective mutual-recognition agreements, experts from Japan and Australia participated in meetings organised by the EMEA on GMP and quality-related issues.
- EMEA and European Commission representatives met with Japanese officials to further progress practical aspects of the mutual-recognition agreement with Japan.
- The EMEA, in collaboration with the European Commission and Swissmedic, co-sponsored a training course on GMP at Beijing University, China, in September 2006.

Visiting experts at the EMEA

The EMEA welcomed visiting experts of non-EU regulatory authorities from Canada, Japan and Taiwan. In addition, national experts from the regulatory authorities of Poland, France, Greece, Hungary and the UK were seconded to the Agency at various periods in 2006.

2. MEDICINES FOR HUMAN USE

2.1 Orphan medicines

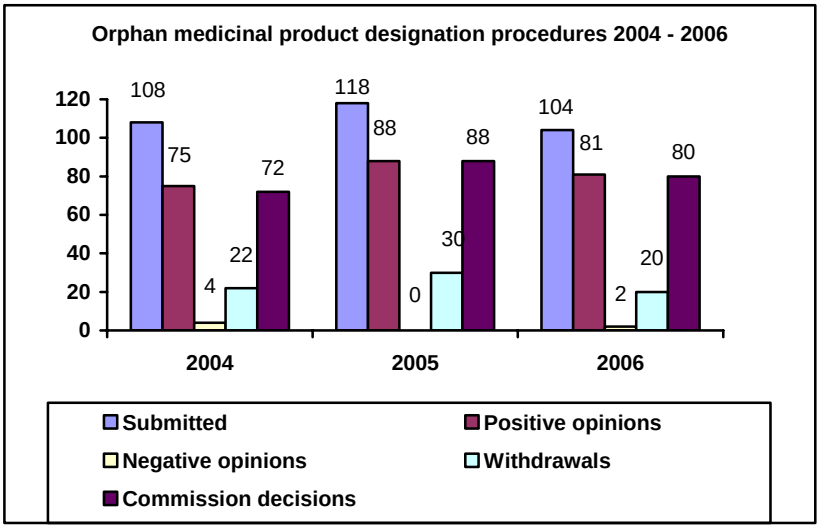
Medicines for rare disorders, so-called orphan medicinal products, are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting no more than five in 10,000 people in the European Union, or where for economic reasons such medicines would not be developed without incentives.

Applications for designation of orphan medicines are reviewed by the EMEA through the Committee for Orphan Medicinal Products (COMP). The composition of the Committee is given in Annex 4.

The third 3-year mandate of the COMP started in May 2006, and a new chairperson and vice-chairperson were elected at the June meeting.

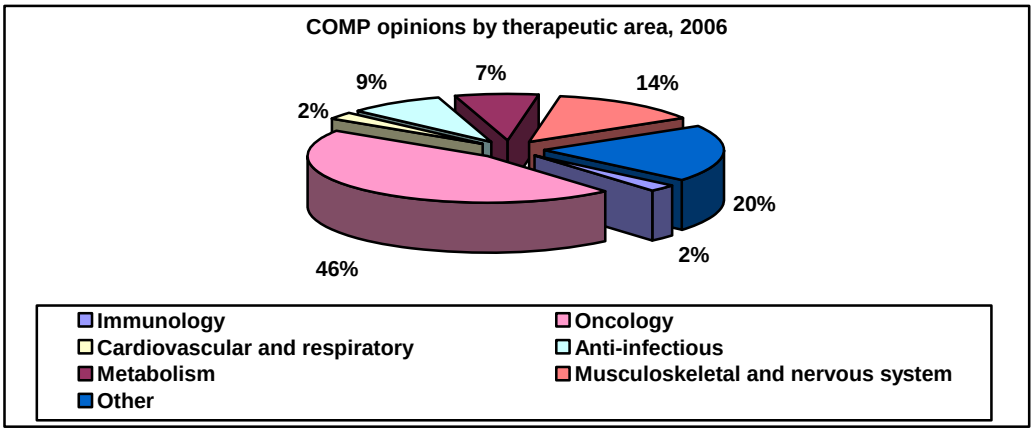
Orphan designation

For the third consecutive year, more than one hundred applications were received for the designation of orphan medicinal products: a total of 104 applications were submitted, on which the COMP adopted 81 positive opinions. The number of withdrawn applications (20) was the lowest in the past six years.



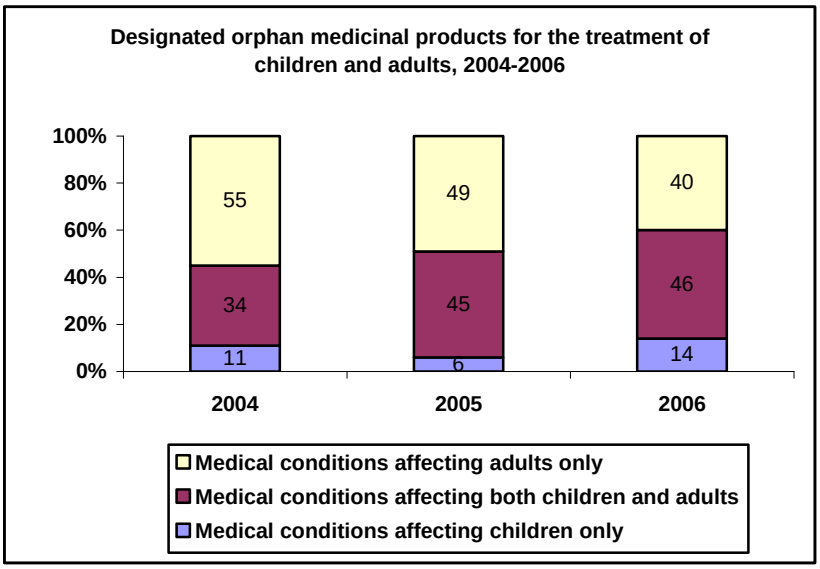
Cancer is still the main therapeutic area concerned

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



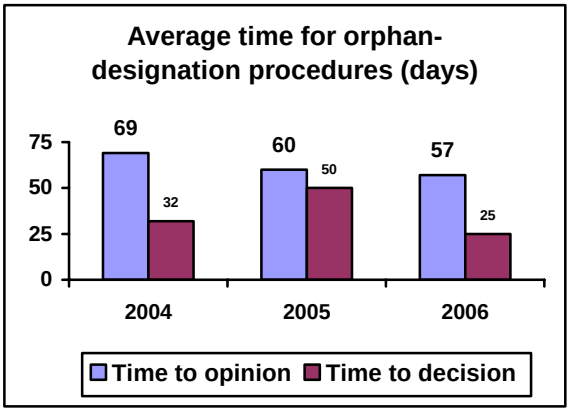
More than half of orphan medicines designated for treatment of children

Sixty percent of orphan products designated in 2006 were for conditions that affect children, including 14% intended exclusively for paediatric use.



Faster processing of orphan designations

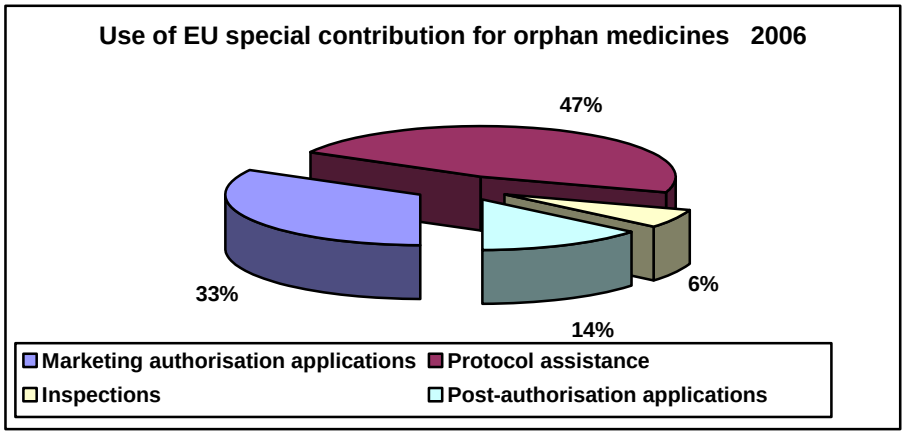
The Agency met its continuing work-programme objective of adhering to regulatory timelines for orphan-designation procedures, and managed to further reduce the average time to 57 days — the shortest average time since the start of the procedure, in 2000.



Special financial support from the EU budget

A total of €6.7 million was granted to fund fee reductions for orphan medicines in 2006, primarily from the EU special contribution.

The Agency's policy on fee reductions for orphan medicines was amended in 2006 to take into account the increasing number of fee-reduction requests being received. The main change to the policy concerned a re-focusing of incentives on support for protocol assistance and other pre-authorisation assistance.



2.2 Scientific advice and protocol assistance

The EMEA provides scientific advice to help companies with their development programmes, thus contributing towards bringing innovative medicines to the market more quickly. The Agency's advice can cover quality, safety or efficacy questions relating to the research and development of a specific product, as well as broader scientific issues not related to a specific product.

Free-of-charge scientific advice, called 'protocol assistance', is offered to sponsors developing orphan-designated medicinal products.

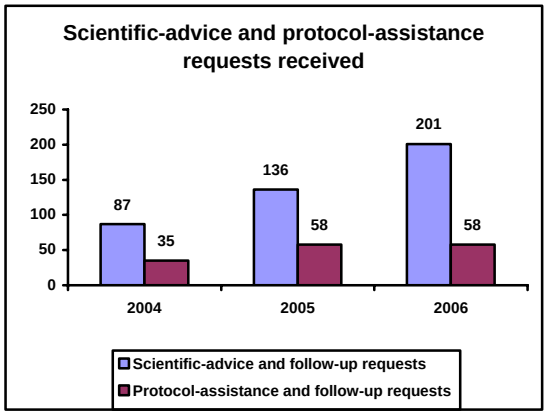
Implementation of the new framework for scientific advice

In July 2006, the Agency implemented a new framework for the provision of scientific advice that helps to improve the management of an increasing workload and new legal requirements in this area. As part of this initiative:

- four additional members were appointed to the Scientific Advice Working Party (SAWP) and its meetings were extended to three days, allowing more discussion meetings to be held with applicant companies;
- the procedure was streamlined to allow finalisation within 40 days (up to a maximum of 70 days), whereas the previous procedure could take up to 100 days;
- coordinators and their assessors/experts are systematically involved in the planning/pre-submission phase of all advice procedures.

Number of requests for scientific advice continues to rise

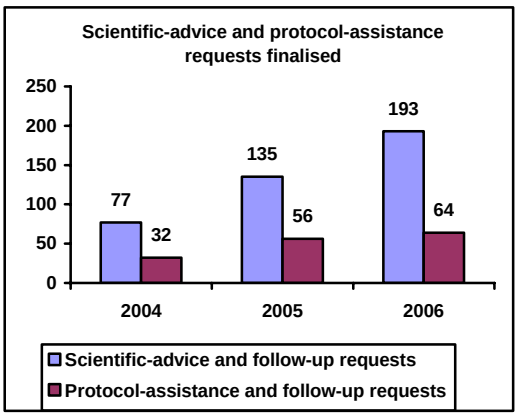
A further increase in the number of requests for scientific advice was registered in 2006, with 33% more requests received than in 2005, indicating that interest in this assistance from the EMEA remains high.

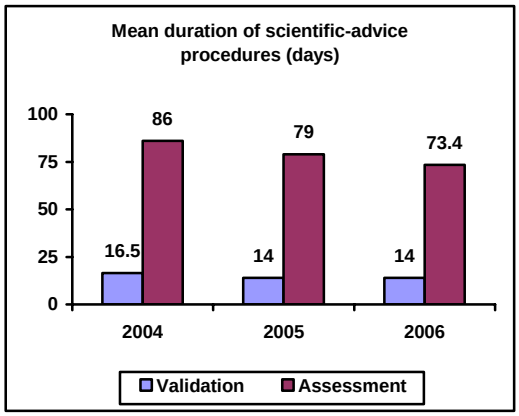


More procedures finalised, in shorter time

A total of 257 scientific-advice, protocol-assistance and follow-up requests were finalised in 2006, compared to 191 in 2005.

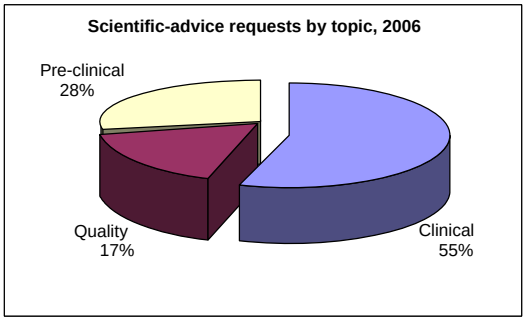
Thanks to the newly streamlined procedure, the SAWP was able to complete these scientific advice procedures more quickly than in previous years.

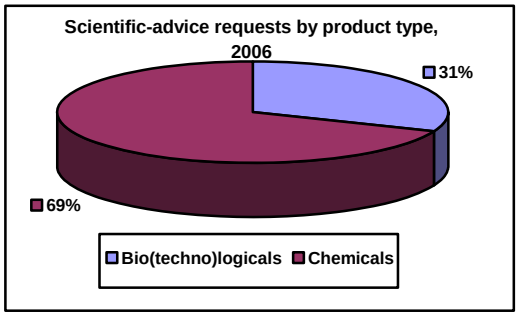




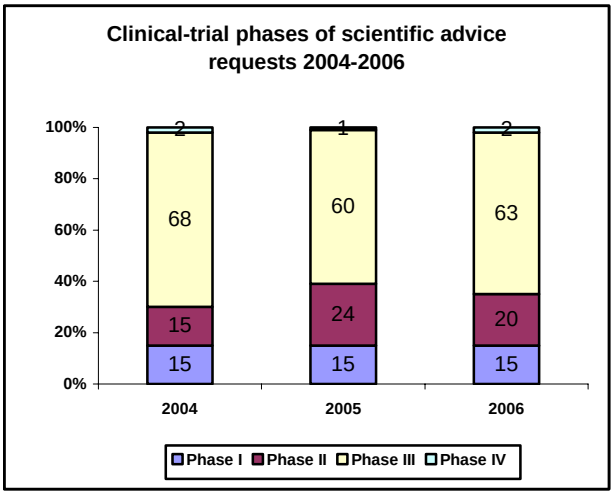
Distribution by topic, product type and clinical-trial phase largely unchanged

The distribution of scientific-advice requests by topic and by product type, as illustrated in the charts below, is fairly consistent with what has been seen over the past few years.



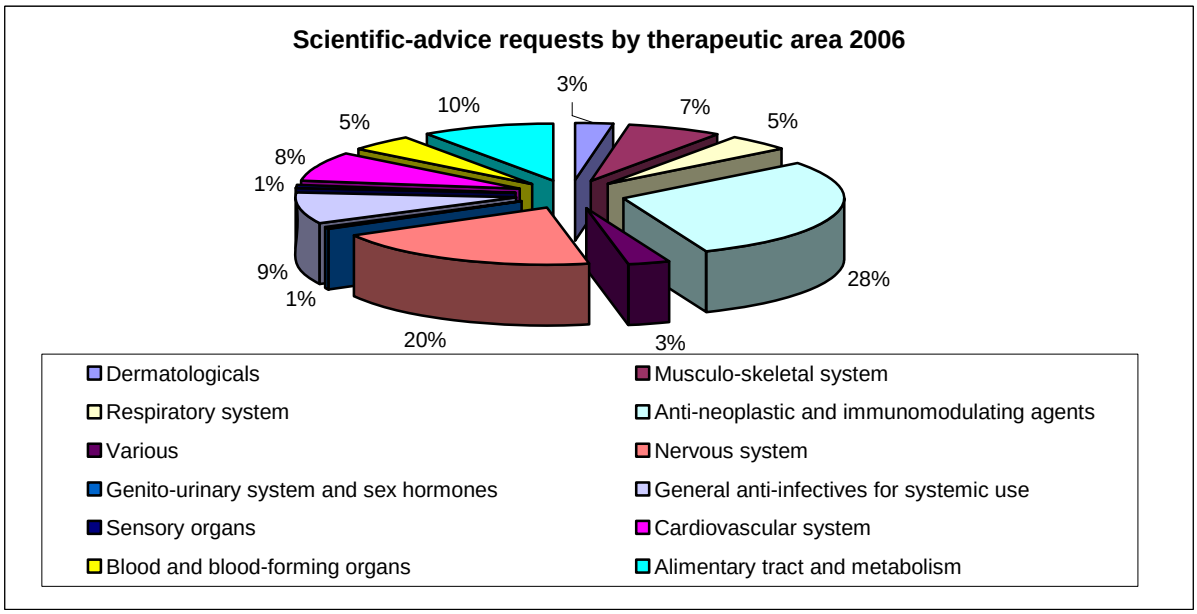


The distribution of scientific advice by clinical-trial phase was largely similar to the distribution in previous years, with minor differences between the proportions of requests at phase II and phase III.



Cancer and nervous system still the predominant therapeutic areas concerned

The highest numbers of requests received concerned medicinal products for conditions related to cancer or the nervous system, with those relating to the alimentary tract and metabolism forming the third most-represented therapeutic area.



Gene and cell-therapy products

More scientific advice and protocol assistance was provided in relation to gene and cell-therapy products than in previous years, reflecting progress made in the field. The number of requests is expected to continue to grow as more marketing-authorisation applications are submitted.

Scientific advice and the CHMP working parties

During 2006, the CHMP working parties increased their contribution of experts, thus improving the scientific advice given to companies.

2.3 Initial evaluation

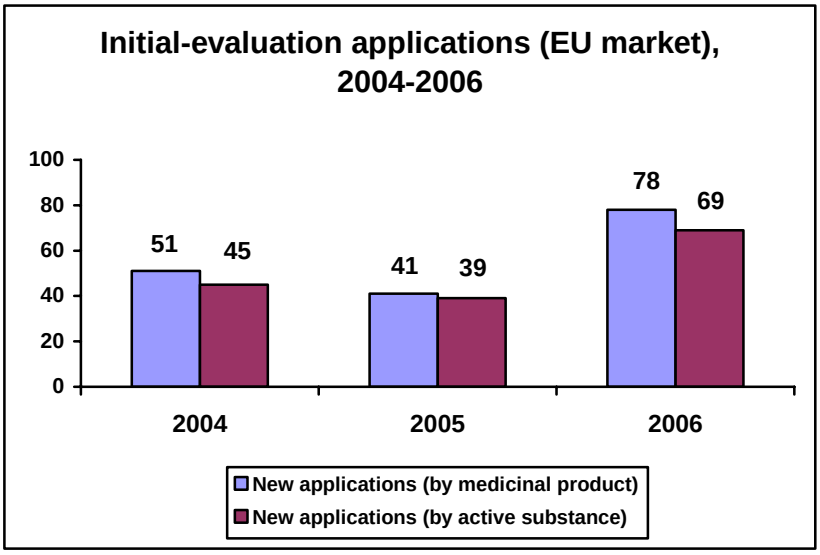
Applications for new medicines are reviewed by the Agency through the Committee for Medicinal Products for Human Use (CHMP). The Committee assesses the quality, safety and efficacy of a medicine and, based on an overall balance of the benefits and risks of the medicine, gives its opinion on whether or not the European Commission should grant a Community-wide marketing authorisation.

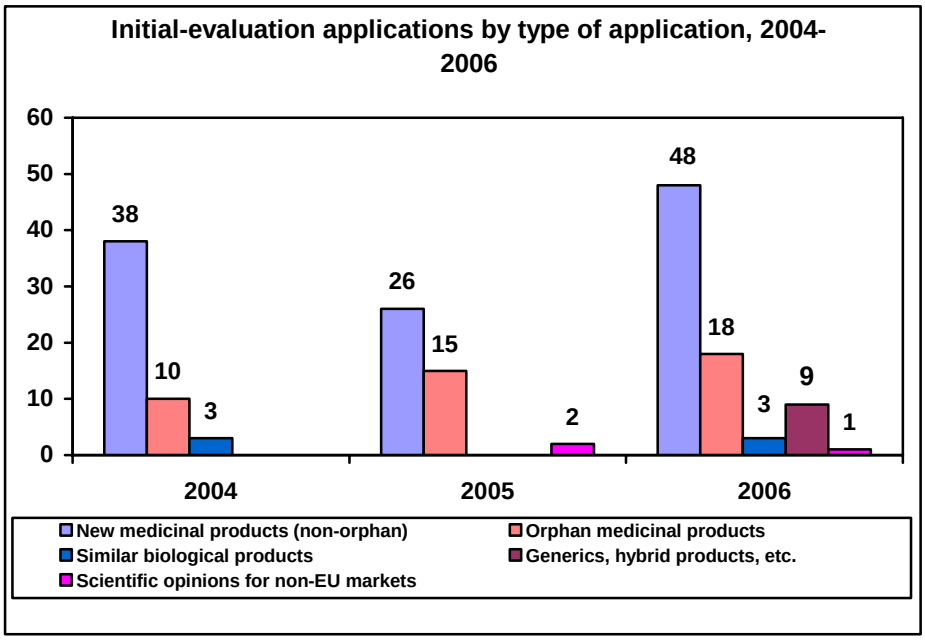
The composition of the Committee is given in Annex 2.

New applications in 2006

Number of applications received in excess of forecast

A greater number of initial marketing-authorisation applications were received in 2006 than had initially been expected. Whereas 62 such applications had been forecast for the year, a total of 79 were actually received (including one concerning a medicinal product intended exclusively for use outside the EU).





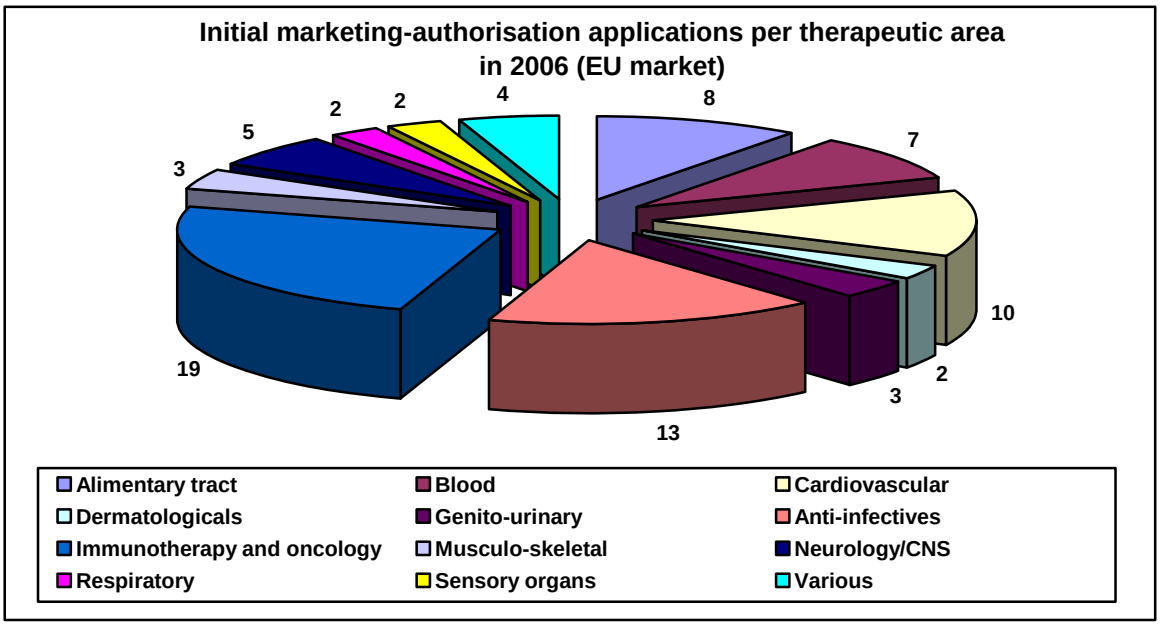
New dossiers concerning generics and novel aspects of pharmaceutical development

A new development in 2006 was the receipt of the first applications for generics of centrally authorised products whose 10-year data-exclusivity period has ended: three such applications were received. Although these generic medicines are not innovative, they are considered to represent an important contribution to public health in the EU.

A number of dossiers received in 2006 concerned novel aspects of pharmaceutical development, including new approaches involving the design-space concept and process-analytical technologies.

Therapeutic areas concerned: cancer still dominates

Applications for new products for use in the treatment of cancer once again represented the highest proportion by therapeutic area in 2006. Anti-infectives and cardiovascular products were the two next most-represented therapeutic groups, overtaking alimentary tract and central nervous system treatments that held these positions in 2005.



One third of accelerated-procedure requests accepted

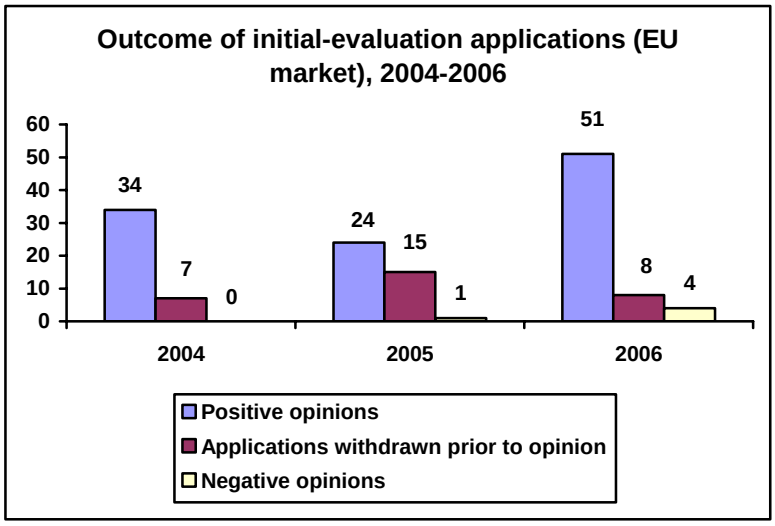
The CHMP accepted 4 out of 13 requests received in 2006 for use of the accelerated-assessment procedure. Two applications that were accepted in 2005 for the accelerated procedure had to be converted to the normal 210-day procedure at the end of the first phase of assessment.

The first CHMP opinions in such procedures are expected to be delivered in 2007.

Summary of accelerated procedures in 2006					
Product type	Requests to CHMP	Rejected by CHMP	Accepted by CHMP	Procedures started	CHMP opinions given
Chemical	10	8	2	1	0
Biological	3	1	2	0	0

Opinions adopted in 2006

The CHMP adopted 51 positive opinions and 4 negative opinions on initial marketing-authorisation applications evaluated in 2006. Eight applications were withdrawn by applicants before an opinion could be adopted.



Europe first to approve biosimilars

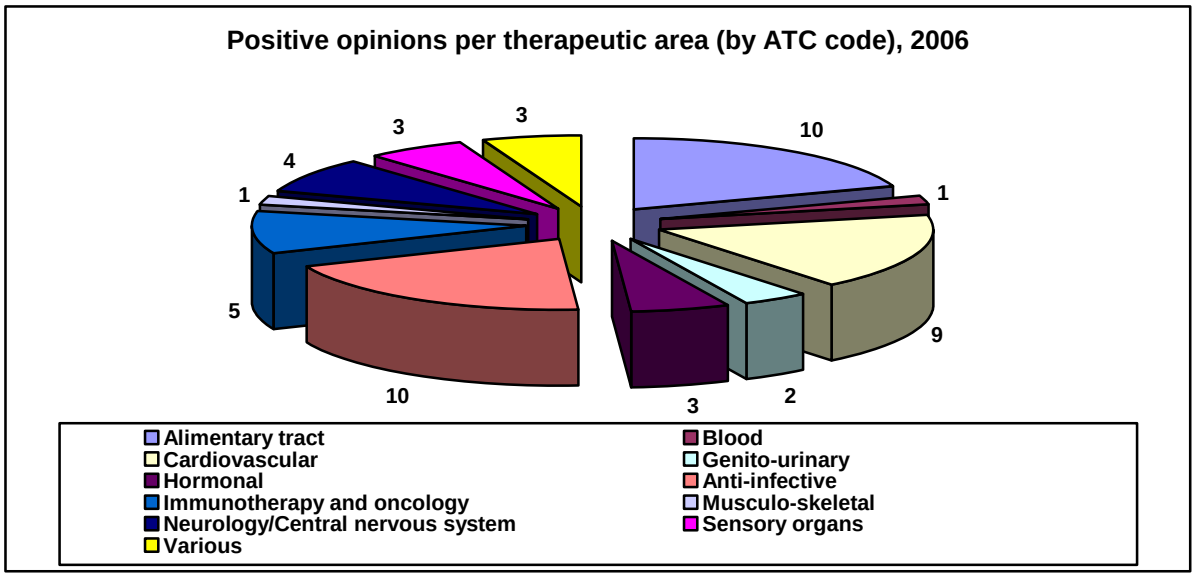
Among the positive opinions adopted, 11 concerned new orphan products and 2 concerned similar biological (biosimilar) products containing human DNA-recombinant growth hormone. The approval of biosimilar products places Europe at the forefront of medicines regulation in this area and represents an important contribution to public health in the EU.

Use of special authorisation procedures

The CHMP adopted positive opinions in 3 conditional-approval procedures (concerning products for treatment of cancer, epilepsy and HIV infection) and approved a further 3 products under exceptional circumstances (concerning one product for cancer, one for an enzyme-deficiency disease, and one pandemic-influenza mock-up vaccine). No opinions were adopted on products evaluated through compassionate-use or accelerated-assessment procedures.

Anti-infectives once again amongst the most-represented therapeutic areas

More positive opinions were adopted in respect of anti-infectives and alimentary-tract products than other types, with those relating to the cardiovascular system forming the third major group.



Public-health benefits of medicines recommended for approval in 2006

Medicinal products of notable public-health interest that received a positive opinion from the CHMP in 2006 included:

- The first medicinal product produced by transgenic biotechnology in animals: a copy of the human protein that prevents blood-clots, extracted from the milk of goats which have had a gene inserted that enables them to produce the human protein.
- The first vaccine against human papilloma virus — a widespread cause of genital infections that can lead to cervical cancer.
- The first pandemic-influenza mock-up vaccine, containing the reverse genetic H5N1 strain. (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.).
- Targeted agents for renal cancer, leukaemia and pancreatic cancer, intended for conditions where there has been a high unmet need.
- Products for rare forms of epilepsy in children, such as Lennox-Gastaut and Dravet's syndrome.
- Products to be used as enzyme-replacement treatment for Pompe disease, for smoking cessation and for opioid-dependency substitution treatment.
- A new treatment option for type-2 diabetes mellitus, introducing a new class of medicinal products called incretin mimetics.

One opinion was adopted in the context of cooperation with the World Health Organization (WHO) on medicines intended exclusively for use in countries outside the EU. The product concerned was for the treatment of HIV infection.

Increasing availability of medicines for rare diseases

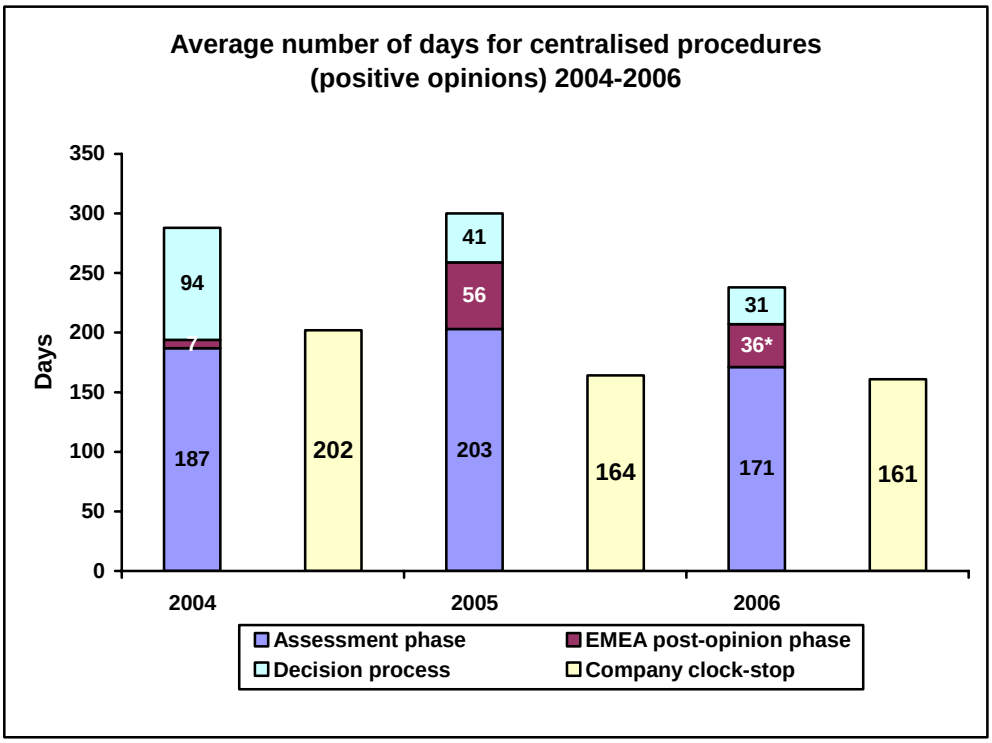
By the end of 2006, a total of 31 orphan medicinal products had been granted a centralised marketing authorisation by the European Commission since the launch, in 2000, of Regulation (EC) No 141/2000. These products potentially benefit some 1.6 million European patients suffering from 24 different rare conditions.

Timelines for opinions

Applications processed more quickly

The average overall time required for approval of a marketing-authorisation application decreased significantly in 2006, with marked reductions compared to 2005 in the average times for the assessment, post-opinion and decision phases of the procedure. A further improvement was also registered in the average clock-stop time required by applicant companies.

The 36-day EMEA post-opinion phase in 2006 accounts for the Agency's processing time as well as the time required by applicants and Member States to carry out their post-opinion translation checks.



* The 36-day EMEA post-opinion phase in 2006 accounts for the Agency's processing time as well as the time required by applicants and Member States to carry out their post-opinion translation checks.

Plasma master files and vaccine antigen master files

Twelve applications were received for certification or re-certification of plasma master files (PMFs). This was higher than the initial 2006 forecast.

No applications were received for certification of vaccine antigen master files.

Ancillary medicinal substances incorporated in medical devices

In 2006, the second positive opinion for a human-blood derivative incorporated in a medical device was given by the CHMP. This represents an important contribution to the safe use of these products.

Due to the increasing number of applications for assessment of ancillary medicinal substances used in a medical device, the EMEA drafted a guideline on the relevant procedural aspects and dossier requirements, which was released for public consultation in 2006.

EMEA Innovation Task Force (ITF)

The ITF is a multidisciplinary group that includes scientific, regulatory and legal competencies to ensure EMEA-wide coordination in the areas of emerging therapies and technologies. The task force monitors emerging therapies and provides companies developing such therapies a platform for early discussion and regulatory advice, and can offer them an early opinion on whether their innovative product will be eligible for EMEA procedures. Briefing meetings for informal exchanges of information can be held with ITF members early in the development process, in liaison with EMEA scientific committees, working parties or expert groups, as appropriate.

During 2006, the ITF received 22 requests for regulatory classification and 15 reports were adopted by the CHMP. The ITF also held 9 briefing meetings with companies.

Improving the quality of assessments

In 2006, the CHMP looked at ways to improve the quality-assurance of the lists of questions which the committee adopts at Day 120 of the assessment procedure. CHMP members assigned as peer reviewers reviewed, together with the EMEA scientific secretariat, the proposed questions in light of the scientific justifications and argumentation presented by the (Co-)Rapporteurs in their initial assessment reports. This initiative helped to improve the quality and clarity of the adopted Day 120 lists of questions, thus meeting one of the objectives set out in the EMEA Road Map.

Product Information Management (PIM) project

The first 'live' marketing-authorisation application using the PIM system was submitted in June 2006, and the first phase of evaluation was successfully completed with the adoption of the 'List of Questions' in October.

PIM is an approach introduced by the EMEA as a joint initiative between industry and regulators. It increases the efficiency of the management and exchange of product information by all parties involved in the evaluation process, using electronic means. In addition, it helps improve the quality and consistency of the published product information.

Work will continue in 2007 to conclude the assessment procedure for the first live submission, including the assessment of the applicant's responses and the linguistic review. On a project level, analysis will continue into the business process and requirements, with a view to accepting further new applications using PIM.

2.4 Post-authorisation activities

Changes to the terms of marketing authorisations are made frequently during the life of a medicine. These changes, known as variations, often relate to the addition of new treatment options, the introduction of warnings or contraindications, or changes in the way the product is manufactured. All variations, whether minor (type IA and type IB) or major (type II), require formal approval, often involving a decision from the European Commission.

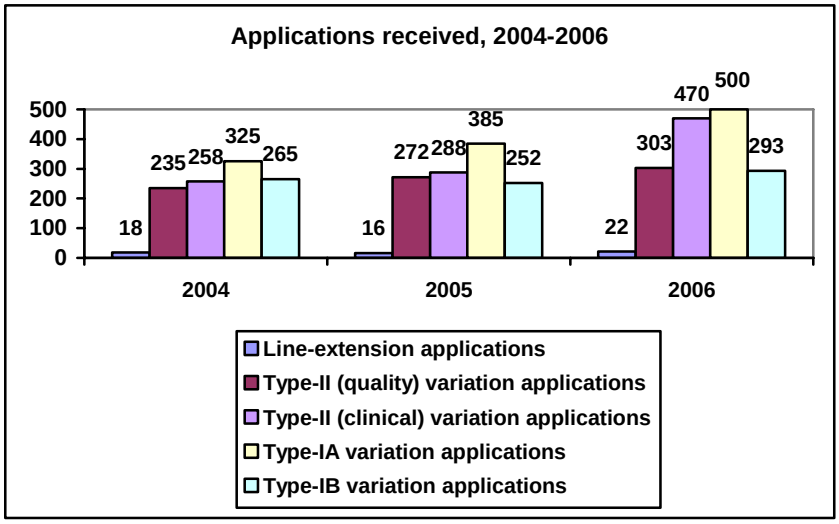
Variations in 2006

Number of variation applications up by almost one third

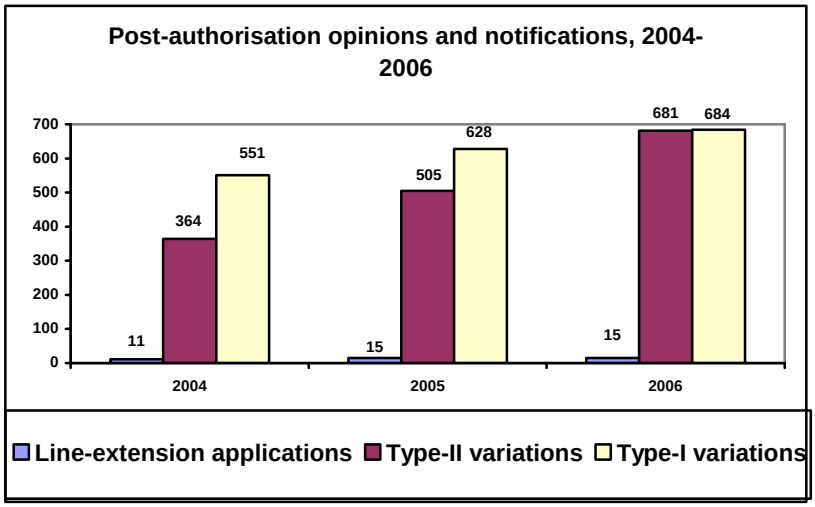
A total of 1,588 applications for variations and line extensions were received in 2006 — an increase of 31% over the number received in 2005.

The number of post-authorisation opinions adopted was also significantly higher (20%) than in the previous year. In particular, the total number of type-II variations (including extensions of indication) finalised during 2006 indicates a 35% increase compared to 2005 (60% of these related to safety and efficacy, and 40% related to quality changes).

The total number of type-I variations handled during the year represents a 9% increase compared to the previous year. Two thirds of these were type-IA variations.



The EMEA undertook various initiatives in 2006 to look at possible process improvements for the handling of variation applications. These efforts are ongoing, and will seek in particular to identify efficiency gains in the handling of type-I and type-II variations.



Public-health impact of post-authorisation activities

New indications broaden scope of existing medicines

A particularly high number of extensions of indication — 41 (46% more than in 2005) — were introduced in 2006, providing additional treatment options for patients.

The majority of the new indications related to medicinal products approved for the treatment of various forms of cancer, including early-stage breast cancer, squamous cell cancer of the head and neck, metastatic gastric adenocarcinoma, cervix carcinoma, follicular lymphoma, dermatofibrosarcoma protuberans, myelodysplastic syndromes, myeloproliferative diseases, and myelodysplastic/myeloproliferative diseases.

Several extensions of indication were also granted for the diagnosis or treatment of central-nervous-system disorders (notably advanced Parkinson's disease and epilepsy), of diabetes, and of cardiovascular, infectious, rheumatoid and inflammatory-bowel diseases.

The use of Scientific Advisory Groups (SAGs) by the CHMP for the assessment of extensions of indications increased in 2006, in particular in the fields of diabetes and oncology.

Contra-indications, class labeling and warnings

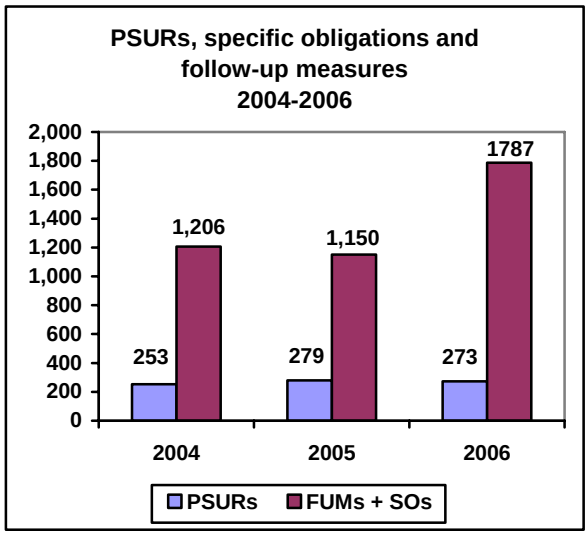
A total of 79 type-II variations (relating to special warnings and precautions for use) were finalised in 2006. Six new contra-indications were also adopted, for medicinal products used in fields such as depression, diabetes and infectious diseases.

Warnings and contra-indications were added for entire classes of medicinal products (class labelling), as outlined here:

- New contra-indication for the use of PDE-5 inhibitors in patients suffering from vision loss in one eye because of non-arteritic anterior ischemic optic neuropathy
- New warning for HIV products relating to the possible risk of osteonecrosis associated with their use
- New warning for glitazones relating to the possible risk of macular oedema associated with their use in diabetic patients
- New warning for biphosphonates relating to the possible risk of osteonecrosis of the jaw associated with their use
- Alleviation of contra-indications and concomitant strengthening of warnings for beta-interferon-containing medicinal products used in the treatment of multiple sclerosis.

Periodic safety update reports (PSURs), follow-up measures (FUMs) and specific obligations (SOs)

The Agency dealt with a high workload relating to PSURs, FUMs and SOs. The sharp increase in the number of FUMs/SOs observed in 2006 (+55%) is partly explained by the assessment of the responses to the EMEA letters sent out in 2005, reminding marketing authorisation holders of their obligation to submit any data (including paediatric data) that might be available and not previously provided to the EMEA.



2.5 Safety of medicines

Major safety reviews

The EMEA dealt with a number of major safety issues in 2006, involving both centrally and non-centrally authorised medicines for human use. Notably, the Agency finalised the following safety reviews, in line with the provisions of Regulation (EC) No 726/2004:

- A review, under Article 5(3), of the cardiovascular safety of non-selective non-steroidal anti-inflammatory drugs (NSAIDs), stemming from new clinical and epidemiological study data. The CHMP concluded that it cannot be excluded that non-selective NSAIDs may be associated with a small increase in the absolute risk for thrombotic events, especially when used at high doses for long-term treatment. However, these medicinal products are important treatments for arthritis and other painful conditions, and the overall benefit-risk balance for non-selective NSAIDs remains favourable when used in accordance with the product information.
- A review, under Article 20, of centrally authorised tacrolimus-containing medicinal products (Protopic, Protopy), in relation to a potential risk of skin cancer and lymphoma. The CHMP concluded that the benefits associated with the use of these dermatological medicinal products outweigh the risks, but that they should be used with greater caution in order to reduce potential risks of skin cancer and lymphoma as far as possible. The same review was conducted for non-centrally authorised pimecrolimus-containing medicinal products (Elidel) under Article 31 of Directive 2001/83/EC, with the same outcome.
- A review, under Article 20, of centrally authorised recombinant hepatitis B vaccines (HBVAXPRO and Procomvax), in relation to the efficacy of the vaccines. The CHMP concluded that these medicinal products continue to offer effective protection against hepatitis B, but recommended some changes to the prescribing information.
- A review, under Article 20, of a centrally authorised perflutren-containing microspheres medicinal product (Optison), further to the suspension of a manufacturing authorisation due to concerns over compliance with good manufacturing practice (GMP). The marketing-authorisation holder and the manufacturer are currently undertaking an extensive corrective-action plan to restore GMP compliance at the site of manufacture, and the matter is under close monitoring by the CHMP.

At the time of adoption of CHMP opinions for these procedures, the EMEA released advice to healthcare professionals and patients in the form of question-and-answer documents.

Risk-management strategy

The EMEA, in close collaboration with the Heads of Medicines Agencies, made good progress in 2006 on a variety of initiatives within the framework of the 2nd implementation phase of the European Risk Management Strategy (ERMS).

Implementation and further development of risk-management plans (RMPs)

The concept of RMPs was fully implemented in 2006 as part of the new legislative provisions of Regulation (EC) No 726/2004.

The Agency reviewed at least once 80% of the RMPs submitted as part of new applications. Of those not reviewed, most related to active substances whose safety profile was well known. Risk-management input was also provided in the early phase of the evaluation of new applications, through the peer-review process at CHMP level.

In order to review the experience gained with risk-management plans to date, and to introduce further improvements, a Review and Learning Project was set up, involving the EMEA, CHMP, PhVWP and CMD(h). The EMEA will continue this and other efforts to further improve the quality and usefulness of RMPs, and will continue to keep industry informed about new developments.

Progress with the ENCePP project

The EMEA has been working to establish a European Union Network of Centres of Pharmacovigilance and Pharmacoepidemiology (ENCePP). This EU-wide network of academic and independent research centres will carry out intensive monitoring of targeted medicinal products through a range of pharmacoepidemiological methodologies. A detailed inventory of 59 research centres (including 7 paediatric ones) from 18 Member States was established in 2006, and European industry associations were contacted to obtain feedback on the initiative. The EMEA also started to develop a detailed working model for the network.

Detection of pharmacovigilance signals

The availability of an adequate pharmacovigilance signals detection system is an important element for the Agency to take appropriate action. In 2006, the list of products reviewed by the Agency for detection of pharmacovigilance signals was extended to include medicinal products submitted for authorisation under the centralised procedure but not yet authorised.

A total of 1,282 suspected signals concerning 122 intensively monitored products, and 365 suspected signals concerning 105 not-intensively monitored products, were identified. This represents a sharp increase compared to 2005. Following further investigation, the Rapporteur was involved in 84 cases, and the CHMP took regulatory action in 47 cases.

Update of Volume 9A of the Rules Governing Medicinal Products in the EU

The Agency worked closely with the European Commission to finalise the revised Volume 9A (Pharmacovigilance, medicinal products for human use), taking into account the public consultation conducted in 2006. The EMEA had rapporteurship for several chapters as well as the overall co-ordinating role. The revised Volume 9A includes the new pharmacovigilance requirements stemming from the revised EU legislation, including those for risk management systems and electronic reporting.

Adverse-reaction reporting and EudraVigilance

Further progress with electronic reporting

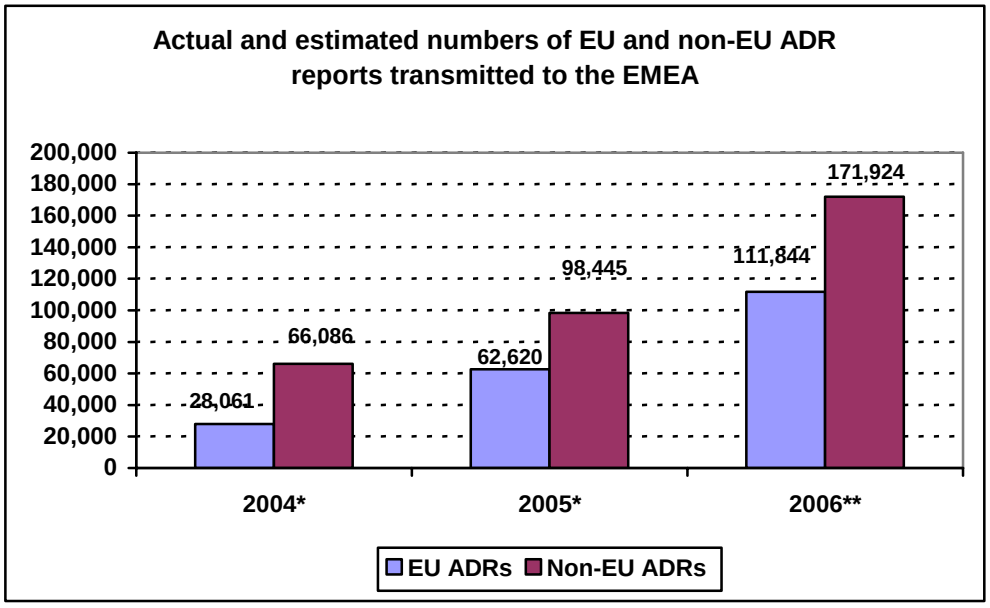
The good progress observed in 2005 with EudraVigilance (EV) continued in 2006. By the end of the year, a total of 26 national competent authorities (NCAs) were reporting electronically to EV, as were 201 marketing-authorisation holders (MAHs). More than 95% of MAHs of centrally authorised products are now in production with EudraVigilance. At the end of 2006, EudraVigilance contained a total of 677,976 individual case safety reports (ICSRs), corresponding to 409,138 individual cases.

EudraVigilance and authorised products

A breakdown of the most salient data is given here:

- The number of ICSRs reported to EudraVigilance in 2006 was three times the 2005 figure
- A total of 283,768 ICSRs were transmitted to the EudraVigilance Post-Authorisation module (EVPM) in 2006, relating to both centrally and non-centrally authorised products, and corresponding to 181,401 individual cases[2]
- One third of the total number of ICSRs received through EudraVigilance in 2006 related to centrally authorised products
- The retrospective electronic population of EudraVigilance progressed in 2006, with the transmission of a further 13,698 ICSRs.

[2] An individual case may consist of one or more ICSRs, i.e. an initial report and additional information provided at a later time in one or more follow-up reports.



* The figures for 2004 and 2005 have been revised to taken into account the report submitted for non-centrally authorised products

** With the implementation of the mandatory electronic reporting of ICSRs and the EudraVigilance Data Warehouse and Analysis System, a new method has been developed to present the number of ICSRs received/expected over time. This new method has been used for the numbers as of 2006.

EudraVigilance and clinical trials

By the end of the year, 161 sponsors of clinical trials being conducted in the European Economic Area were reporting suspected unexpected serious adverse reactions to the EudraVigilance Clinical Trial Module (EVCTM). To date, a total of 53,642 ICSRs, corresponding to 26,997 individual cases, have been transmitted to EVCTM.

Ongoing development of EudraVigilance

Further progress in the development of EudraVigilance was made in 2006, particularly with regard to the Data Analysis system. This system is designed to allow users to analyse safety data collected in EudraVigilance to better define safety profiles of medicinal products. It contains a range of analytical tools within the administrative and scientific query libraries, as well as quantitative signal-detection tools. Once validated, the Data Analysis system will be rolled out to the EU NCAs, together with the relevant training.

Activities of the EudraVigilance Steering Committee and Expert Working Group

The EudraVigilance Steering Committee (EV-SC) and the EudraVigilance Expert Working Group (EV-EWG) continued their work to coordinate the implementation of electronic reporting in the pre- and post-authorisation phases.

The two groups conducted a survey to assess the reporting requirements of suspected adverse reactions in Member States, and prepared a pilot project to improve stakeholders' compliance with regard to expedited reporting timelines. Following a request from the European Commission, the EMEA drew up an action plan to rectify the areas of disharmony identified in the survey.

The groups also drafted an initial proposal for EudraVigilance access policies, in accordance with Community legislation, and held two EV Info Days in collaboration with the Drug Information Association (DIA).

The EV-SC and EV-EWG prepared a 'Guideline on the use of statistical signal detection methods in the EV data analysis system' (EMEA/106464/06), and released it for a 6-month consultation period. Finally, the groups continued to support the ICH activities, mainly in relation to the revision of the E2B(M) Guideline on ICSRs and M5 for Drug Dictionaries.

The first pharmacovigilance training course, 'Excellence in Pharmacovigilance: Clinical Trials and Post Marketing', organised in collaboration with the DIA, took place in 2006.

2.6 Arbitration, Community referrals and opinions on scientific matters

Arbitration procedures (either under Article 29 of Directive 2001/83/EC or Article 6(12) and 6(13) of Commission Regulation (EC) No 1084/2003) are initiated because of disagreement between Member States in the framework of the mutual-recognition procedure.

Referral procedures under Article 30 of Directive 2001/83/EC are mainly initiated in order to obtain harmonisation within the Community of the conditions of authorisation for products already authorised by the Member States.

Referral procedures under Articles 31 and 36 of Directive 2001/83/EC are mainly initiated in cases involving the interests of the Community or concerns relating to the protection of public health.

Procedures under Article 5(3) of Council Regulation (EC) 726/2004 concern requests to the Committee for Medicinal Products for Human Use (CHMP) to draw up an opinion on any scientific matter concerning medicinal products.

Further details on referrals started and finalised are available in Annex 14.

Substantial increase in arbitration and referral activity in 2006

The number of procedures for arbitrations, referrals and opinions initiated in 2006 increased significantly (79%) compared with 2005. Procedures finalised in 2006 reached a total of 32 opinions (five times more than in 2005), including procedures started late in 2005 as well as new procedures started in 2006. This number also includes the first Article 5(3) opinions on scientific matters, following the entry into force of the new pharmaceutical legislation.

Procedure type	2004		2005		2006	
	Started	**Finalised**	**Started**	**Finalised**	**Started**	Finalised
Article 6(12) of Commission Regulation (EC) No 1084/2003	**3**	**0**	**3**	**1**	**0**	2
Article 6(13) of Commission Regulation (EC) No 1084/2003	**0**	**0**	**4**	**0**	**0**	4
Article 29 of Directive 2001/83/EC	**2**	**2**	**7**	**5**	**20**	12
Article 30 of Directive 2001/83/EC	**1**	**2**	**3**	**0**	**1**	4
Article 31 of Directive 2001/83/EC	**1**	**1**	**2**	**0**	**3**	1
Article 36 of Directive 2001/83/EC	**0**	**0**	**0**	**0**	**7**	7
Article 5(3) of Directive 2001/83/EC	**0**	**0**	**0**	**0**	**3**	2
Totals:	**7**	**5**	**19**	**6**	**34**	**32**

Arbitration and referral procedures of high public health interest in 2006

Procedures started but not finalised in **2006:**

- Review of a bicalutamide 150mg-containing medicinal product triggered by safety concerns, in particular heart problems, when the medicinal product is used in the treatment of early prostate cancer (*Article 31 procedure*)
- Review of veralipride-containing medicinal products triggered by safety concerns regarding reported psychiatric and neurological reactions (*Article 31 procedure*)
- Review of piroxicam-containing medicinal products triggered by safety concerns in relation to gastrointestinal and skin disorders (*Article 31 procedure*).

Procedures finalised in 2006:

- Review of a pimecrolimus-containing medicinal product in relation to a potential risk of skin cancer and lymphoma. The CHMP concluded that the benefits associated with the use of these dermatological medicinal products outweigh the risks, but that they should be used with greater caution in order to reduce potential risks of skin cancer and lymphoma as far as possible (*Article 31 procedure*)
- Review of atorvastatin-containing medicinal products due to concerns over the extension of the indication to the prevention of cardiovascular events in patients with multiple risk factors. The CHMP recommended the grant of an extension of indication to patients who have a high risk of a first cardiovascular event (*Article 6(12) procedure*)
- Review of fluoxetine-containing medicinal products due to concerns over the extension of indication to children. The CHMP recommended to extend the indication to include the treatment of children of 8 years of age or older who suffer from moderate to severe depression and who do not respond to psychological therapy as the benefits of using fluoxetine in this indication outweigh its potential risks. However, this conclusion was associated with a recommendation that the MAHs carry out additional studies to ensure that the safety profile of fluoxetine remains acceptable (*Article 6(12) procedure*)
- Review of fixed dose combinations salmeterol / fluticasone propionate medicinal products. The CHMP recommended that the products could be tried for a short period of time as initial maintenance therapy in adults and adolescents with moderate asthma for whom rapid control of asthma is essential, after which a decision should be taken whether or not to continue treatment with the product (*Article 6(13) procedure*)
- Review of four cetirizine dihydrochloride 10mg-containing generic medicinal products. The CHMP recommended the suspension of these products due to concerns over good clinical practices (GCP) and good laboratory practices (GLP) compliance and the possible impact on the quality and reliability of bioequivalence studies supporting the marketing authorisations (*Article 36 procedure*)
- Review of a simvastatine-containing generic medicinal product. The CHMP recommended the suspension of the concerned product due to non-compliance with GCP in the conduct of a bioequivalence study used to demonstrate comparability with the originator product (*Article 36 procedure*)
- Review of two gadobutrol-containing generic medicinal products. The CHMP recommended the restriction of the extension of indication originally applied for by the marketing authorisation holder in the context of the mutual recognition procedure to include the contrast-enhanced MRI of liver and kidneys (*Article 36 procedure*).

Opinions on scientific matters in 2006

Procedures started and finalised:

- Adequacy of guidance relating to conduct of clinical trials on the elderly to address the specific pharmaco-therapeutic needs of the elderly, which are often excluded from clinical trials, on the request of the European Commission (*Article 5(3) procedure*)

Review of cardiovascular safety of non-selective non-steroidal anti-inflammatory drugs (NSAIDs) stemming from new clinical and epidemiological study data, on the request of the French national medicines agency, Agence française de sécurité sanitaire des produits de santé (Afssaps) (*Article 5(3) procedure*).

Procedures started but not yet finalised:

- Use of certain categories of substances (potential carcinogens, mutagens, substances toxic to reproduction) as excipients in medicinal products for human use and need to strengthen existing

guidelines or for legislative changes, on the request from European Commission (*Article 5(3) procedure*).

2.7 Herbal medicines

The Agency's activities in the area of herbal medicines include: the provision by the Committee on Herbal Medicinal Products of scientific opinions on questions relating to herbal medicines; the establishment of Community herbal monographs for traditional and well-established herbal medicinal products; the establishment of a draft list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products; the provision of opinions on herbal substances at the request of the CHMP; and the evaluation for referral and arbitration procedures concerning traditional herbal medicinal products.

The composition of the Committee is given in Annex 5.

The Committee on Herbal Medicinal Products (HMPC) met 6 times in 2006.

New working party

In March 2006, the HMPC established a permanent Working Party on Community Monographs and Community List (MLWP), which replaced the temporary Safety & Efficacy Drafting Group.

Community herbal monographs

The HMPC finalised 9 Community herbal monographs in 2006, for: valerian root, linseed, ispaghula husk, ispaghula seed, psyllium seed, senna pods, senna leaf, frangula bark and aloes (cape and barbados). These monographs were released for public consultation prior to being finalised.

The Committee also released for public consultation 5 new draft Community herbal monographs, for aniseed, anis oil, bitter-fennel fruit, sweet-fennel fruit and bitter-fennel fruit oil.

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

The Committee released for public consultation 2 new draft entries to the Community list, for bitter-fennel fruit and sweet-fennel fruit.

Publication of regulatory and scientific documents

To support its work on Community herbal monographs and the Community list, the HMPC developed, in particular:

- a procedure for the publication of calls for scientific data for use in HMPC assessment work;
- a guideline on the assessment of clinical safety and efficacy in the preparation of monographs and list entries.

To assist national competent authorities in their implementation of the simplified registration scheme, as well as to help applicants in their preparation of marketing-authorisation or traditional-use-registration applications, the HMPC released:

- guidance on the non-clinical documentation required for (traditional) herbal medicinal products
- a concept paper on the assessment of genotoxic constituents in herbal substances/preparations.

In December 2006, the HMPC presented to the European Commission a comprehensive overview of its activities and achievements since its establishment in September 2004. This overview aids the Commission in the preparation of its report to the European Parliament and to the Council concerning the application of the relevant legislative provisions relating to traditional herbal medicinal products.

The Community herbal monographs and entries to the Community list are listed in Annex 12a and 12b of this report. The HMPC guidelines and working documents adopted or released for consultation in 2006, are listed in Annex 13.

2.8 Management and organisation of EMEA scientific committees for human medicines

Scientific committees

Three EMEA human scientific committees are responsible for formulating the Agency's opinions on all questions relating to medicinal products for human use.

	Plenary meetings in 2006
Committee for Medicinal Products for Human Use (CHMP)	11
Committee for Orphan Medicinal Products (COMP)	11
Committee on Herbal Medicinal Products (HMPC)	6

The CHMP/EMEA Implementation Task Force, which had a crucial role during the implementation of the new pharmaceutical legislation, held its last meeting in July 2006. Further implementation and monitoring of the review were integrated in the plenary CHMP meeting.

Working parties

The work of the human scientific committees is currently supported by a total of eighteen permanent working parties and temporary working groups, composed of members selected from the list of European experts maintained by the EMEA.

The working parties are involved, according to their specific area of responsibility, in the development and revision of guidelines, including work stemming from ICH activities. They also provide recommendations and advice on medicinal products that are the subject of applications for orphan designation, scientific advice, protocol assistance, marketing authorisation or post-authorisation activities.

New working party creates permanent forum for patients and consumers

The first cross-committee working party was established in December 2006: the EMEA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP). The PCWP replaces the temporary working group, the EMEA/CHMP Working Group with Patients' and Consumers' (POWG), and will continue to build on the achievements of that group.

Work continued on implementing the final recommendations and proposals for actions developed by the POWG in 2005. All recommendations relating to the Product Information (PI) that could be directly implemented by the EMEA were implemented. Preparatory work was also done for the future involvement of patients and consumers in the review of Package Leaflets and EPAR summaries, which is intended for 2007.

Scientific guidelines

In 2006, the working parties developed a number of guidelines and other working documents on a wide range of specialist subjects. Further information is available in Annex 13.

Full details of guidelines and other working documents prepared by the working parties can be found in the 'Human Medicines' section of the EMEA website:

(http://www.emea.europa.eu/htms/human/humanguidelines/background.htm).

Scientific advisory groups (SAGs)

Scientific advisory groups support the CHMP on the scientific evaluation of medicinal products, depending on the area of expertise of each group. Six SAGs have now been established covering all therapeutic areas in the mandatory scope of the centralised procedure (anti-infectives, central nervous system, diabetes and endocrinology, diagnostics, HIV and viral diseases, oncology). The seventh, the SAG on cardiovascular issues, was in the process of being established at the end of the year.

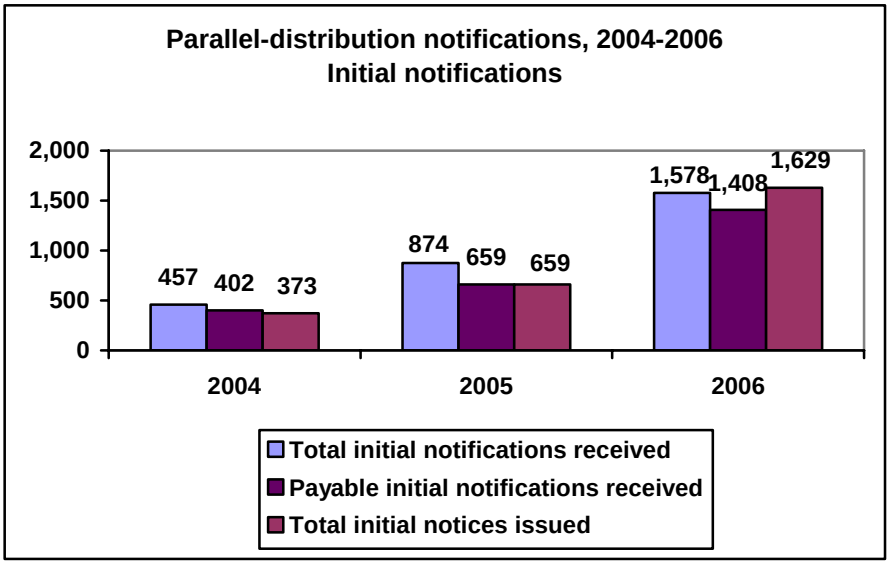
Organisation of and contribution to scientific workshops

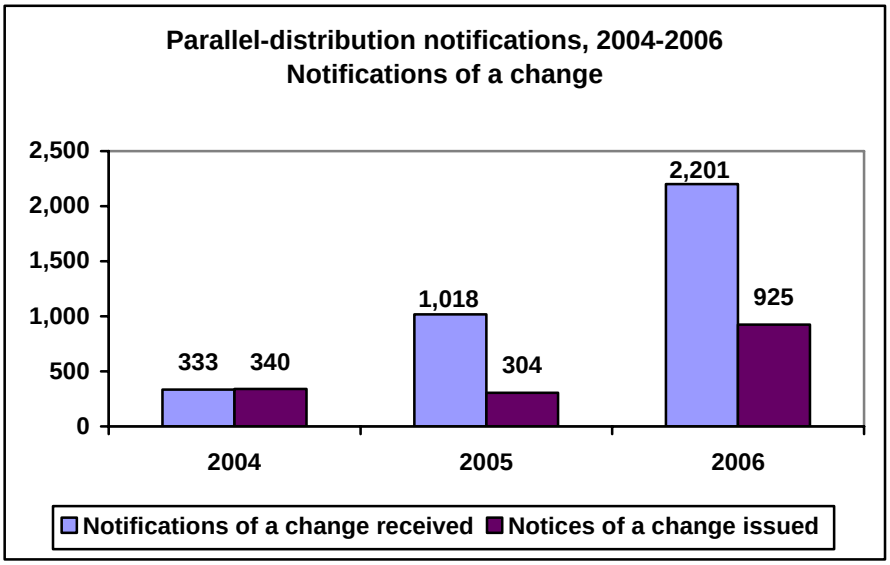
The EMEA scientific committees, with the support of their working parties and scientific advisory groups and the EMEA secretariat, contributed to workshops on the following subjects in 2006:

- Transmissible spongiform encephalopathy (TSE) (Biologics Working Party).
- Cell-based products (organised jointly by the Biologics Working Party and the Working Party on Cell-based Products).
- Concomitant administration of vaccines (Vaccine Working Party).
- Development of medicines for the neonate (Paediatric Working Party).
- Neurodegenerative diseases and development requirements for disease modifiers, with particular attention to the role of biomarkers and neuro-imaging (SAG on central nervous system).
- Second workshop on the development and use of biomarkers (Scientific Advice Working Party)

2.9 Parallel distribution

Parallel distribution is the distribution of a centrally authorised medicinal product from one Member State to another by a pharmaceutical company independent of the marketing-authorisation holder. The task of the EMEA is to check compliance of products distributed in parallel with the conditions laid down in Community legislation on medicinal products and in the marketing authorisation of the product.





In 2006, a total of 1,408 payable initial notifications of parallel distribution were made to the EMEA, including a carryover of 350 notifications from 2005, which was due to the introduction of a new invoicing system. This corresponds to a 113% increase compared to 2005 (659). This high number of notifications was attributed to: new parallel distributors starting this activity; parallel distributors complying with the mandatory notification procedure; recently authorised medicinal products entering the parallel-distribution chain; enlargement by existing parallel distributors of their range of products.

In addition to initial notifications, the Agency received 2,201 notifications of a change, representing a 120% increase compared to 2005 (1,018). This was due to the frequent update of the Annexes to the Community marketing authorisations of parallel-distributed products and to other changes proposed by parallel distributors (e.g. addition of countries of origin).

Handling the parallel-distribution notifications within the timeframe of 5 working days for validation and 30 working days for the regulatory check was identified as the most important key performance indicator by parallel distributors. The Agency strengthened its efforts in order to achieve this objective in 2006 and was able to reduce the delays for starting the procedure encountered in 2005 from 4 months to 1 month.

With the feedback from all stakeholders (both parallel distributors and marketing-authorisation holders), the Agency prepared a revision of the post-authorisation guidance for parallel distribution to further clarify the process and to incorporate new topics, such as the Braille requirement.

2.10 Coordination Group for Mutual Recognition and Decentralised Procedures–Human

Websites:

Heads of Medicines Agencies–Human: *http://www.hma.eu/human.html*

European product index: *http://www.hma.eu/mri.html*

EMEA/CMD(h) secretariat e-mail: *mrp@emea.europa.eu*

This is an adapted summary of a full report on the CMD(h)'s activities in 2006. The full report is available on the Heads of Medicines Agencies–Human website.

2006 was the first full year of operation of the Coordination Group for Mutual Recognition and Decentralised Procedures–Human (CMD(h) — formerly the Mutual Recognition Facilitation Group), set up under the revised EU pharmaceutical legislation for the examination of any question relating to the marketing authorisation of a medicinal product in two or more Member States, in accordance with the mutual-recognition procedure (MRP) or the decentralised procedure (DCP).

The CMD(h) met eleven times in 2006 under the chairmanship of Mrs Truus Janse-de Hoog.

The implementation of the new pharmaceutical legislation, including the development and update of guidance documents, and arrangements for the CMD(h) were permanent items on the agendas of CMD(h) meetings.

The CMD(h) worked in close collaboration with the EMEA on the development of guidance for the authorisation and supervision of medicinal products for human use in line with the provisions of the revised EU pharmaceutical legislation.

The EMEA and CMD(h) organised a workshop on user-consultation in the context of readability-testing of package leaflets for medicines, focusing on the layout and design of a good package leaflet, the review of user-testing reports, and the assessment of justification for not performing user-testing.

The CMD(h) devoted considerable time and resources to trying to reach agreement for mutual-recognition-procedure applications in situations where a Member State cannot approve the assessment report, the summary of product characteristics, the labelling and the package leaflet on the grounds of potential serious risk to public health, in accordance with Article 29(1) of Directive 2001/83/EC, as amended.

Of the Mutual Recognition Procedures finalised in 2006 (535), 19% (104) were referred to the CMD(h) whilst only 2% (1) of the decentralised procedures finalised in 2006 (57) were referred to the CMD(h) in this time period. There were 20 oral explanations from applicants. Of the 75 procedures finalised by the CMD(h) in 2006, the CMD(h) was able to reach agreement for 71% of the procedures (53), and referred 29% of the procedures (22) to the CHMP. 5 applications were withdrawn in the RMS and all CMSs within the CMD(h) referral procedure.

However, the 22 applications for marketing authorisation were referred to the CHMP for arbitration on 10 different grounds: 5 on bioequivalence; 3 on divergences between the proposed SPC and the SPC authorised for the national reference medicinal product; 1 on safety and efficacy; and 1 on efficacy and bioequivalence. All but 1 of the applications referred to the CHMP for arbitration were for generic medicinal products, and concerned 9 different active substances.

With a view to avoiding referrals to the CMD(h)/CHMP other than on grounds of a potential serious risk to public health, the CMD(h) agreed that a deviation in indications (more or fewer) in the generic product from the national reference product in the concerned Members State is not considered to be, per se, an appropriate reason to refuse licensing of a medicinal product. The CMD(h) developed a paper regarding processing of generic applications when the generic product has more or fewer indications than the reference product in the concerned Members State.

The CMD(h) established 2 new working groups, one to evaluate the Decentralised Procedure and to consider the need for revision of the Decentralised Procedure SOP and the other to analyse validation issues and national requirements within the framework of the MRP and DCP.

The CMD(h) in cooperation with representatives of National Competent Authorities set up another working group to prepare for the new tasks and work generated by the Paediatric Regulation, in particular on the submission of paediatric data, to set up the requirements in collaboration with the EMEA, and the type of information to be collected on a systematic basis.

The CMD(h) Sub-group on harmonisation of SPCs, met 6 times in 2006, one of which with Interested Parties, to hear their views on future harmonisation of authorisations for medicinal products authorised in the Community. The sub-group defined the criteria for the selection of products for SPC harmonisation and agreed a list of products for SPC harmonisation, in accordance with Article 30(2) of Directive 2001/83/EC, as amended. The list was forwarded to the European Commission together with the comments received during the public consultation.

The number of new applications submitted in 2006 via the mutual recognition and decentralised procedures (1,046) increased by approximately 20% compared to 2005. However, the number of applications finalised via the MRP and DCP (592) has decreased compared to 2005. This might be explained by the number of decentralised procedure applications submitted in 2006, with a calendar of 210 days as opposed to the 90 days of the MRP. The number of variations finalised in 2006 has increased compared to 2005. In addition, there was an increase in the number of arbitrations for new applications. This increase might be explained by the fact that the withdrawal of an application at any time point in the MRP or after circulation of the draft Assessment Report in the DCP no longer prevents the issue of disagreement on the grounds of potential serious risk to public health from being referred to the CMD(h).

There were no variations referred to the CHMP for arbitration in 2006.

	Total submitted in 2006*	Under evaluation in 2006*	Ended positively in 2006*	Referrals to CMD(h) in 2006	Referrals to CHMP in 2006
New applications MRP	596	217	535	105	22
New applications DCP	450	402	57	1	0
Type-IA variations	4701	115	4524	N/A	N/A
Type-IB variations	2292	178	2209	N/A	0
Type-II variations	2284	509	1916	N/A	0

*The numbers include multiple procedures as stated at 31 December 2006.

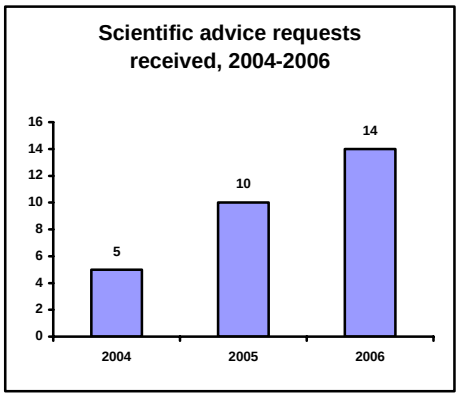
3. VETERINARY MEDICINES

3.1 Scientific advice

Scientific advice is a priority area for the EMEA. Its provision helps companies with their development programmes, and thus contributes towards bringing innovative medicines to the market more quickly.

The Agency provides advice on specific questions that typically arise during the research and development of medicinal products, relating to quality, safety or efficacy, or to the establishment of maximum residue limits.

Scientific advice activity increased significantly in 2006: 14 requests for scientific advice were received (2 more than the forecast), compared to the 10 received in 2005.



The average time required to finalise procedures for provision of scientific advice in 2006 was 55 days.

Free scientific advice for minor uses and minor species

In December 2006, the EMEA Management Board further extended the pilot scheme for free scientific advice for veterinary medicines for minor uses and minor species (MUMS). The scheme is part of the Agency's strategy to improve the availability of such medicines.

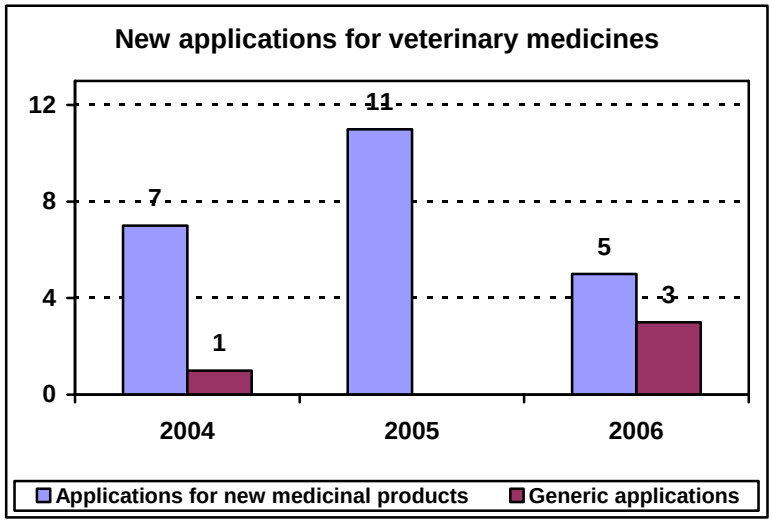
Three scientific advice requests were deemed eligible in 2006 for free advice under the provisions of the programme for minor uses and minor species. These related to: an antimicrobial for turkeys and gamebirds (pheasants); a live vaccine for wild rabbits; and development of a vaccine for sheep, goats and cattle.

3.2 Initial evaluation

Applications for new medicines are reviewed by the Agency through the Committee for Medicinal Products for Veterinary Use (CVMP). The Committee assesses the quality, safety and efficacy of every new veterinary product that is subject to the Community or centralised procedure and, based on the overall balance of the benefits and risks of the medicine, gives its opinionb on whether or not the European Commission should grant a Community-wide marketing authorisation.

The Composition of the Committee is given in Annex 3.

Eight initial marketing-authorisation applications were received, 5 of which were for pharmaceuticals and 3 for immunologicals. The 5 pharmaceutical applications, 3 of which were generic applications, concerned medicinal products for dogs, while the 3 immunological applications were for chickens principally.



In 2006, the Committee for Medicinal Products for Veterinary Use (CVMP) adopted a total of 13 positive opinions for initial marketing-authorisation applications. There was 1 negative opinion, which was also subject to a re-examination, for an antimicrobial for treatment of specific skin and soft-tissue infections and specific acute infections of the upper respiratory tract and the urinary tract in cats and dogs.

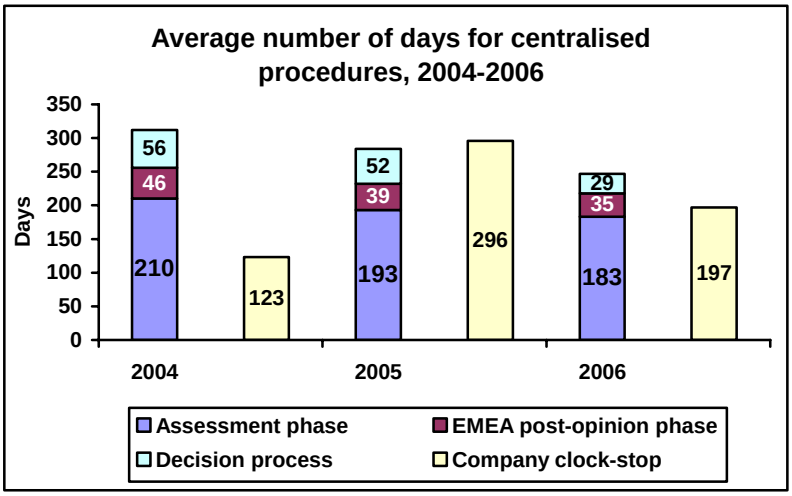
Among the 13 positive opinions were:

- 2 vaccines for chickens, against avian influenza, which were evaluated on an accelerated timetable with the opinions adopted in 79 days, taking into account the epidemiological situation within the EU. These led to authorisations 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 for ectoparasiticides for treatment and prevention of flea and tick infestations in dogs;
- 1 for an ectoparasiticide for treatment and prevention of flea infestations in cats;
- 1 for oxygen intended for oxygen supplementation and as a carrier gas during inhalation anaesthesia;
- 1 for a steroid for treatment of inflammatory and pruritic dermatoses in dogs;
- 1 for a product for treatment of benign prostatic hypertrophy in dogs;
- 1 for a product for treatment of overweight and obese dogs;
- 1 for a cephalosporin for treatment of specific skin, soft-tissue and urinary-tract infections in cats and dogs;
- 1 for a product for treatment and prevention of emesis in dogs.

All opinions are listed in Annex 10 of this report.

Average assessment time quicker than in 2005

All initial evaluations were carried out within the 210-day regulatory time limit. For those new applications for which the Commission delivered a decision in 2006, the average CVMP assessment time was 183 days — noticeably shorter than the average of 193 days in 2005, partly due to the accelerated assessment of avian influenza vaccine applications.



3.3 Availability of veterinary medicines

The EMEA continued its initiatives aimed at improving the availability of medicines. In particular, major progress was made on adapting the data requirements for products for minor uses and minor species. The CVMP finalised guidelines for quality, safety and efficacy testing of such products, and published for consultation a similar guideline regarding immunological products. Further work is being done to better define minor uses and limited markets, in order to facilitate use of the guidelines and to allow for a harmonised implementation across the EU.

The CVMP continued to extrapolate maximum residue limits (MRLs) to further species, at the request of companies concerned. This required no fee or formal application, provided the scientific criteria allowing such extrapolations were met.

In December 2006, the EMEA Management Board further extended the pilot scheme for the provision of free scientific advice from the CVMP for marketing-authorisation applications and establishment of MRLs for veterinary medicines for minor uses and minor species.

The Agency sought the views of stakeholders on the kind of measures they would like to see put in place for implementing the new legal provisions (under Article 79 of Regulation (EC) No 726) for the supply of administrative assistance to companies intending to submit applications through the centralised procedure for products that have limited markets or that are intended for diseases of a regional nature. The provisions under this Article are further supported by a separate regulation on support for small and medium-sized enterprises (Commission Regulation (EC) No 2049/2005).

The above activities are seen by industry as key initiatives to provide incentives for the development of new veterinary medicines for minor uses and minor species.

The EMEA proposal for a list of essential substances for the treatment of certain indications in equidae with no MRL but with a withdrawal period of at least six months was approved by the Commission and Member States, and the Regulation establishing this list was adopted (Commission Regulation (EC) No 1950/2006).

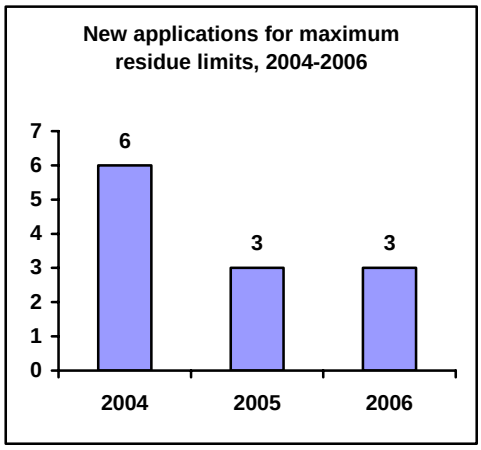
The EMEA provided input and advice to the Heads of Medicines Agencies-Veterinary's task force on availability, as well as to the European Technology Platform for Global Animal Health, to ensure that due attention be given to the Community priority to increase the number of medicines available within the EU, particularly for minor uses and minor species, and to minimise the development time for new products.

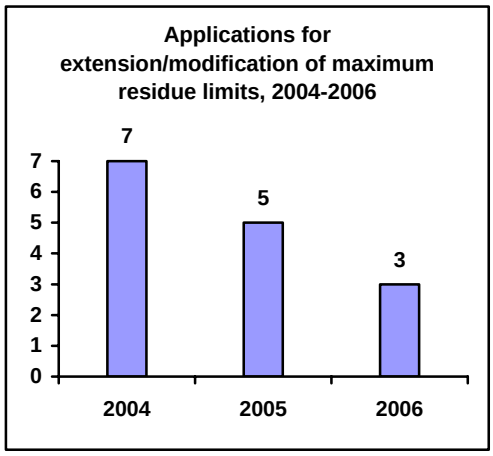
3.4 Maximum residue limits

If food-producing animals are treated with medicines, residues may remain in the food produced by or from them. To obtain a marketing authorisation for a veterinary medicinal product intended for use in a food-producing species, so-called maximum residue limits (MRLs) for all pharmacologically active substances must be established in advance for the animal species concerned and for its tissues or products, e.g. meat, milk, honey etc. An MRL is the safe level of residue in food that can be consumed by a person every day over a lifetime without it causing a harmful effect.

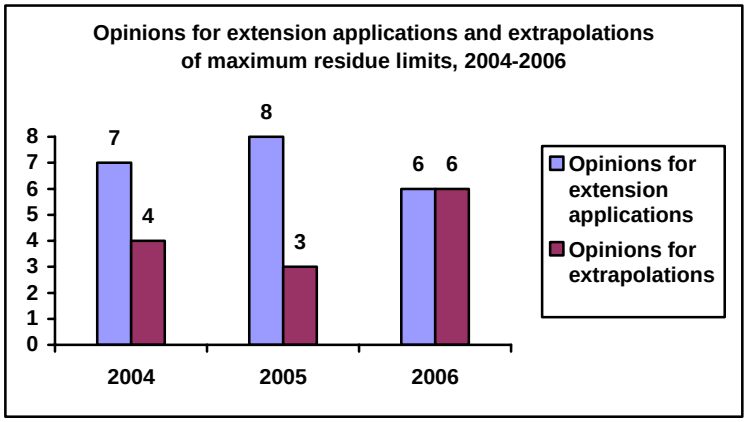
Fewer MRL applications submitted than expected

In 2006 the EMEA received and validated 3 new applications for MRLs — the same number as in 2005, and 2 fewer than were forecast for the year. The small number of new MRL applications is consistent with the comparatively greater interest currently seen for the development of new veterinary medicines for companion animals than for food-producing animals.





There was also a shortfall in the number of applications submitted for extension or modification of MRLs, with only 3 of the forecast 7 being submitted. The declining number of these applications over recent years is probably due to the fact that it has become possible, when the criteria for MRL extrapolations are met, to extend MRLs to further species without a formal application (i.e. without a fee and detailed application dossier). Thus, with 6 of these requests received in 2006, the overall number of applications and requests for extensions and extrapolations of MRLs received for the year was in fact 9.



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

CVMP opinions on maximum residue limits

The CVMP adopted:

- 2 positive opinions for the establishment of new MRLs;
- 3 positive opinions for the establishment of final MRLs further to previous provisional MRLs for new substances;
- 6 positive opinions for the extension of existing MRLs to other species;
- 6 positive opinions for the extrapolation of existing MRLs to further species in line with the CVMP policy on availability of veterinary medicines.

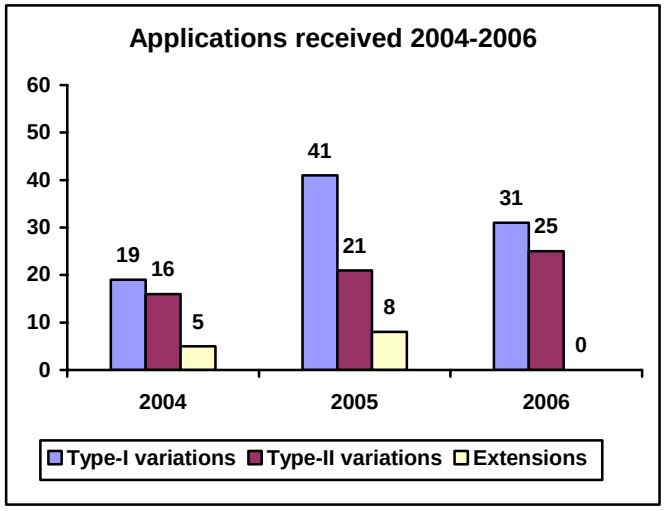
All opinions are listed in Annex 10 of this report.

3.5 Post-authorisation activities

Changes to the terms of marketing authorisations are made frequently during the life of a medicine. Marketing authorisation holders may want to change the manufacturing process, alter or improve the medicinal product, or introduce additional warnings and contraindications. These changes, known as variations, require formal approval. Variations can involve either minor (type IA or IB) or major (type II) changes.

Besides variations, post-authorisation activities also include line extensions and transfers of marketing authorisation.

The overall number of applications for variations to marketing authorisations received in 2006 was lower than in 2005, despite the greater number of centrally authorised products on the market.



A total of 31 type-I variation applications were received, relating to 18 type-IA and 13 type-IB variations.

There were also 25 applications relating to the more complex type-II variations. Of these, 14 concerned pharmaceutical products and 11 concerned immunological products. Nine of the variations concerning pharmaceuticals related to changes in quality and 5 related to clinical changes. All variations concerning immunologicals related to quality changes.

There were no applications for extension of marketing authorisation.

The total number of Type II opinions adopted in 2006 was 18. Of these, 2 were received in 2004 (both for a new indication), 3 were received in 2005 (1 new indication and 2 quality changes) and 13 were received in 2006 (2 update of SPC and PL, 1 new presentation and 10 other quality changes).

All variation applications were evaluated within the regulatory time limits.

3.6 Safety of medicines

Pharmacovigilance in the veterinary sector in the EU is undergoing changes triggered by the new legislation. The electronic exchange of pharmacovigilance information within the EU is improving, as are active surveillance, harmonisation and risk management.

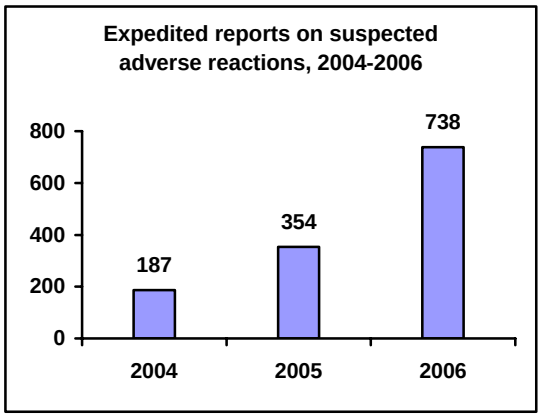
Marked increase in expedited reporting of suspected adverse reactions

For centrally authorised veterinary products (for which pharmacovigilance falls within the remit of the EMEA), a total of 738 expedited spontaneous reports of suspected adverse reactions were reported within the 15-day legal timeframe in 2006.

This is a considerable increase – more than twice the number of such reports received in 2005 – and would appear to result, among others, from the Agency's efforts to promote awareness of expedited reporting.

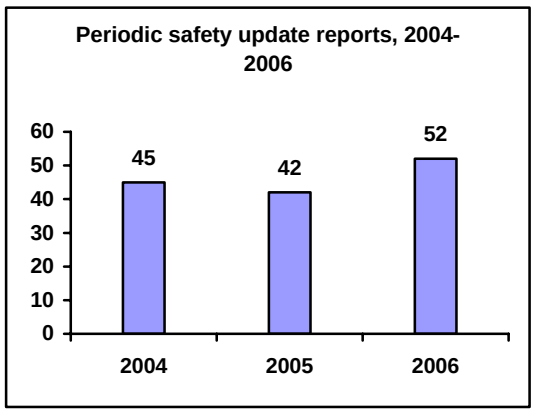
Of the 738 reports received:

- 638 related to suspected adverse reactions in animals and 100 to reactions in humans;
- 53 related to food-producing animals (mainly cattle, pigs and horses), following treatment of 2,251 animals, of which 559 showed suspected adverse reactions;
- 380 related to suspected adverse reactions in dogs;
- 200 related to suspected adverse reactions in cats;
- 300 originated within the EU.



Review of PSURs

Fifty-two periodic safety update reports (PSURs) were received in 2006 for centrally authorised products. Following its review of these reports, the CVMP recommended in 7 cases that variations be submitted for the products concerned, mainly concerning the addition of new adverse reaction information to the product literature.



First 'Article 78' procedure

Following a request for consideration from a Member State, the CVMP recommended that new precautionary measures concerning user safety be added to the product literature of 21 veterinary medicinal products containing alpha2-adrenoreceptor agonists. This was the first procedure conducted under the new pharmacovigilance provision under Article 78 of Directive 2001/82/EC, as amended.

Confirmation of CVMP opinion on veterinary Cox-2s and NSAIDs

The CVMP further reviewed the safety of Cox-2 inhibitors and non-steroidal anti-inflammatory drugs for use in veterinary medicine as a result of the recently concluded review of concerns related to human use of these substances. The Committee reconfirmed its previous conclusion that no action was required regarding concerns of possible cardiovascular effects and skin reactions for this class of medicines.

Developments in veterinary pharmacovigilance

The preparation of guidance documents is a continuous activity for the CVMP and its working parties. In 2006, this activity focused on the provision of new guidance for marketing authorisation holders and applicants concerning the pharmacovigilance systems that need to put in place, as well as on guidance for regulatory authorities concerning the assessment of PSURs. Simple guidance was also finalised for veterinarians and other health professionals concerning the reporting of adverse reactions.

In order to further progress the direct electronic reporting of adverse reactions into the EudraVigilance Veterinary database, a simplified electronic reporting tool was made available, designed particularly for the use of smaller companies in the veterinary industry. A web-reporting tool for veterinarians was developed for pilot-testing in 2007.

EudraVigilance Veterinary became the main reporting tool used by national competent authorities in 2006. Marketing authorisation holders have started reporting electronically and implementation plans for full electronic reporting are being finalised by major veterinary pharmaceutical companies. It is anticipated that many more companies will move to electronic reporting in early 2007.

Further progress was made on developing the DataWarehouse tool to facilitate continuous monitoring and signal detection of pharmacovigilance data in EudraVigilance Veterinary. The DataWarehouse is expected to become operational in 2007.

The EMEA continued to hold training sessions on the use of EudraVigilance Veterinary to support the Member State competent authorities.

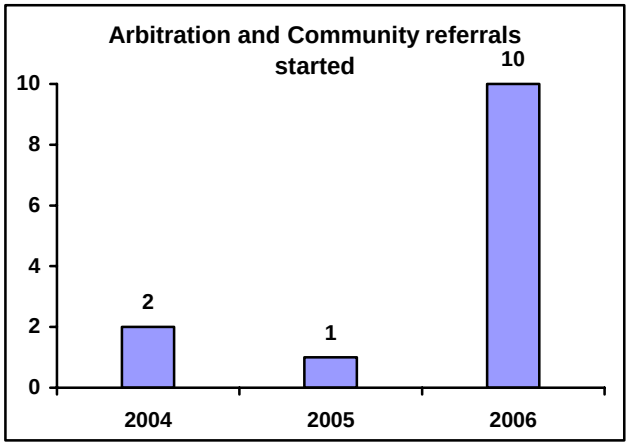
3.7 Arbitration and Community referrals

Arbitration procedures are initiated because of disagreement between Member States in the framework of the mutual recognition procedure (Article 33 of Directive 2001/82/EC). Referrals are initiated either in order to obtain harmonisation within the Community of the conditions of authorisation for products already authorised by the Member States (Article 34 of Directive 2001/82/EC), or in cases involving the interests of the Community or concerns relating to the protection of human or animal health or the environment (Articles 35 and 40 of Directive 2001/82/EC).

Procedures started in 2006

In line with expectations, the number of referrals made to the CVMP in the framework of the mutual recognition procedure increased significantly in 2006. A total of 10 referral procedures were initiated, including:

- 6 Article 33 referrals;
- 1 Article 34 referral;
- 2 Article 40 referrals;
- 1 referral under Article 6(13) of Regulation (EC) No 1084/2003 following a type-II variation procedure for a mutual recognition product.



Four of the referrals related to the demonstration of efficacy and concerned pharmaceuticals. Six related to safety issues or benefit/risk evaluation, of which 3 were for pharmaceuticals and 3 were for vaccines.

Referral procedures concluded in 2006

The CVMP completed the assessment and issued opinions in 3 of the referral procedures started in 2006 and in 1 of the referral procedures started in 2005.

Measures to avoid unnecessary referrals

Discussions were held during the year on how to avoid unnecessary referral procedures. In particular, this issue was addressed at the Joint Informal CVMP/CMD(v) meeting under the Finnish presidency, and at further meetings between the chairs of these two bodies, which continue within the context of the CVMP Strategic Planning Group. Concrete measures have been agreed which should ensure that only unavoidable referrals will be passed to CVMP.

A list of referral procedures can be found in Annex 14.

3.8 Management and organisation of the Committee for Medicinal Products for Veterinary Use

The Committee for Medicinal Products for Veterinary Use (CVMP) met 11 times in 2006.

Activities relating to antimicrobial resistance

Based on the recommendations of its Scientific Advisory Group on Antimicrobials (SAGAM), the CVMP:

- adopted a new strategy on antimicrobials for the years ahead;
- adopted a reflection paper on the use of quinolones and fluoroquinolones in the EU, critically reviewing recent data on their use and the potential impact on human and animal health;
- proposed risk-management actions, including a recommendation for harmonised prudent-use guidance in the product literature of all (fluoro)quinolone-containing veterinary medicines for food-producing animals.

Activities relating to risk assessment

The CVMP asked its Working Party on Environmental Risk Assessment to provide advice that would help the European Commission with the practical implementation of the requirements of the amended Veterinary Directive (Directive 2004/28/EC). This proved to be a challenging task, given the need to balance the legislative requirements with the need for science-based assessment. The potential impact that substantially increased data requirements for products that have a track record of safe use might have on availability of veterinary medicines also needed to be taken into account.

Ultimately, the CVMP was able to provide advice which should be useful in terms of promoting a harmonised and pragmatic interpretation of the requirements of the Directive throughout the Community.

Methodology for systematic risk assessment

The amended Veterinary Directive places particular emphasis on risk/benefit assessment as the basis for authorisation of veterinary medicines. The CVMP considered in detail how to develop a methodology to ensure that these analyses are conducted in a systematic and scientifically robust manner. This led to the publication of a concept paper, which will be developed into a guideline on this subject during 2007.

3.9 Coordination Group for Mutual Recognition and Decentralised Procedures–Veterinary

Website:

Heads of Medicines Agencies–Veterinary: *http://www.hma.eu/veterinary.html*

The Coordination Group for Mutual Recognition and Decentralised Procedures–Veterinary (CMD(v)) met on a monthly basis in 2006. One informal meeting was held in Helsinki, Finland.

Procedures started and concluded in 2006

Ninety-nine mutual recognition procedures (MRPs) were started for a total of 77 products, and 29 decentralised procedures (DCPs) were started for a total of 25 products.

Ninety-five mutual recognition procedures were finalised for a total of 77 products, including 4 referrals carried over from 2005. Three decentralised procedures were finalised for a total of 3 products.

Eight MRP products and 1 DCP product were referred to the CMD(v) and 6 products were referred to the CVMP for arbitration.

	Started Products (procedures)	Finalised Products (procedures)	CMD(v) referrals	CVMP referrals
MRP	77 (99)	77 (95)	8	6
DCP	25 (29)	3 (3)	1	0

For the first time, a product was referred to the group over environmental concerns. During the CMD(v) referral, agreement was reached after environmental-risk-mitigation measures were put in place.

The CMD(v) addressed a number of questions from industry and from Member States, in particular in relation to generic veterinary medicinal products. The administrative handling of diluents, industry's packaging proposals, and the acceptance of indications, withdrawal periods and target species for generic products were the subjects of continuing discussions.

The group also drafted various best-practice guides, standard operating procedures and Q&A documents.

A new sub-group was set up for the annual CMD(v)/IFAH-Europe survey, and the survey conducted in 2005 was completed. The sub-group for SPC harmonisation, however, was disbanded because the CMD(v) could not identify products for which an SPC harmonisation exercise would be beneficial to the availability or the safety of products.

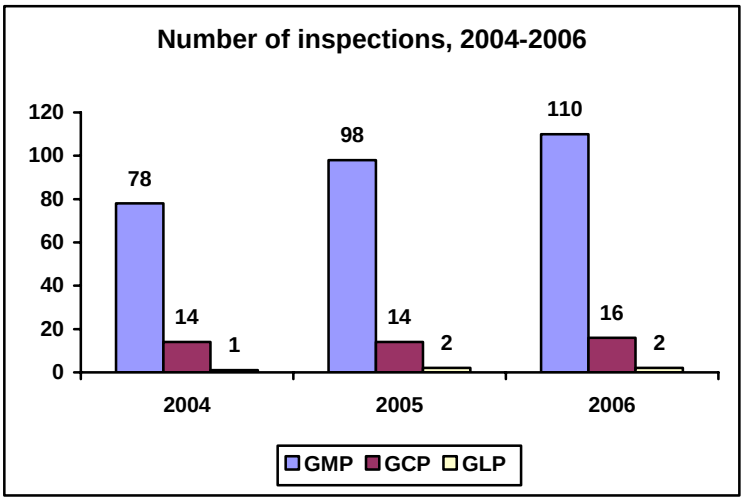
Four meetings were held with IFAH-Europe and the European Group for Generic Veterinary Products (EGGVP) to discuss regulatory issues.

The EMEA provided full secretariat and administrative support to the CMD(v).

4. INSPECTIONS

4.1 GMP, GCP, pharmacovigilance and GLP inspections

The EMEA continued to support all Member States on good manufacturing practice (GMP), good clinical practice (GCP) and pharmacovigilance inspection procedures. Support was provided primarily through the ad hoc GMP and GCP inspectors meetings, which worked on harmonisation of procedures and interpretation of related requirements.



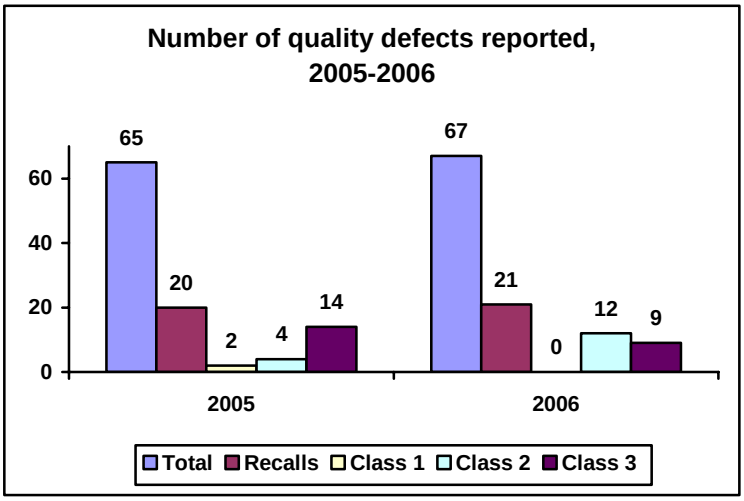
All inspections were completed within the legal timeframes and to the standards required by the Agency's quality-management system.

A report on major deficiencies found during GMP inspections coordinated by EMEA was completed and published.

Product defects and deviations

Marketing authorisation holders are required to notify the EMEA of any defect or abnormal restriction in the supply of a centrally authorised medicinal product that could result in a recall.

In 2006, the EMEA received 64 quality-defect reports concerning human medicinal products and 3 quality-defect reports concerning veterinary medicinal products. Of these, 21 resulted in a product recall (19 human medicines and 2 veterinary medicines); the remainder of the defects reported were classified as minor.



None of the 21 recalls were classified as 'Class 1' recalls (which relate to defects that are potentially life-threatening or could cause serious risk to health). Twelve of the recalls were 'Class 2' recalls (which relate to defects that could cause illness or mistreatment) and the remaining 9 were classified as 'Class 3' recalls, which are not associated with serious public-health hazards.

An analysis of all defects reported during 2005 was completed and published.

Meetings and activities of the inspectors groups

The EMEA organised and chaired 4 meetings each for the ad hoc GMP and GCP inspectors groups. A first meeting of pharmacovigilance inspectors was also held, while a planned meeting of the GLP (good laboratory practice) inspectors was postponed to 2007.

These groups contribute to the harmonisation of inspection-related procedures across the EU. They also develop guidance and other working documents, which this year included:

- draft guidelines on pharmacovigilance systems and inspections;
- a policy on performing GCP inspections;
- draft revisions of GMP annexes on herbal medicines, radiopharmaceuticals and medicinal gases.

Meetings with stakeholders were also held to discuss draft guidance on the manufacture of sterile products and on facilities to be used in the manufacture of potent or sensitising medicinal products.

Good progress with EudraGMP

The ad hoc GMP inspectors are also responsible for overseeing the implementation of the EudraGMP database of manufacturing authorisations and GMP certificates. A first version of the database was put into final testing during the year, and is expected to be made available in 2007.

Meetings and activities of the Quality Working Party

The Agency provided secretarial support to the Joint CHMP/CVMP Quality Working Party (QWP), which continued its work on:

- development of EU quality guidelines;
- provision of support relating to ICH and VICH;
- cooperation with the European Directorate for the Quality of Medicines (EDQM).

In cooperation with the Heads of Medicines Agencies, a pilot procedure for work-sharing on complex variations was agreed and launched.

One joint meeting of the QWP and ad hoc GMP inspectors took place, building on cooperation between assessors and inspectors on quality-related matters. The meeting included a workshop on anti-counterfeiting techniques. These groups also contributed jointly to the publication of a reflection paper on dealing with minor manufacturing deviations.

Training activities

The EMEA organised training courses for EU GCP inspectors (in conjunction with the Austrian inspectorate) and on Process Analytical Technology. The Agency also supported a training conference on 'design space' concepts, as well as a conference with the Parenteral Drug Association on understanding the European GMP environment.

Joint audit programme for GMP inspectorates

In the context of the joint audit programme for EEA GMP inspectorates, the EMEA coordinated activities designed to ensure consistent quality standards and harmonised approaches.

The Compliance Group, a subgroup of the GMP Inspection Services Group, met twice in 2006. The group finalised the revision of documentation and procedures for the joint audit programme.

PAT (Process Analytical Technologies) team

PAT is a system for designing, analysing and controlling manufacturing through the timely measurement (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and processes, with the goal of ensuring final product quality (= identifying and monitoring factors that affect product quality).

The EMEA PAT team held 4 meetings in 2006 to review the implications of PAT, with a view to ensuring that the European regulatory framework and the authorities are prepared to conduct thorough and effective evaluations of PAT-based submissions. The PAT team also heard presentations from 3 industry groups, participated in 2 site visits and published a question-and-answer document aimed at clarifying certain dossier provisions.

4.2 Mutual recognition agreements

Mutual recognition agreements (MRAs) between the European Community (EC) and partner countries allow EU Member States and the MRA partner to mutually recognise the conclusions of each other's inspections of manufacturers, and to mutually recognise certificates of conformity to manufacturing specifications. The EMEA is responsible for implementation and operational aspects of these MRAs. MRAs with Australia, New Zealand, Switzerland, Canada and Japan are currently operational, but with slightly different provisions as to scope and applicability.

The harmonisation of operational aspects of all EC MRAs continued in 2006. All MRA partners have agreed to share annual reporting on GMP with each other as part of the maintenance programme. MRA partners have been closely involved in the changes to the EU GMP requirements to ensure ongoing equivalency. Work began on including active pharmaceutical ingredients (APIs) within the scope of the MRAs. The exchange of GMP certificates of API manufacturers will begin in 2007 for Switzerland, Australia and New Zealand, while for Canada and Japan it was agreed that APIs would continue to be excluded.

Good progress was made on including further product types within the scope of the MRA with Japan. Changes to Japanese GMP requirements for biological products were reviewed and a list of activities for 2007 was agreed with the Japanese authorities.

In the context of the EC-Canada MRA, the preparatory evaluation work performed by EU competent authorities for all new Member State GMP authorities was completed. Canada completed assessments of human and veterinary authorities in the Czech Republic and Hungary, and began accepting GMP certificates for these countries as of June 2006. Canadian evaluations of Cyprus, Malta and the Slovak

Republic are ongoing, while those for Estonia, Poland, Lithuania, Slovenia and Latvia will be initiated in 2007.

Mutual recognition agreement (MRA) implementation status and coverage

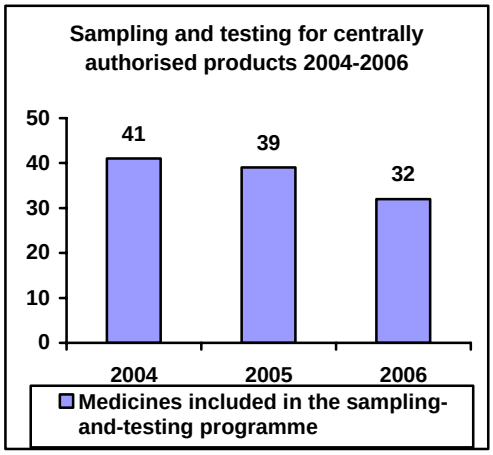
MRA	Implementation status	Coverage
European Community – Australia	Human medicinal products: 1 January 1999 Veterinary medicinal products: 1 June 2001	Human and veterinary medicinal products and active substances Official batch release excluded
European Community – Canada	Operational since 1 February 2003. Czech Republic and Hungary included since June 2006 Assessment of other new Member States ongoing	Human and veterinary medicinal products Veterinary immunologicals and vaccines excluded
European Community – Japan	Operational since 29 May 2004	Human medicinal products only Currently excludes sterile and biological medicinal products, active substances, investigational medicinal products, medicinal gases Official batch release excluded
European Community – New Zealand	Human medicinal products: 1 January 1999 Veterinary medicinal products: 1 June 2002	Human and veterinary medicinal products and active substances Official batch release excluded
European Community – Switzerland	1 June 2002	Human and veterinary medicinal products and active substances and recognition of official batch control of biologicals (human)
European Community – United States	Not in operation. Transitional period ended. No decision on formal extension of the transitional period has been taken	Human and veterinary medicinal products Official batch release excluded

4.3 Sampling and testing

The objectives of the sampling and testing programme are to supervise the quality of centrally authorised medicinal products placed on the market, and to check compliance of these with their authorised specifications.

Sampling from the market in different countries is carried out by national inspectorates, and testing is performed by official medicines control laboratories coordinated through the European Directorate for the Quality of Medicines (EDQM). A selection of centrally authorised products is included in each annual programme.

The 2006 programme for sampling and testing included 32 centrally authorised products.



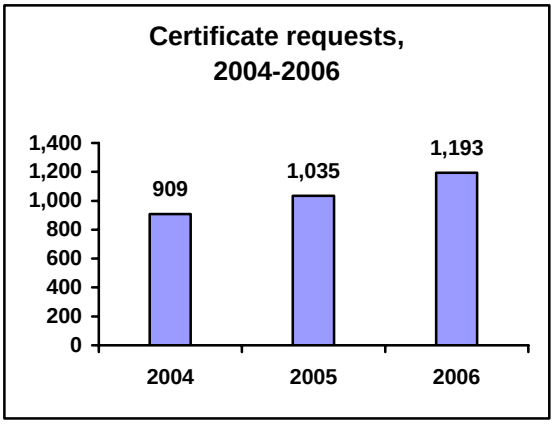
Testing results showed that the majority of the products were of high quality. However, 2 products were found not to comply with their authorised specifications. In one case this resulted in the recall of a batch of the product. Results requiring further investigation were found in 18 products. The investigations revealed some regulatory and scientific discrepancies, which were mainly addressed through amendment of the testing documentation by the marketing authorisation holders concerned.

Work continued on improving the operation of the sampling and testing programme. Procedures for ad hoc or emergency testing of centrally authorised products and for handling of out-of-specification results were finalised and adopted. A first proposal for a risk-based approach to the selection of products and parameters to be tested was under discussion in the relevant EMEA working parties. New contract negotiations with EDQM were also initiated in 2006.

4.4 Certificates of a medicinal product

The EMEA issues certificates of medicinal products to confirm their marketing authorisation status if they have been authorised through the centralised procedure, or to confirm that a centralised marketing authorisation application has been submitted to the EMEA. The purpose of this certification scheme is to support the work of health authorities outside the European Union, in particular those in developing countries.

The number of certificate requests continued to climb in 2006, with 15% more being received than in 2005. Since 2000, requests for certificates have increased by more than 300%.



Main developments in 2006:

- The year saw two firsts: the first certificates issued within the context of cooperation with the World Health Organization, and the first certificates provided free of charge to SMEs.
- A meeting with stakeholders held early in the year confirmed the successful removal of the legalisation step previously performed by the European Commission's UK representation.
- A new system of revenue (invoicing) was introduced and implemented successfully.

4.5 Implementation of the Clinical Trials Directive

The EMEA continued to support the European Commission and Member States with the implementation of Directive 2001/20/EC on clinical trials. It did this through:

- activities of the ad hoc meetings of GCP and GMP inspection services;
- participation in working groups of the Commission;
- support to the Heads of Medicines Agencies' Clinical Trials Facilitation Group;
- support to the Commission and Member States on developing and updating guidance on various aspects of clinical trials;
- progressing work on harmonised procedures.

A joint group of GMP and GCP inspectors developed guidance documents on the content of the batch release certificate and on certification by the Qualified Person, thereby facilitating harmonisation of inspection practices. Further development of the EudraCT database was also supported.

5. EU TELEMATICS STRATEGY

Various initiatives are currently underway to implement the EU Telematics Strategy drawn up by the European Commission, the Member States and the EMEA. Their objective is to support and facilitate the operation of procedures established in accordance with European policy and legislation in the field of pharmaceuticals, whilst also increasing their efficiency and transparency.

EU telematics and EMEA internal systems are backed by dedicated support and maintenance systems and services, which ensure high levels of availability, security and confidentiality.

As at the end of 2006, versions of the following systems were in production:

- EudraNet (secure communication between stakeholders in the European Medicines Regulatory Network). The network is in place, connecting regulatory authorities in the European Economic Area, including the two new EU Member States, Bulgaria and Romania.
- EudraVigilance (web-based information system to support the pharmacovigilance obligations laid down by Community legislation). The base system is in place. Work is required in order to complete the data warehouse and business intelligence functionality, sophisticated signal detection, signal tracking, and implementation of the access policies with regard to all stakeholders.
- EudraPharm (database of medicinal products authorised in the European Union to support regulatory activities and to make information on medicinal products available to the public). The base system is in place. Work is required to implement extended search, technical structuring of the content, incorporation of data from national competent authorities, and a multilingual approach.
- EudraCT (Community database of information on the content, commencement and termination of clinical trials). The base system is in place. Requests for enhancements have been received.
- PIM (Product Information Management — a process that supports the electronic exchange of product information between applicant and EMEA, and the review of this information). The system for the centralised procedure is nearly complete, adjustments for post-authorisation procedures being planned for early 2007. Thereafter, subject to budgetary capacity, it is hoped to extend the system to the decentralised and mutual recognition procedures.

The following systems were in development as at the end of 2006:

- EudraGMP (Community database of manufacturing authorisations and of certificates of good manufacturing practice). The core system was in testing as at the end of 2006. Enhancements to permit semi-automatic batch upload are planned for 2007. Further requests for enhancements have been received.
- EU Telematics Controlled Terms (a central hub providing agreed and authoritative look-up information for medicinal products in as many EU/EEA languages as possible). Planning of development work on a production system, following two successful prototypes in 2006, was ongoing at the end of the year.

Project	Initiatives/deliverables
EudraPharm	▪ This database of authorised medicinal products in the EU was released to the public in December 2006. The database contains information and links to product information in English on all products authorised via the centralised procedure. ▪ Data from 2 national competent authorities were successfully transferred and imported into a test version of the database
EudraVigilance, data	▪ Version 7.1 of EudraVigilance (Human) and version 2.2 of

Project	Initiatives/deliverables
warehouse and business intelligence	EudraVigilance (Veterinary) were deployed. ▪ The simple form for reporting by occasional users in the veterinary sector was released. ▪ The EudraVigilance Interim Data Warehouse System was deployed in the production environment and validation activities were initiated. ▪ The Member State Edition was deployed and installed in 5 of the 7 national competent authorities currently involved in the programme. ▪ The architectural foundations of the Eudra Data Warehouse were put into place and 10 pre-defined reports for the Veterinary Unit were developed and made available to EMEA users.
Product information management (PIM)	▪ Version 4.0 of the PIM Review System, Version 2.0 of the Light Authoring Tool, and version 2.3 of the Data Exchange Standard were put into production. ▪ The first pilot submission through the centralised procedure was received and successfully processed to the appropriate stage in the procedure.
EudraGMP	▪ The initial version of the system was developed and was in test as at the end of the year.
EudraCT	▪ Versions 3 and 4 were released in 2006.
Implementation of e-submissions	▪ The decision to implement eCTD as part of the process-improvement exercise was taken ▪ The tender process for the European Review System was completed during the year.
Infrastructure	▪ A first prototype of a system for the maintenance and making available of controlled-term lists was successfully completed during the year. ▪ A second prototype of a system for the maintenance and making available of controlled-term lists was successfully completed in support of the EU's participation in the preparation of a guideline on data elements and standards for drug dictionaries in the context of ICH.
Reference-data model used as a reference for current and future databases and projects	▪ The project was re-oriented. ▪ Work on expanding the model for information contained in four systems (EudraVigilance. EudraCT, PIM and the Medicinal Product Identifier) in parallel was initiated.

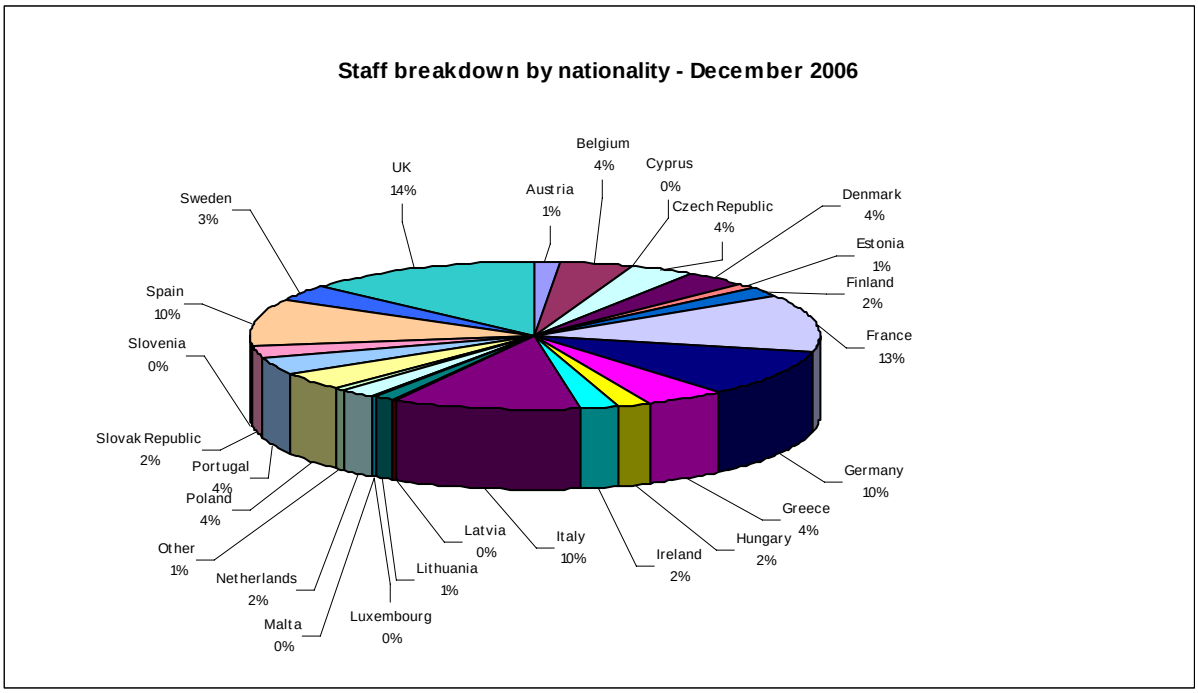
6. SUPPORT SERVICES

6.1 Personnel and budget

Activities in this area relate to the administration of the Agency's personnel and the management of its revenue and expenditure.

By the end of 2006, the Agency employed a total of 497 staff. In addition, about 45 people worked at the agency on a contractual basis, mainly on IT projects.

There is a balanced geographical representation of EU Member State nationalities among the EMEA staff, with emphasis being made in recent years on recruiting from the new accession countries.



The gender balance overall is slightly in favour of women in that about two thirds of agency staff are female.

Staff of the agency are comparatively young: over 70% of are aged below 40 and less than 10% are aged 50 or above.

Staffing and recruitment data	2004	2005	2006
Total established staff (AT/CA)	314 + 65*	372 + 44*	435 + 62*
Selection procedures (external & internal)	27	41	49

* Number of interims, trainees, auxiliary agents and national experts.

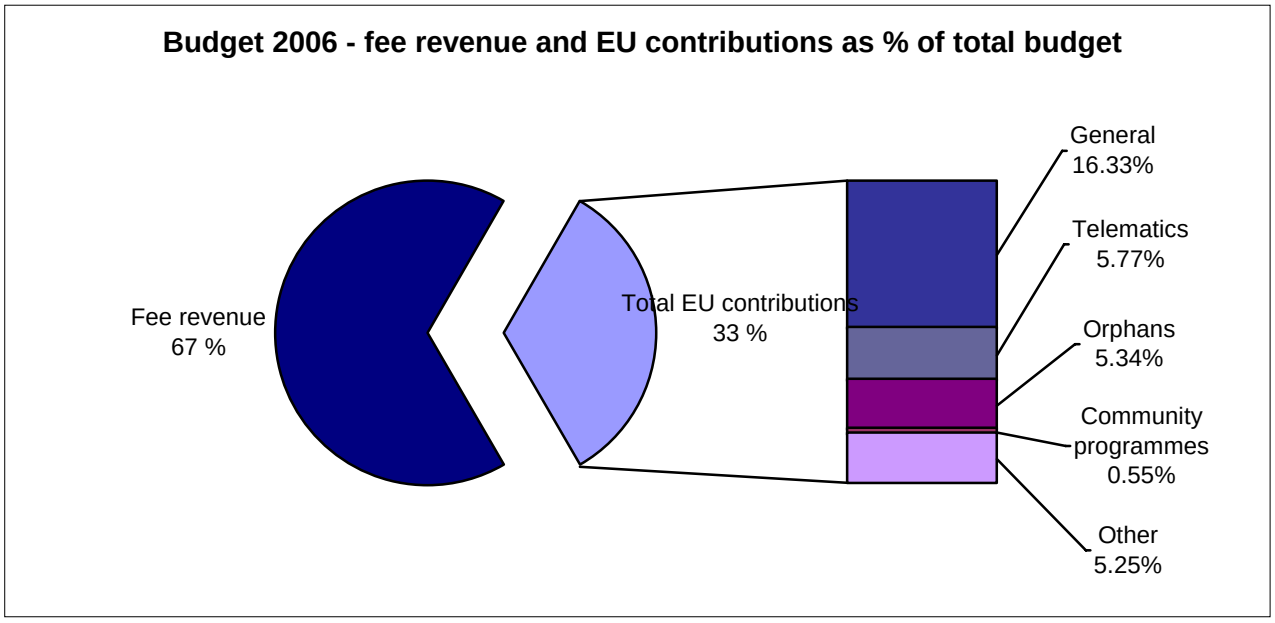
Main personnel-related developments in 2006

- The Agency's training budget was increased by €150,000. This allowed further training opportunities to be provided, including additional courses on scientific subjects, financial competency and other business-related training. A process to revise the training rules was begun, and an annual fellowship programme was put in place to allow temporary work-exchanges between the EMEA and other related organisations.

- Training profiles were implemented to provide a 'training map' for new staff. Introduction of this system began in May 2006 and has largely been implemented in 2006.
- A policy on equal opportunities was adopted, and an annual report on its functioning will be prepared in 2007.
- Progress was made with the development of implementing rules, several of which can be finalised in 2007, once responses are received from the European Commission.

Main budget-related developments in 2006

The Agency's total budget in 2006 was € 138,676,000, an increase of 27 % over 2005. Revenue from fees paid by industry accounts for about two thirds of the EMEA budget, the remainder is made up of community contributions.



- Support was given to the 2007 budget-negotiation process, and a policy was developed to support the 2008 and future budget-negotiation processes. Support was also provided to the Management Board's long-term financing and costing groups.
- ActiTrak, the costing system of the Agency, was substantially revised and is now an even more comprehensive and precise tool for budgetary and operational-costing analysis and activity-based budgeting.

6.2 Accounts

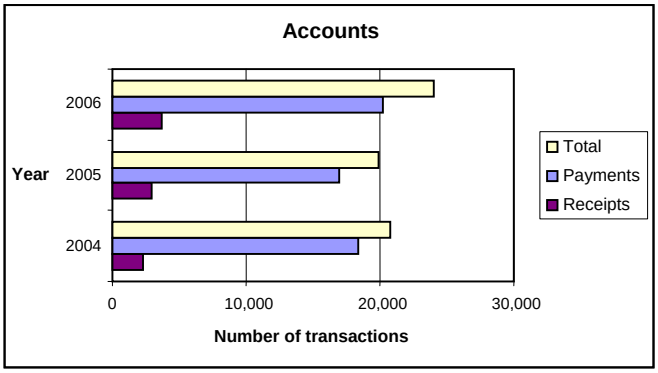
The account sector maintains the accounts, makes payments, and collects revenue in accordance with the procedures laid down in the Financial Regulation. It manages the cash resources of the Agency, maintains the Agency's relationship with its banks, and provides accurate and timely financial information to management.

The main factors shaping activity in this area in 2006 were the implementation of new financial accounting rules and the modification of accounting systems.

Main developments in 2006

- The first accrual-based accounts were completed for 2005, and consolidated with the European Commission accounts. The EMEA 2005 accounts are available on the Agency's website.

- Consolidation of the revenue/customer-invoicing system resulted in a significant process improvement.
- Having looked at available options, the Agency has commissioned a feasibility study to examine the suitability of migrating the current accounting system to an enterprise resource planning system in order to achieve integration with other processes and systems relating to human resources, supply chain, costing, customer and revenue management, etc.



6.3 Verification service

The Agency's verifying officer is responsible for the mandatory ex-ante verification of each operation that has a financial impact. The verifying officer verifies whether operations are legal, regular and compliant with the principle of sound financial management, and ensures that all tasks have been carried out in conformity with the rules and regulations in force.

Main developments in 2006

- The verifying service carried out ex-ante checks on 34,100 financial and operational transactions, including commitments, contracts, payments and recovery orders. This total is 12.5% higher than the 2005 figure.
- A new approach on risk-analysis using appropriate reports and a strong relationship between the financial actors has been implemented. The system offers a better interaction but requires more support and advice from the verifying service prior to the transaction initiation. This transparent approach aims to prevent possible mistakes and improves the workflow. In 2006, no cases were referred to the Executive Director.
- The internal control method was complemented by an appropriate ex-post control. Both ex-ante checks and ex-post reports provide the authorising officer the assurance that the budget execution has respected principles of sound financial management.

6.4 Infrastructure services

Activities in this field relate to the provision and running of the necessary infrastructure services for the effective functioning of the Agency, including the management of procurement procedures.

The main factor influencing activity in this area during 2006 was the extension of the Agency's premises.

- Main developments in 2006
- The seventh floor of the EMEA building was completely refurbished. The project was completed according to schedule and within budget. Refurbishment of meeting rooms and office accommodation for the Meeting Management & Conferences sector on the second floor was

started. On the basis of a risk assessment on the need for additional office space, management agreed that an option would be exercised to take over one floor of the adjacent building.

- A new access system was installed on the ground floor to enhance the overall security of the premises and security guards were contracted to provide additional security throughout the building.
- The EMEA health and safety policy was updated and a number of fire, health & safety campaigns and training sessions were undertaken.
- A business continuity exercise was carried out, which included testing of the crisis management plan and disaster recovery facilities.
- Contacts were established with a number of procurement officers in other EU Agencies, leading to valuable collaboration on contracts and procurement.

6.5 Meetings and conferences at the EMEA

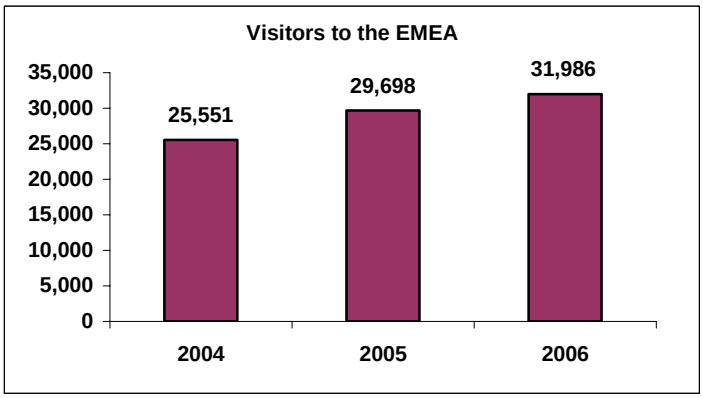
The EMEA organises hundreds of meetings on its premises every year and hosts tens of thousands of delegates and other visitors.

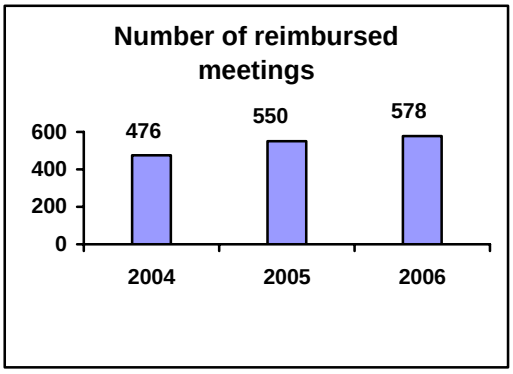
To ensure these meetings are organised as efficiently as possible, the EMEA has a dedicated sector – the Meeting Management and Conferences (MM&C) sector – responsible for managing meeting-related facilities and services.

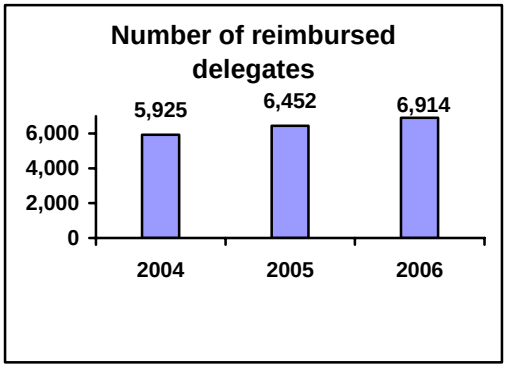
The MM&C sector makes practical and logistical arrangements for in-house meetings and for external conferences that the EMEA hosts or attends, including travel and accommodation arrangements for delegates, reimbursement of expenses, organisation of supplies, etc.

Steady increase in EMEA meetings activity

The number of meetings organised by the EMEA rose once again in 2006. A total of 578 meetings were held this year (up 5% on 2005), involving over 30,000 visitors and almost 7,000 reimbursement operations for delegates (7.2% more than in 2005).







Main developments in 2006

- MM&C sector laid down procedures for organising emergency meetings within 24 hours, whether on working days, weekends or national holidays.
- Phase III of the meeting-management system was tested, implemented and released. MM&C provided technical support and assistance to EMEA users through ad-hoc training and by answering queries. The tracking system for hotel and travel details was finalised, and work was begun on the online booking facility for delegates.
- MM&C was extensively involved in the Agency's preparations for the accession of Bulgaria and Romania to the EU, as well as in preparatory work for the involvement of Croatia and Turkey in EMEA activities.

6.6 EMEA document management and publishing

The Agency ensures full compliance with all regulatory and quality requirements in the areas of document and records management. This includes ensuring best practice in document and records management, verifying the quality of published documents, providing access to internal and external information for staff to perform their duties, verifying the accuracy of translations, and organising and supporting the Agency's exhibitions.

Activity in this area is assured by the Document Management & Publishing (DM&P) sector.

Management of documents, records and information is a key task of the EMEA, and continuous effort is made to enhance the quality and efficiency of the systems and services that support this activity.

A number of processes have been developed – or are currently being developed – to optimise the effective management of the ever-increasing number of documents and records that the Agency receives. In 2006, these included:

- initial development of an electronic records management project (i.e. best practices for the systematic control of the creation, maintenance, use, retention, preservation and disposition of records);
- further upgrading of the Agency's electronic document management system;
- processes for implementation of Regulation (EC) No 1049/2001 on access to documents;

DM&P activities	2005	2006	Change (%)	Monthly average (2006)
External requests for information*	3,006	3,024	+ 0.6	252
Internal requests for information	4,505	3,479	– 23	290
Visitors to the library	1,301	1,934	+ 49	161

Translated pages	14,177	20,819	+ 47	1,735
New documents published on EMEA website	4,952	5,113	+ 3	426

* Includes requests for access to documents (where a single request may encompass hundreds of documents).

Access to documents

This was the second full year of operation of the Rules for the implementation of Regulation (EC) No 1049/2001 on access to EMEA documents, adopted by the Management Board in May 2004. The rules were revised twice in 2006, following consultation with the European Commission.

Access to EMEA documents*	2006	Monthly average
Requests		
Total requests received	55	4.6
Access granted	25	2
Partial access granted	4	0.3
Access denied	15	1.25
Appeals		
Total appeals received	5	0.4
Appeals granted	0	0
Appeals partially granted	2	0.2
Appeals denied	2	0.2

* In accordance with the provisions of Regulation (EC) No 1049/2001 on access to documents.

The main reasons for refusal of access at the initial as well as the appeals stage concerned the protection of the Agency's decision-making process (Article 3(3) of the rules) and the protection of commercial interests of a natural or legal person (Article 3(2)(a) of the rules). Each exception accounts for 50% of the refusals. In approximately 9% of cases the document in question did not exist.

6.7 Information technology

The principal aim in the IT environment for 2006 was to ensure timely progress with the development of a programme of corporate projects, while providing support services to all IT activities relating to the Agency's increasing range of tasks and responsibilities. Progress was monitored using key performance indicators such as systems availability, response times and on-time delivery, within budget and to specifications, for new or improved information systems.

Several new IT systems were set up as part of the Agency's efforts to promote the use of virtual meetings, videoconferencing and web-streaming technologies as alternatives to physical meetings and conferences.

New management systems and enhanced Helpdesk services were implemented to improve the corporate and EU telematics infrastructure, enabling a high level of service to be maintained.

Main developments in 2006

- Meetings-management system (MMS). A new module that allows delegates to register and to make hotel and travel arrangements via the Internet was added.

- Managing meeting documents (MMD). A system that involves the electronic provision of documentation for meetings and the use of alternative technologies for electronic meetings was piloted.
- Virtual meeting room (VITERO). A second pilot was set up involving an audio-conference software package that allows delegates to use their own PC to participate in a meeting, with the ability to chair the meeting, to speak, to vote and to access presentation materials.
- Several improvements were made to the underlying IT infrastructure, including the implementation of a single sign-on process for Java applications developed in-house and migration to the latest releases of Linux and Oracle.
- A critical project that was progressed in 2006 concerns business-continuity arrangements which ensure that, in the case of a disaster, the Agency's core business will not be interrupted for more than one working day, and that IT systems can be recovered. This included further work on the development and implementation of remote off-site disaster-recovery facilities, as well as a pilot test of a system that offers a location-independent working capability.
- SIAMED II. The underlying database was migrated to Oracle (expected to go live in Q1/07) and a final draft of the SIAMED II Vision document was submitted for approval.
- Eudra Common Directory (ECD). The integration of ECD into new applications was extended, to prepare for the introduction of delegated-user management in 2007.
- The new Scientific Advice database was rolled out including the generation of the Scientific Advice Working Party agendas as well as the monitoring of implementation of the new Scientific Advice Framework.
- The experts database was rolled out. It is now linked to ECD for contacts and for user-authentication and authorisation.

ANNEXES

Annex 1 Members of the Management Board

Annex 2 Members of the Committee for Medicinal Products for Human Use

Annex 3 Members of the Committee for Medicinal Products for Veterinary Use

Annex 4 Members of the Committee on Orphan Medicinal Products

Annex 5 Members of the Committee on Herbal Medicinal Products

Annex 6 National competent authority partners

Annex 7 EMEA budget summaries 2005–2007

Annex 8 EMEA Establishment Plan

Annex 9 CHMP opinions in 2006 on medicinal products for human use

Annex 10 CVMP opinions in 2006 on medicinal products for veterinary use

Annex 11 COMP opinions in 2006 on designation of orphan medicinal products

Annex 12A HMPC Community herbal monographs

Annex 12B Entry to List of Herbal Substances, Preparations and Combinations thereof for use in Traditional Herbal Medicinal Products

Annex 13 Guidelines and working documents in 2006

Annex 14 Arbitration and Community referrals overview 2006

Annex 15 EMEA contact points

Annex 1 Members of the Management Board

Chair: Hannes WAHLROOS
EMEA contact: Martin HARVEY ALLCHURCH

Members

▪ European Parliament	Gianmartino BENZI (†), José-Luis VALVERDE LÓPEZ
▪ European Commission	Heinz ZOUREK[3], Andrzej RYŚ[4] (*Alternates:* Georgette LALIS, Bernard MERKEL[5])
▪ Belgium	Johan van CALSTER (*Alternate:*nomination awaited[6])
▪ Czech Republic	Milan ŠMÍD (*Alternate:* Alfred HERA)
▪ Denmark	Jytte LYNGVIG *(vice-chairman)* (*Alternate:* Paul SCHÜDER)
▪ Germany	Walter SCHWERDTFEGER (*Alternate:* Ilse-Dore SCHÜTT)
▪ Estonia	Kristin RAUDSEPP (*Alternate:* Alar IRS)
▪ Greece	Dimitrios VAGIONAS (*Alternate:* Vassilis KONTOZAMANIS)
▪ Spain	Cristina AVENDAÑO-SOLÀ[7] (*Alternate:* Teresa PAGÉS)
▪ France	Jean MARIMBERT[8] (*Alternate:* Pascale BRIAND[9])
▪ Ireland	Pat O'MAHONY (*Alternate:* Joan GILVARRY)
▪ Italy	Nello MARTINI (*Alternate:* Silvia FABIANI)
▪ Cyprus	Panayiota KOKKINOU (*Alternate:* Louis PANAYI)
▪ Latvia	Inguna ADOVIĈA
▪ Lithuania	Mindaugas PLIESKIS (*Alternate:* Juozas JOKIMAS)
▪ Luxembourg	Mariette BACKES-LIES (*Alternate:* Claude A HEMMER)
▪ Hungary	Tamás L PAÁL (*Alternate:* Beatrix HORVÁTH)
▪ Malta	Patricia VELLA BONANNO (*Alternate:* Kenneth MIFSUD)
▪ Netherlands	Aginus A W KALIS
▪ Austria	Marcus MÜLLNER[10] (*Alternate:* Christian KALCHER)
▪ Poland	Piotr BLASZCZYK (*Alternate:* Jacek SPŁAWINSKI)
▪ Portugal	Vasco MARIA (*Alternate:* Hélder MOTA FILIPE)
▪ Slovenia	(*Alternate:* Vesna KOBLAR)
▪ Slovakia	Ján MAZÁG (*Alternate:* Dagmar STARÁ)
▪ Finland	Hannes WAHLROOS (*Alternate:* Pekka JÄRVINEN)
▪ Sweden	Gunar ALVÁN (*Alternate:* Anders BROSTRÖM)
▪ United Kingdom	Kent WOODS (*Alternate:* Steve DEAN)
▪ Representatives of patients' organisations	Mary BAKER, Jean GEORGES
▪ Representative of doctors' organisations	Lisette TIDDENS-ENGWIRDA
▪ Representative of veterinarians' organisations	Fritz Rupert UNGEMACH

[3] Replaced Horst REICHENBACH as of June 2006 meeting
[4] Replaced Fernand SAUER as of June 2006 meeting
[5] Replaced Patricia BRUNKO as of June 2006 meeting
[6] Nomination awaited following the departure of André PAUWELS in October 2006
[7] Replaced Maria del Val DÍEZ RODRIGÁLVAREZ as of December 2006 meeting
[8] Replaced Philippe DUNETON as of September 2006 meeting
[9] Replaced Jean MARIMBERT following his nomination as member as of September 2006 meeting
[10] Replaced Robert SCHLÖGEL as of March 2006 meeting

Observers	
▪ Iceland	Ingolf J PETERSEN (Alternate: Rannveig GUNNARSDÓTTIR)
▪ Liechtenstein	Brigitte BATLINER (Alternate: Peter MALIN)
▪ Norway	Gro Ramsten WESENBERG (Alternate: Hans HALSE)
▪ Bulgaria	Emil IVANOV HRISTOV (Alternate: Meri BORISLAVOVA PEYCHEVA)
▪ Romania	Magdalena BADULESCU (Alternate: Rodica BADESCU)

Annex 2 Members of the Committee for Medicinal Products for Human Use

Chair: Daniel BRASSEUR
EMEA contact: Anthony HUMPHREYS

Members

- Eric ABADIE (France) *(vice-chairman)*
  Alternate: Jean-Hugues TROUVIN
- John Joseph BORG (Malta)
  Alternate: Patricia VELLA BONANNO
- János BORVENDÉG (Hungary)
  Alternate: Agnes GYURASICS
- Gonzalo CALVO ROJAS (Spain)
  Alternate: Concepcion PRIETO YERRO
- Nikolaos DRAKOULIS (Greece)
  Alternate George AISLAITNER[1]
- Harald ENZMANN (Germany)
  Alternate: Karl BROICH
- Jacqueline GENOUX-HAMES (Luxembourg)
  Alternate: nomination awaited[2]
- Manfred HAASE (Germany) *(co-opted)*
- Ian HUDSON (United Kingdom)
  Alternate: Julia DUNNE
- Arthur ISSEYEGH (Cyprus)
  Alternate: Panayiota KOKKINOU
- Alar IRS [3](Estonia)
  Alternate: Raul KIIVET[4]
- Pekka KURKI (Finland) *(co-opted)*
- Nomination awaited [5](Finland)
  Alternate: Pirjo LAITINEN-PARKONNEN[6]
- Metoda LIPNIK-STANGELJ (Slovenia)
  Alternate: Barbara RAZINGER-MIHOVEC
- David LYONS (Ireland)
  Alternate: Patrick SALMON
- Romaldas MAČIULAITIS (Lithuania)
  Alternate: Donatas STAKIŠAITIS[7]
- Ján MAZÁG (Slovakia)
  Alternate: nomination awaited[8]
- Pieter NEELS (Belgium)
  Alternate: Bruno FLAMION
- Giuseppe NISTICÒ (Italy)
  Alternate: Pasqualino ROSSI
- Sif ORMARSDÓTTIR (Iceland)
  Alternate: Magnús JÓHANNSSON
- Ingemar PERSSON (Sweden) *(co-opted)*
- Michał PIROŻYŃSKI (Poland)
  Alternate: Piotr SIEDLECKI
- Heribert PITTNER (Austria)
  Alternate: Josef SUKO
- Juris POKROTNIEKS (Latvia)
  Alternate: Indulis PURVINŠ
- Jean-Louis ROBERT (Luxembourg)
  (co-opted)
- Frances ROTBLAT (United Kingdom)
  (co-opted)
- Tomas SALMONSON (Sweden)
  Alternate: Bengt LJUNGBERG
- Beatriz SILVA LIMA (Portugal)
  Alternate: Cristina SAMPAIO
- Eva SKOVLUND (Norway)
  Alternate: Liv MATHIESEN
- Milan ŠMÍD (Czech Republic)
  Alternate: nomination awaited
- Steffen THIRSTRUP (Denmark)
  Alternate: Jens ERSBØLL
- Barbara VAN ZWIETEN-BOOT (Netherlands)
  Alternate: Frits LEKKERKERKER

[1] Replaced Michalis AVGERINOS as alternate in January 2006
[2] Nomination awaited following appointment of Jean-Louis ROBERT as co-opted member in September 2004
[3] Replaced Raul KIIVET as of January 2006 meeting
[4] Replaced Alar IRS as of January 2006 meeting
[5] Nomination awaited following departure of Tapio KUITUNEN in May 2006
[6] Replaced Riita TOKOLA in June 2006
[7] Replaced Valdas LIUKAITIS (nominated in June 2006 as replacement for Mykolas MAURICAS) as of November 2006
[8] Nomination awaited following departure of Leila FARAH in September 2005

Observers

- Bulgaria Dimiter TERZIIVANOV NIKOLOV (*Alternate:* Ivanka ATANASOVA)
- Romania Viorel Robert ANCUCEANU[1] (*Alternate:* Victoria SUBTIRICA)

Working parties, ad hoc groups and scientific advisory groups

Scientific Advice Working Party
Chair: Bruno FLAMION
EMEA contact: Agnès SAINT-RAYMOND

Biologics Working Party
(formerly Biotechnology Working Party)
Chair: Jean-Hugues TROUVIN
EMEA contact: John PURVES

Blood Products Working Party
Chair: Manfred HAASE
EMEA contact: John PURVES

Cell-based Products Working Party

Efficacy Working Party
Chair: Barbara VAN ZWIETEN-BOOT
EMEA contact: Xavier LURIA

Gene Therapy Working Party

Joint CHMP/CVMP Quality Working Party
Chair: Jean-Louis ROBERT
EMEA contact: Emer COOKE

Pharmacogenetics Working Party

Pharmacovigilance Working Party
Chair: June RAINE
EMEA contact: Panos TSINTIS

Safety Working Party

Vaccine Working Party
Chair: Roland DOBBELAER
EMEA contact: John PURVES

Paediatric Working Party

Working Party on Similar Biological (Biosimilar) Medicinal Products
Chair: Pekka KURKI
EMEA contact: Marisa PAPALUCA AMATI

Scientific Advisory Group on Anti-infectives

Scientific Advisory Group on Cardiovascular Issues
Chair: To be appointed
EMEA contact: Xavier LURIA

Scientific Advisory Group on Central Nervous System

[1] Replaced Rodica BADESCU as of May 2006 meeting.

Scientific Advisory Group on Diabetes/Endocrinology
Chair: Edwin GALE
EMEA contact: Xavier LURIA

Scientific Advisory Group on Diagnostics

Scientific Advisory Group on HIV/Viral Diseases
Chair: Ian WELLER
EMEA contact: Xavier LURIA

Scientific Advisory Group on Oncology

CHMP/EMEA Implementation Task Force
(until July 2006)
Chair: Daniel BRASSEUR
EMEA contact: Anthony HUMPHREYS

Invented Name Review Group

EMEA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations
Chair: Frits LEKKERKERKER/Isabelle MOULON
EMEA contact: Isabelle MOULON

EMEA/CHMP Working Group with Healthcare Professionals' Organisations
Chair: Noël WATHION/Giuseppe NISTICO

Working Group on Quality Review of Documents
Chair: Hilde BOONE, as from March 2006 Isabelle MOULON
EMEA contact: Hilde BOONE, as from March 2006 Isabelle MOULON

Annex 3 Members of the Committee for Medicinal Products for Veterinary Use

Chair: Gérard MOULIN
EMEA contact: David MACKAY

Members

- Margarita ARBOIX (Spain)
  Alternate: Ricardo de la FUENTE LÓPEZ
- Gabriel BEECHINOR (Ireland)
  Alternate: David MURPHY
- Rory BREATHNACH (Irland) *(co-opted)*
- Ivo CLAASEN (Netherlands) *(co-opted)*
- Johannes DICHTL (Austria)
  Alternate: Jean-Pierre BINDER
- Peter EKSTRÖM (Sweden) *(co-opted)*
- Lorenzo José FRAILE SAUCE (Spain) *(co-opted)*
- Christian FRIIS (Denmark) *(co-opted)*
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- Tonje HØY (Norway)
  Alternate: Hanne BERGENDAHL
- Martin ILOTT[3] (UNITED KINGDOM)
  Alternate: Lesley Anne JOHNSON[4]
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  Alternate: Valda SEJANE
- Laimi JODKONIS (Lithuania)
  Alternate: Juozas JOKIMAS
- Liisa KAARTINEN (Finland)
  Alternate: Tita-Maria MUHONEN
- Reinhard KROKER (Germany)
  Alternate: Manfred MOOS
- Katarzyna KRZYŻAŃSKA (Poland)
  Alternate: Roman LECHOWKSI
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- Maria Helena PONTE (Portugal)
  Alternate: Leonor Maria MEISEL
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  Alternate: Joseph VELLA
- Cristina MUÑOS MADERO (Spain)[5]
  Alternate: Consuelo Rubio MONTEJANO[6]
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  Alternate: Ioanna TALIOTI
- Eugen OBERMAYR[7] (Austria)
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  Alternate: Henrik HOLST
- Bruno URBAIN (Belgium)
  Alternate: Lionel LAURIER
- Marc WIRTOR (Luxembourg)
  Alternate: Maurice HOLPER

[1] replaced Lotte Winther in May 2006
[2] until October 2006
[3] replaced John O'Brien in April 2006
[4] replaced Martin Ilott in April 2006
[5] replaced Margarita Arboix
[6] replaced Ricardo de la Fuente López
[7] replaced Johannes Dichtl

Efficacy Working Party
Chair: Michael HOLZHAUSER-ALBERTI
EMEA contact: Jill ASHLEY-SMITH

Immunologicals Working Party
Chair: Jean-Claude ROUBY
EMEA contact: Jill ASHLEY-SMITH

Pharmacovigilance Working Party
Chair: Cornelia IBRAHIM
EMEA contact: Kornelia GREIN

Joint CHMP/CVMP Quality Working Party
Chair: Jean-Louis ROBERT
EMEA contact: Emer COOKE

Safety Working Party
Chair: Christian FRIIS
EMEA contact: Kornelia GREIN

Scientific Advice Working Party
Chair: Reinhard KROKER
EMEA contact: Jill ASHLEY-SMITH

Scientific Advisory Group on Antimicrobials
Chair: Karolina TÖRNEKE[1]
EMEA contact: Kornelia GREIN

Environmental Risk Assessment (temporary working party)
Chair: Johannes Petrus HOOGLAND[2]
Vice Chair: Joop A DE KNECHT
EMEA contact: Kornelia GREIN

[1] replaced Liisa Kaartinen in December 2006
[2] until October 2006

Annex 4 Members of the Committee on Orphan Medicinal Products

Chair: Kerstin WESTERMARK (replaced Josep TORRENT-FARNELL as of June 2006 meeting)
EMEA contact: Agnès SAINT-RAYMOND

Members

- Gianmartino BENZI (†) (EMEA representative)
- Brigitte BLÖCHL-DAUM (Austria)
- Andrew BORG (Malta)
- Heidrun BOSCH TRABERG (Denmark)
- Birthe BYSKOV HOLM[1] (patients' organisation representative) *(vice-chairman)*
- Yann LE CAM (patients' organisation representative)
- Ana CORRÊA NUNES (Portugal)
- Bożenna DEMBOWSKA-BAGIŃSKA[2] (Poland)
- Julia DUNNE[3] (EMEA representative)
- Judit EGGENHOFER (Hungary)
- Rembert ELBERS (Germany)
- Pauline EVERS[4] (patients' organisation representative)
- Lars GRAMSTAD (Norway)
- Emmanuel HÉRON (France)
- Ioannis KKOLOS (Cyprus)
- Kateřina KUBÁČKOVÁ (Czech Republic)
- Magdaléna KUŽELOVÁ (Slovakia)
- André LHOIR (Belgium)
- David LYONS (EMEA representative)
- Greg MARKEY (United Kingdom)
- Aušra MATULEVIČIENĖ[5] (Lithuania)
- Henri METZ (Luxembourg)
- Martin MOŽINA (Slovenia)
- Kristina PAVLOVSKA (Latvia)
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- Miranda SIOUTI[6] (Greece)
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- Sigurður B. THORSTEINSSON (Iceland)
- Vallo TILLMANN (Estonia)
- Josep TORRENT i FARNELL[7] (Spain)
- Bettie VOORDOUW[8] (the Netherlands)

[1] Replaced Yann LE CAM as a vice-chairman as of June 2006 meeting
[2] Replaced Jolanta WIĘCKOWSKA as of May 2006 meeting
[3] Replaced Eric ABADIE as of May 2006 meeting
[4] Replaced Alastair KENT as of May 2006 meeting
[5] Replaced Algirdas UTKUS as of May 2006 meeting
[6] Replaced George STATHOPOULOS as of May 2006 meeting
[7] Replaced Fernando ANDRES-TRELLES as of May 2006 meeting
[8] Replaced Harrie J. J. SEEVERENS as of May 2006 meeting

Working parties and ad hoc groups

Ad hoc Biotechnology Working Group
Chair: Harrie SEEVERENS/Jean-Hugues TROUVIN
EMEA contact: Spiros VAMVAKAS

Working Group with Interested Parties
Chair: Yann LE CAM/Agnès SAINT-RAYMOND
EMEA contact: Frida RIVIÈRE

Annex 5 Members of the Committee on Herbal Medicinal Products

Chair: Konstantin KELLER
EMEA contact: Anthony HUMPHREYS

Members

- Linda ANDERSON (United Kingdom)
  Alternate: Sue HARRIS
- Mariette BACKES-LIES (Luxembourg)
  Alternate: Jacqueline GENOUX-HAMES
- Steffen BAGER (Denmark)
  Alternate: Kristine HVOLBY
- Zsuzsanna BIRÓ-SÁNDOR (Hungary)
  Alternate: Nomination awaited[1]
- Per CLAESON (Sweden)
  Alternate: Ubonwan CLAESON
- Christian CUSCHIERI (Malta)
  Alternate: Caroline ATTARD
- Dairíne DEMPSEY (Ireland)
  Alternate: Cora NESTOR[2]
- Wojciech DYMOWSKI (Poland)
  Alternate: Elżbieta WOJTASIK
- Anneli TÖRRÖNEN (Finland)
  Alternate: Sari KOSKI
- Emiel VAN GALEN (Netherlands)
  Alternate: Burt H KROES
- Gloria GARCÍA LORENTE (Spain)
  Alternate: Adela VELÁZQUEZ
- Ioanna CHINOU (Greece)
  Alternate: Eleni SKALTSA
- Marie HEROUTOVÁ (Czech Republic)
- Thorbjörg KJARTANDSDÓTTIR (Iceland)
  Alternate: Sesselja ÓMARSDOTTIR
- Dáša SALUGOVÁ (Slovakia)
-
  Alternate: Pavol MUČAJI
- Artūras KAŽEMEKAITIS[3] (Lithuania)
- Steinar MADSEN (Norway)
  Alternate: Gro FOSSUM
- Ana Paula MARTINS (Portugal)
  Alternate: Maria Helena PINTO FERREIRA
- Samo KREFT (Slovenia)
  Alternate: Barbara RAZINGER-MIHOVEC
- Dailonis PAKALNS (Latvia)
  Alternate: Dace KALKE
- Heribert PITTNER (Austria) *(vice-chairman)*
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- Werner KNÖSS[4] (Germany)
  Alternate: Christine WERNER
- Marie ZERNANT (Estonia)
  Alternate: Ain RAAL
- Antoine SAWAYA (France)
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- Vittorio SILANO (Italy)
  Alternate: Marisa DELBÓ
- Panayiotis TRIANTAFYLLIS (Cyprus)
  Alternate: Maria STAVROU
- Arnold J Vlietinck (Belgium)
  Alternate: Heidi NEEF

[1] Nomination awaited following the departure of Gyöngyi BACS who resigned in February 2005

[2] Replaced Elaine BRESLIN as of May 2006 meeting

[3] Replaced Audronis LUCKOSIUS as of April 2006 meeting

[4] Replaced Klaus REH as of July 2006 meeting

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- Ulrike WISSINGER-GRÄFENHAHN (Germany)
- Olavi Pelkonen (Finland)
- Gert Laekeman (Belgium)
- Kurt WIDHALM (Austria)

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- Ellen PEL (EDQM) (on maternity leave from September 2005)
- Michael WIERER (EDQM)
- Stefan NIKOLOV (Bulgaria)
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- Maria NICULESCU (Romania)
  Alternate: Laurentia RUSCAN

Working parties, ad hoc groups and Scientific Advisory Groups

Working party on Community Monographs and Community List
Chair: Heribert PITTNER
EMEA contact: Anthony HUMPHREYS

Organisational Matters Drafting Group
Chair: Emiel VAN GALEN
EMEA contact: Anthony HUMPHREYS

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Chair: Dairíne DEMPSEY
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Annex 6 National competent authority partners

Further information on the national competent authorities is also available on the national authorities' Internet sites: http://www.hma.eu/human.html and http://www.hma.eu/veterinary.html

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Annex 7 EMEA budget summaries 2005–2007

The summarised comparative budget statements for 2005 to 2007 are as follows:

		2005[1]		2006[2]		2007[3]	
		€ '000	%	€ '000	%	€ '000	%
Revenue							
Fees		71,895	*65.72*	92,580	*66.76*	105,870	*68.51*
General EU contribution		19,588	*17.91*	22,000	*15.87*	25,836	*16.71*
EU contribution for IT Telematics strategy		7,500	*6.86*	8,000	*5.77*	9,164	*5.93*
Special EU contribution for orphan medicinal products		6,110	*5.59*	7,400	*5.34*	6,000	*3.88*
Contribution from EEA		536	*0.49*	650	*0.47*	798	*0.52*
Community programmes		0	*0.00*	760	*0.55*	490	*0.32*
Other		3,767	*3.44*	7,286	*5.25*	6,380	*4.13*
TOTAL REVENUE		**109,396**	*100.00*	**138,676**	*100.00*	**154,538**	*100.00*
Expenditure							
Staff							
11	Staff in active employment	36,463	*33.98*	41,376	*29.84*	47,708	*30.87*
13	Mission expenses	560	*0.52*	586	*0.42*	610	*0.39*
14	Socio-medical infrastructure	436	*0.41*	440	*0.32*	499	*0.32*
15	Exchange of civil servants and experts	726	*0.68*	1,119	*0.81*	1,375	*0.89*
16	Social welfare	6	*0.01*	155	*0.11*	240	*0.16*
17	Entertainment and representation expenses	52	*0.05*	31	*0.02*	24	*0.02*
18	Staff insurances	1,065	*0.99*	1,214	*0.88*	1,457	*0.94*
	Total Title 1	*39,307*	*36.63*	*44,921*	*32.39*	*51,913*	*33.59*
Building/equipment							
20	Investment in immovable property, renting of building and ass costs	12,475	*11.62*	17,260	*12.45*	16,606	*10.75*
21	Expenditure on data processing	10,889	*10.15*	14,623	*10.54*	18,223	*11.79*
22	Movable property and ass costs	1,482	*1.38*	1,057	*0.76*	3,148	*2.04*
23	Other administrative expenditure	540	*0.50*	756	*0.55*	792	*0.51*
24	Postage and communications	624	*0.58*	684	*0.49*	983	*0.64*
25	Expenditure on formal and other meetings	4	*0.00*	74	*0.05*	75	*0.05*
	Total Title 2	*26,015*	*24.24*	*34,454*	*24.84*	*39,827*	*25.77*
Operational expenditure							
300	Meetings	5,825	*5.43*	6,355	*4.58*	7,298	*4.72*
301	Evaluations	34,727	*32.36*	49,827	*35.93*	51,089	*33.06*
302	Translation	1,043	*0.97*	2,215	*1.60*	3,593	*2.32*
303	Studies and consultants	150	*0.14*	170	*0.12*	150	*0.10*
304	Publications	122	*0.11*	124	*0.09*	178	*0.12*
305	Community programmes	132	*0.12*	610	*0.44*	490	*0.32*
	Total Title 3	*42,000*	*39.13*	*59,301*	*42.76*	*62,798*	*40.64*
TOTAL EXPENDITURE		**107,322**	*100.00*	**138,676**	*100.00*	**154,538**	*100.00*

[1] Outturn 2005 as per Final Accounts
[2] Appropriation/Budget 2006 as of 31 December 2006
[3] Appropriation/Budget 2007 as adopted by the Management Board on 19 December 2006

Annex 8 EMEA Establishment Plan

Function Group & Grade	**TEMPORARY POSTS**		
	Occupied as per 31.12.05	Authorised for 2006	Authorised for 2007
AD 16	-	1	1
AD 15	1	3	3
AD 14	6	4	4
AD 13	4	4	4
AD 12	33	34	34
AD 11	32	33	33
AD 10	34	34	34
AD 9	10	13	13
AD 8	31	32	36
AD 7	37	43	43
AD 6	-	12	12
AD 5	-	-	10
Total Function Group AD	*188*	*213*	*227*
AST 11	-	-	-
AST 10	6	6	6
AST 9	-	2	2
AST 8	9	10	10
AST 7	12	14	14
AST 6	27	30	30
AST 5	29	32	32
AST 4	46.5	54	54
AST 3	14	23	24
AST 2	2	10	10
AST 1	4	30	32
Total Function Group AST	*149.5*	*211*	*214*
Total Staff	**337.5**	**424**	**441**

Annex 9 CHMP opinions in 2006 on medicinal products for human use

CHMP positive opinions in 2006 on non-orphan medicinal products for human use

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Proquad ▪ measles, mumps, rubella and varicella vaccine (live)	▪ Sanofi Pasteur MSD	▪ J07BD54 ▪ Simultaneous vaccination against measles, mumps, rubella and varicella in individuals 12 months through 12 years of age.	▪ 18.10.2004 ▪ 23.02.2006 ▪ 209 days ▪ 123 days	▪ 14.02.2006 ▪ 06.04.2006 ▪ 10.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4
▪ Preotact ▪ parathyroid hormone	▪ Nycomed Danmark	▪ H05AA03 ▪ Treatment of osteoporosis in postmenopausal women at high risk of fractures.	▪ 28.03.2005 ▪ 23.02.2006 ▪ 224 days ▪ 105 days	▪ 27.03.2006 ▪ 24.04.2006 ▪ 24.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4
▪ M-M-RVAXPRO ▪ measles, mumps and rubella vaccine (live)	▪ Sanofi Pasteur MSD	▪ J07BD52 ▪ Simultaneous vaccination against measles, mumps, and rubella in individuals 12 months or older.	▪ 19.07.2004 ▪ 23.02.2006 ▪ 193 days ▪ 388 days	▪ 02.05.2006 ▪ 05.05.2006 ▪ 11.05.2006 ▪ OJ C 152, ▪ 30.06.2006, p. 8
▪ Duotrav ▪ travopost/ timolol maleate	▪ Alcon Laboratories	▪ S01ED51 ▪ Decrease of intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues.	▪ 18.05.2005 ▪ 23.02.2006 ▪ 196 days ▪ 82 days	▪ 03.03.2006 ▪ 24.04.2006 ▪ 26.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4
▪ Tygacil ▪ tigecycline	▪ Wyeth Europa	▪ J01AA12 ▪ Treatment of complicated skin and soft tissue infections and complicated intra-abdominal infections.	▪ 24.01.2005 ▪ 23.02.2006 ▪ 182 days ▪ 210 days	▪ 23.03.2006 ▪ 24.04.2006 ▪ 26.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4
▪ Ganfort ▪ bimatoprost/ timolol	▪ Allergan	▪ SO1ED51 ▪ Reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues.	▪ 18.05.2005 ▪ 23.03.2006 ▪ 196 days ▪ 113 days	▪ 24.04.2006 ▪ 19.05.2006 ▪ 23.05.2006 ▪ OJ C 152, ▪ 30.06.2006, p. 8

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Zostavax ▪ varicella - zoster live virus	▪ Sanofi Pasteur MSD	▪ Not yet assigned ▪ Prevention of herpes zoster ("zoster" or shingles) and herpes-zoster related post-herpetic neuralgia. Immunisation of individuals 60 years of age or older.	▪ 15.06.2005 ▪ 23.03.2006 ▪ 202 days ▪ 79 days	▪ 02.05.2006 ▪ 19.05.2006 ▪ 23.05.2006 ▪ OJ C 152, ▪ 30.06.2006, p. 8
▪ Avaglim ▪ rosiglitazone/ glimepiride	▪ SmithKline Beecham	▪ A10BD04 ▪ Treatment of type 2 diabetes mellitus patients insufficiently controlled on optimal dosage of sulphonylurea monotherapy and for whom metformin is inappropriate.	▪ 15.06.2005 ▪ 27.04.2006 ▪ 204 days ▪ 112 days	▪ 24.05.2006 ▪ 27.06.2006 ▪ 29.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19
▪ RotaTeq ▪ rotavirus vaccine	▪ Sanofi Pasteur MSD	▪ J07BH01 ▪ Active immunisation of infants from the age of 6 weeks for prevention of gastroenteritis due to rotavirus infection.	▪ 18.05.2005 ▪ 27.04.2006 ▪ 190 days ▪ 154 days	▪ 31.05.2006 ▪ 27.06.2006 ▪ 29.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19
▪ Baraclude ▪ entecavir	▪ Bristol Myers Squibb Pharma	▪ J05AF10 ▪ Treatment of chronic hepatitis B virus infection in adults with compensated liver disease and evidence of active viral replication, persistently elevated serum alanine aminotransferase levels and histological evidence of active inflammation and/or fibrosis.	▪ 18.10.2004 ▪ 27.04.2006 ▪ 210 days ▪ 343 days	▪ 24.05.2006 ▪ 26.06.2006 ▪ 28.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19
▪ Tysabri ▪ natalizumab	▪ Elan Pharma International	▪ L04AA23 ▪ Treatment of highly active relapsing remitting forms of multiple sclerosis as a single disease modifying therapy in patients with high disease activity despite treatment with beta-interferon or in patients with rapidly evolving severe disease.	▪ 21.06.2004 ▪ 27.04.2006 ▪ 176 days ▪ 496 days	▪ 01.06.2006 ▪ 27.06.2006 ▪ 30.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Zimulti ▪ rimonabant	▪ Sanofi-Synthelabo Recherche	▪ Not yet assigned ▪ As an adjunct to diet and exercise for the treatment of obese patients (BMI>30 kg/m^2), or overweight patients (BMI>27 kg/m^2) with associated risk factor(s), such as type 2 diabetes or dyslipidaemia.	▪ 28.09.2005 ▪ 27.04.2006 ▪ 85 days ▪ 66 days	▪ 24.05.2006 ▪ 19.06.2006 ▪ 19.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19
▪ Acomplia ▪ rimonabant	▪ Sanofi-Synthelabo Recherche	▪ Not yet assigned ▪ As an adjunct to diet and exercise for the treatment of obese patients (BMI>30 kg/m^2), or overweight patients (BMI>27 kg/m^2) with associated risk factor(s), such as type 2 diabetes or dyslipidaemia.	▪ 18.05.2005 ▪ 27.04.2006 ▪ 202 days ▪ 142 days	▪ 24.05.2006 ▪ 19.06.2006 ▪ 19.06.2006 ▪ OJ C 176, ▪ 28.07.2006, p. 19
▪ Intrinsa ▪ testosterone	▪ Procter & Gamble Pharmaceuticals	▪ G03BA03 ▪ Treatment of hypoactive sexual desire disorder in bilaterally oophorectomised and hysterectomised (surgically-induced menopause) women receiving concomitant estrogen therapy.	▪ 15.11.2004 ▪ 01.06.2006 ▪ 210 days ▪ 353 days	▪ 29.06.2006 ▪ 28.07.2006 ▪ 03.08.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Livensa ▪ testosterone	▪ Procter & Gamble Pharmaceuticals	▪ G03BA03 ▪ Treatment of hypoactive sexual desire disorder in bilaterally oophorectomised and hysterectomised (surgically-induced menopause) women receiving concomitant estrogen therapy.	▪ 15.11.2004 ▪ 01.06.2006 ▪ 210 days ▪ 353 days	▪ 29.06.2006 ▪ 28.07.2006 ▪ 01.08.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Competact ▪ pioglitazone/ metformin	▪ Takeda Europe R&D Centre	▪ Not yet assigned ▪ Treatment of type 2 diabetes mellitus patients, insufficiently controlled at their maximally tolerated dose of oral metformin alone	▪ 28.03.2005 ▪ 01.06.2006 ▪ 204 days ▪ 226 days	▪ 06.06.2006 ▪ 28.07.2006 ▪ 01.08.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Atryn ▪ recombinant antithrombin alfa	▪ Genzyme Europe	▪ B01AB02 ▪ Indicated in patients with congenital antithrombin deficiency for the prophylaxis of deep vein thrombosis and thromboembolism in clinical risk situations.	▪ 23.02.2004 ▪ 01.06.2006 ▪ 207 days ▪ 521 days	▪ 29.06.2006 ▪ 28.07.2006 ▪ 02.08.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Exjade ▪ deferasirox	▪ Novartis Europharm	▪ V03AC03 ▪ Treatment of chronic iron overload in patients with beta thalassaemia major aged 6 years and older.	▪ 18.05.2005 ▪ 28.06.2006 ▪ 174 days ▪ 202 days	▪ 26.07.2006 ▪ 28.08.2006 ▪ 31.08.2006 ▪ OJ C 236, ▪ 30.09.2006, p. 2
▪ Champix ▪ varenicline tartrate	▪ Pfizer	▪ N07BA03 ▪ Smoking cessation in adults.	▪ 23.11.2005 ▪ 27.07.2006 ▪ 175 days ▪ 71 days	▪ 23.08.2006 ▪ 26.09.2006 ▪ 28.09.2006 ▪ OJ C 259, ▪ 27.10.2006, p. 6
▪ Silgard ▪ human papilloma recombinant virus vaccine	▪ Merck Sharp & Dohme	▪ J07BM01 ▪ Prevention of high-grade cervical dysplasia, cervical carcinoma, high-grade vulvar dysplastic lesions, and external genital warts.	▪ 24.05.2006 ▪ 27.07.2006 ▪ 117 days ▪ 28 days	▪ 24.08.2006 ▪ 20.09.2006 ▪ 22.09.2006 ▪ OJ C 259, ▪ 27.10.2006, p. 6
▪ Gardasil ▪ human papilloma recombinant virus vaccine	▪ Sanofi	▪ J07BM01 ▪ Prevention of high-grade cervical dysplasia, cervical carcinoma, high-grade vulvar dysplastic lesions, and external genital warts.	▪ 28.12.2005 ▪ 27.07.2006 ▪ 177 days ▪ 34 days	▪ 24.08.2006 ▪ 20.09.2006 ▪ 22.09.2006 ▪ OJ C 259, ▪ 27.10.2006, p. 6
▪ Suboxone ▪ buprenorphine/ naloxone	▪ Schering Plough Europe	▪ N07B C51 ▪ Substitution treatment for opioid drug dependence, within a framework of medical, social and psychological treatment of adults and adolescents over 15 years of age who have agreed to be treated for addiction.	▪ 26.10.2005 ▪ 27.07.2006 ▪ 196 days ▪ 78 days	▪ 24.08.2006 ▪ 26.09.2006 ▪ 28.09.2006 ▪ OJ C 259, ▪ 27.10.2006, p. 6
▪ Luminity ▪ perflutren	▪ Bristol-Myers Squibb Pharma	▪ V08DA04 ▪ Ultrasound contrast-enhancement for use in patients in whom non-contrast echocardiography was suboptimal and who have suspected or established coronary artery disease.	▪ 21.02.2005 ▪ 27.07.2006 ▪ 207 days ▪ 314 days	▪ 23.08.2006 ▪ 20.09.2006 ▪ 22.09.2006 ▪ OJ C 259, ▪ 27.10.2006, p. 6
▪ Byetta ▪ exenatide	▪ Eli Lilly and Company	▪ A10BX04 ▪ Treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonlylureas in patients insufficiently controlled on maximally tolerated doses of these oral therapies.	▪ 23.11.2005 ▪ 21.09.2006 ▪ 208 days ▪ 94 days	▪ 19.10.2006 ▪ 20.11.2006 ▪ 22.11.2006 ▪ OJ C 321, ▪ 29.12.2006, p.13

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Tandemact ▪ glimepiride/ pioglitazone	▪ Takeda Europe R&D Centre	▪ Not yet assigned ▪ Treatment of type 2 diabetes mellitus patients showing intolerance to metformin or for whom metformin is contraindicated and who are already treated with a combination of pioglitazone and glimepiride.	▪ 17.08.2005 ▪ 18.10.2006 ▪ 196 days ▪ 231 days	▪ 27.11.2006 ▪ 08.01.2007 ▪ 10.01.2007 ▪
▪ Adrovance ▪ alendronate sodium-colecalciferol	▪ Merck Sharp & Dohme	▪ M05BB03 ▪ Postmenopausal osteoporosis in patients at risk of vitamin D insufficiency. Reduces the risk of vertebral and hip fractures.	▪ 21.07.2006 ▪ 18.10.2006 ▪ 89 days ▪ 0 days	▪ 15.11.2006 ▪ 04.01.2007 ▪ 09.01.2007 ▪
▪ Lucentis ▪ ranibizumab	▪ Novartis Europharm	▪ S01LA04 ▪ Treatment of neovascular (wet) age-related macular degeneration.	▪ 01.03.2006 ▪ 16.11.2006 ▪ 195 days ▪ 65 days	▪ 22.11.2006 ▪ 22.01.2007 ▪ 24.01.2007 ▪
▪ Insulin Human Winthrop ▪ insulin human	▪ Aventis Pharma Deutschland	▪ A10AB01 ▪ Treatment of diabetes mellitus where treatment with insulin is required.	▪ 21.07.2006 ▪ 16.11.2006 ▪ 110 days ▪ 8 days	▪ 15.12.2006 ▪ 17.01.2007 ▪ 02/02/2007 ▪
▪ Irbesartan HCT Winthrop ▪ irbesartan/ hydrochloro-thiazide	▪ Sanofi Pharma Bristol Myers Squibb	▪ C09DA04 ▪ Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on irbesartan or hydrochlorothiazide alone.	▪ 27.09.2006 ▪ 16.11.2006 ▪ 50 days ▪ 0 days	▪ 13.12.2006 ▪ 19.01.2007 ▪ 23.01.2007 ▪
▪ Irbersartan HCT BMS ▪ irbesartan/ hydrochloro-thiazide	▪ Bristol Myers Squibb Pharma	▪ C09DA04 ▪ Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on irbesartan or hydrochlorothiazide alone.	▪ 27.09.2006 ▪ 16.11.2006 ▪ 50 days ▪ 0 days	▪ 13.12.2006 ▪ 19.01.2007 ▪ 23/01/2007 ▪
▪ Irbesartan Winthrop ▪ irbesartan	▪ Sanofi Pharma Bristol Myers Squibb	▪ C09DA04 ▪ Treatment of hypertension and treatment of renal disease in patients with hypertension and type -2 diabetes mellitus.	▪ 27.09.2006 ▪ 16.11.2006 ▪ 50 days ▪ 0 days	▪ 13.12.2006 ▪ 19.01.2007 ▪ 23.01.2007 ▪

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Irbesartan - BMS ▪ irbesartan	▪ Bristol Myers Squibb Pharma	▪ C09 CA04 ▪ Treatment of hypertension and treatment of renal disease in patients with hypertension and type -2 diabetes mellitus.	▪ 27.09.2006 ▪ 16.11.2006 ▪ 50 days ▪ 0 days	▪ 13.12.2006 ▪ 19.01.2007 ▪ 23.01.2007 ▪
▪ Exforge ▪ valsartan/ amlodipine	▪ Novartis Europharm	▪ C09DB01 ▪ Treatment of hypertension in patients whose blood pressure is not adequately controlled on amlodipine or valsartan alone.	▪ 01.03.2006 ▪ 16.11.2006 ▪ 173 days ▪ 82 days	▪ 18.12.2006 ▪ 17.01.2007 ▪ 19.01.2007 ▪
▪ Dafiro ▪ valsartan/ amlodipine	▪ Novartis Europharm	▪ C09DB01 ▪ Treatment of hypertension in patients whose blood pressure is not adequately controlled on amlodipine or valsartan alone.	▪ 01.03.2006 ▪ 16.11.2006 ▪ 80 days ▪ 8 days	▪ 18.12.2006 ▪ 16.01.2007 ▪ 18.01.2007 ▪
▪ Copalia ▪ valsartan/ amlodipine	▪ Novartis Europharm	▪ C09DB01 ▪ Treatment of hypertension in patients whose blood pressure is not adequately controlled on amlodipine or valsartan alone.	▪ 01.03.2006 ▪ 16.11.2006 ▪ 80 days ▪ 8 days	▪ 18.12.2006 ▪ 16.01.2007 ▪ 18.01.2007 ▪
▪ Imprida ▪ valsartan/ amlodipine	▪ Novartis Europharm	▪ C09DB01 ▪ Treatment of hypertension in patients whose blood pressure is not adequately controlled on amlodipine or valsartan alone.	▪ 01.03.2006 ▪ 16.11.2006 ▪ 80 days ▪ 8 days	▪ 18.12.2006 ▪ 17.01.2007 ▪ 19.01.2007 ▪
▪ Prezista ▪ darunavir	▪ Tibotec	▪ J05AE10 ▪ Treatment of HIV infection	▪ 01.02.2006 ▪ 14.12.2006 ▪ 204 days ▪ 112 days	▪ 21.12.2006 ▪ ▪ ▪
▪ Daronrix ▪ a/vietnam/1194/2004 (H5N1) whole virus inactivated antigen	▪ GlaxoSmithKline Biologicals	▪ J07BB01 ▪ Prophylaxis of influenza in an officially-declared pandemic situation (in the event of a pandemic, the applicant will file a variation to the marketing authorisation to introduce the exact matching pandemic vaccine strain).	▪ 31.01.2006 ▪ 14.12.2006 ▪ 142 days ▪ 174 days	▪ 31.01.2007 ▪ ▪ ▪

CHMP positive opinions in 2006 on similar biological medicinal products for human use

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Omnitrope ▪ somatropin	▪ Sandoz	▪ H01AC01 ▪ Treatment ofgrowth disturbance and Prader-Willi syndrome in children.	▪ 16.08.2004 ▪ 26.01.2006 ▪ 210 days ▪ 147 days	▪ 09.03.2006 ▪ 12.04.2006 ▪ 20.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4
▪ Valtropin ▪ somatropin	▪ BioPartners	▪ H01AC01 ▪ Long-term treatment of children with growth failure due to an inadequate secretion of normal endogenous growth hormone, replacement therapy in adults with pronounced growth hormone deficiency.	▪ 19.07.2004 ▪ 23.02.2006 ▪ 179 days ▪ 402 days	▪ 27.03.2006 ▪ 24.04.2006 ▪ 26.04.2006 ▪ OJ C 124, ▪ 25.05.2006, p. 4

CHMP positive opinions in 2006 on orphan medicinal products for human use

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Myozyme ▪ recombinant human acid alpha-glucosidase	▪ Genzyme	▪ A16AB07 ▪ Treatment of long term enzyme replacement therapy in patients with a confirmed diagnosis of Pompe disease. The benefits have not been established in the late-onset form of Pompe disease.	▪ 20.12.2004 ▪ 26.01.2006 ▪ 196 days ▪ 206 days	▪ 01.03.2006 ▪ 29.03.2006 ▪ 31.03.2006 ▪ OJ C 102, ▪ 28.04.2006, p. 2
▪ Evoltra ▪ clofarabine	▪ Bioenvision	▪ L01BB06 Treatment of acute lymphoblastic leukaemia in paediatric patients who have relapsed or are refractory after receiving at least 2 prior regimens and where there is no other treatment option anticipated to result in a durable response.	▪ 16.08.2004 ▪ 23.02.2006 ▪ 209 days ▪ 344 days	▪ 24.04.2006 ▪ 29.05.2006 ▪ 31.05.2006 ▪ OJ C 152, ▪ 30.06.2006, p. 8

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Sutent ▪ sunitinib malate	▪ Pfizer	▪ LO1XE04 Treatment of malignant gastrointestinal stromal tumors after failure of imatinib mesylate treatment and treatment of advanced or metastatic renal cell carcinoma after failure of interferon alfa or interleukin-2 therapy.	▪ 28.09.2005 ▪ 27.04.2006 ▪ 177 days ▪ 34 days	▪ 28.06.2006 ▪ 19.07.2006 ▪ 24.07.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Nexavar ▪ sorafenib tosylate	▪ Bayer Healthcare	▪ L01XE05 ▪ Treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.	▪ 28.09.2005 ▪ 27.04.2006 ▪ 177 days ▪ 34 days	▪ 31.05.2006 ▪ 19.07.2006 ▪ 21.07.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Thelin ▪ sitaxentan sodium	▪ Encysive (UK)	▪ Not yet assigned ▪ Treatment of pulmonary arterial hypertension classified as WHO functional class III, to improve exercise capacity.	▪ 17.08.2005 ▪ 01.06.2006 ▪ 196 days ▪ 92 days	▪ 30.06.2006 ▪ 10.08.2006 ▪ 10.08.2006 ▪ OJ C 236, ▪ 30.09.2006, p. 2
▪ Savene ▪ dexrazoxane	▪ TopoTraget UK	▪ V03AF02 ▪ Treatment of anthracycline extravasation.	▪ 17.08.2005 ▪ 01.06.2006 ▪ 204 days ▪ 84 days	▪ 29.06.2006 ▪ 28.07.2006 ▪ 02.08.2006 ▪ OJ C 217, ▪ 08.09.2006, p. 5
▪ Sprycel ▪ dasatinib	▪ Bristol-Myers Squibb Pharma	▪ L01XE06 Treatment of adult patients with chronic myeloid leukaemia with resistance or intolerance to prior therapy including imatinib mesilate or Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia, in adults with resistance or intolerance to prior therapy.	▪ 01.02.2006 ▪ 21.09.2006 ▪ 177 days ▪ 55 days	▪ 19.10.2006 ▪ 20.11.2006 ▪ 22.11.2006 ▪ OJ C 321, ▪ 29.12.2006, p. 13
▪ Diacomit ▪ stiripentol	▪ Laboratoires Biocodex	▪ N03AX17 ▪ Adjunctive therapy (to clobazam and valproate) of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (Dravet's syndrome).	▪ 18.05.2005 ▪ 18.10.2006 ▪ 201 days ▪ 317 days	▪ 22.11.2006 (revised opinion received on 31.1.207) – see table above ▪ ▪ ▪

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Elaprase ▪ idursulfase	▪ Shire Human Genetic Therapies	▪ A16AB09 ▪ Long-term enzyme replacement therapy in patients with Mucopolysaccharidosis Type II (Hunter syndrome).	▪ 28.12.2005 ▪ 18.10.2006 ▪ 207 days ▪ 87 days	▪ 28.11.2006 ▪ 08.01.2007 ▪ 10.01.2007 ▪
▪ Inovelon ▪ rufinamide	▪ Eisai	▪ N03AF03 ▪ Treatment of seizures associated with Lennox-Gastaut syndrome as adjunctive therapy in patients 4 years and older.	▪ 18.05.2005 ▪ 16.11.2006 ▪ 208 days ▪ 339 days	▪ 15.12.2006 ▪ 16.01.2007 ▪ 18.01.2007 ▪
▪ Cystadane ▪ betaine	▪ Orphan Europe	▪ A16A A06 ▪ Treatment of homocystinuria.	▪ 17.08.2005 ▪ 14.12.2006 ▪ 194 days ▪ 290 days	▪ 16.01.2007 ▪

CHMP negative opinions in 2006 on medicinal products for human use

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Alpheon ▪ recombinant human Interferon-alfa-2a	▪ BioPartners	▪ L03AB04 ▪ Chronic hepatitis C.	▪ 21/06/2004 ▪ 29/06/2006 ▪ 204 Days ▪ 534 Days	▪ 03/08/2006 ▪ 05/09/2006 ▪ 07/09/2006 ▪ OJ 259, ▪ 27.10.2006, p. 7
▪ Valdoxan ▪ agomelatine	▪ Les Laboratoires Servier	▪ N06AX22 ▪ Treatment of major depressive disorder.	▪ 28/03/2005 ▪ 27/07/2006 ▪ 207 Days ▪ 279 Days	▪ 27.07.2006 ▪ 16.01.2007 ▪ 18.01.2007 ▪ ongoing
▪ Thymanax ▪ agomelatine	▪ Les Laboratoires Servier	▪ N06AX22 ▪ Treatment of major depressive disorder.	▪ 28/03/2005 ▪ 27/07/2006 ▪ 207 Days ▪ 279 Days	▪ 27.07.2006 ▪ 16.01.2007 ▪ 18.01.2007 ▪ ongoing
▪ Mycograb ▪ myctumab	▪ NeuTec Pharma	▪ Not yet assigned ▪ Treatment of invasive candidiasis.	▪ 14/03/2005 ▪ 16/11/2006 ▪ 207 Days ▪ 391 Days	▪ ▪ ▪ ▪

Centralised applications – Withdrawals prior to opinion

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Date of withdrawel ▪ Active time ▪ Clock stop
▪ Multaq ▪ dronedarone	▪ Sanofi	▪ Not yet assigned ▪ Treatment of atrial fibrillation or atrial flutter.	▪ 20.07.2006 ▪ 06.09.2006 ▪ 48 days ▪ 0 Days
▪ Riquent ▪ abetimus sodium	▪ La Jolla	▪ L04AA22 ▪ Delaying the time to and reducing the incidence of renal flare and/or major SLE flare by lowering anti-dsDNA, antibody levels in patients with SLE who have high affinity antibodies to Riquent.	▪ 21/06/2006 ▪ 13.10.2006 ▪ 114 Days ▪ 0 Days
▪ Synordia ▪ fenofibrate/metformin hydrochloride	▪ Laboratoires FOURNIER SA	▪ A10BA02 ▪ Adjunct to diet and exercise to improve glycemic control and dyslipidemia in patients with type 2 diabetes mellitus.	▪ 16/08/2006 ▪ 08.12.2006 ▪ 114 Days ▪ 0 Days
▪ Scintimun ▪ besilesomab	▪ Cis Bio International	▪ V09 HA03 ▪ Scintigraphic imaging to determine location of infectious /inflammatory lesions. Scintigraphic imaging of bone marrow involvement (detection and extent of carcinoma metastasis).	▪ 21/02/2005 ▪ 27.06.2006 ▪ 119 Days ▪ 372 Days
▪ Retaane ▪ anecortave acetate	▪ Alcon laboratories (UK)	▪ S01XA16 ▪ Treatment of neovascular (wet) age-related macular degeneration.	▪ 20/12/2004 ▪ 28.03.2006 ▪ 176 Days ▪ 287 Days
▪ Orathecin ▪ rubitecan	▪ EuroGen Pharmaceuticals	▪ Not yet assigned ▪ Treatment of patients with advanced adenocarcinoma of the pancreas with progressive disease after two or more therapies.	▪ 19/07/2004 ▪ 27/01/2006 ▪ 177 Days ▪ 380 Days
▪ Surfaxin ▪ lucinactant	▪ GMB Biobusiness	▪ Not yet assigned ▪ Prevention and treatment of Respiratory Distress Syndrome in premature newborns.	▪ 18/10/2004 ▪ 08.06.20069 ▪ 182 Days ▪ 416 Days
▪ Ximelagatran ▪ ximelagatran melag	▪ Astra Zeneca	▪ Not yet assigned ▪ Prevention of stroke and other thromboembolic complications associated with atrial fibrillation.	▪ 28/12/2005 ▪ 28.02.2006 ▪ 62 Days ▪ 0 Days

CHMP Opinions in the context of cooperation with the World Health Organization (WHO) for the evaluation of medicinal products intended exclusively for markets outside the Community

Product ▪ Brand name ▪ INN	**Marketing authorisation holder**	**Therapeutic area** ▪ ATC code ▪ Summary of indication	**EMEA/CHMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop
▪ Aluvia ▪ lopinavir / ritonavir	▪ Abbott Laboratories	▪ J05AE06 ▪ Treatment of HIV-1 infected adults and children above the age of 2 years, in combination with other antiretroviral agents.	▪ 23.07.2006 ▪ 21.09.2006 ▪ 60 days ▪ 0 days

Annex 10 CVMP opinions in 2006 on medicinal products for veterinary use

Centralised applications – Positive opinions

Product ▪ Brand name ▪ INN ▪ Part A or B	**Marketing authorisation holder**	**Therapeutic area** ▪ Target species ▪ Summary of indication	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	European Commission ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Flexicam ▪ MELOXICAM	▪ Omnipharm Ltd	▪ Dogs	▪ 13/12/2004 ▪ 18/01/2006 ▪ 210 ▪ 190	▪ 03/03/2006 ▪ 10/04/2006 ▪ 13/04/2006 ▪ OJ C 124, ▪ 25/05/06, p 9
▪ Convenia ▪ CEFOVECIN ▪ Part B	▪ Pfizer Limited	▪ Cats & dogs	▪ 11/05/2004 ▪ 20/04/2006 ▪ 210 ▪ 463	▪ 26/04/2006 ▪ 19/06/2006 ▪ 21/06/2006 ▪ OJ C 176 ▪ 28/07/2006, p. 19
▪ Cerenia ▪ MAROPITANT CITRATE ▪ Part B	▪ Pfizer	▪ Dogs	▪ 12/07/2005 ▪ 19/07/2006 ▪ 210 ▪ 161	▪ 16/08/2006 ▪ 29/09/2006 ▪ 03/10/2006 ▪ OJ C 259 ▪ 27/10/2006, p. 6
▪ Nobilis Influenza H5N2 ▪ INACTIVATED AVIAN INFLUENZA VIRUS VACCINE	▪ Intervet International bv	▪ Chickens, ducks	▪ 02/05/2006 ▪ 20/07/2006 ▪ 78 ▪ 19.07.06	▪ 21/07/2006 ▪ 01/09/2006 ▪ 07/09/2006 ▪ OJ C 259, ▪ 27/10/2006, p. 6
▪ Poulvac Flufend H5N3 RG ▪ RECOMBINANT INACTIVATED AVIAN INFLUENZA VIRUS	▪ Fort Dodge Animal Health	▪ Chickens, Turkeys, Ducks	▪ 02/05/2006 ▪ 20/07/2006 ▪ 78 ▪ 19.07.2006	▪ 21/07/2006 ▪ 01/09/2006 ▪ 07/09/2006 ▪ OJ C 259, ▪ 27/10/2006, p. 6
▪ Yarvitan ▪ MITRATAPIDE	▪ Janssen	▪ Dogs	▪ 21/12/2005 ▪ 13/09/2006 ▪ 210 ▪ 63	▪ 13/10/2006 ▪ 14/11/2006 ▪ 16/11/2006 ▪ OJ C 321, ▪ 29/12/2006, p 13
▪ Medicinal Oxygen Air Liquide Santé ▪ OXYGEN	▪ Air Liquide Sante	▪ Dogs, cats, horses	▪ 21/12/2005 ▪ 11/10/2006 ▪ 210 ▪ 50	▪ 12/10/2006 ▪ 20/12/2006 ▪ ▪
▪ Prac-Tic ▪ PYRIPROLE ▪ Part B	▪ Novartis Sanidad Animal S.L	▪ Dogs	▪ 09/05/2005 ▪ 11/10/2006 ▪ 204 ▪ 315	▪ 12/10/2006 ▪ 18/12/2006 ▪ ▪
▪ ProMeris ▪ METAFLUMIZONE ▪ Part B	▪ Fort Dodge Animal Health ▪	▪ Cat	▪ 12/07/2005 ▪ 11/10/2006 ▪ 210 ▪ 252	▪ 12/10/2006 ▪ 19/12/2006 ▪ ▪

Product ▪ Brand name ▪ INN ▪ Part A or B	**Marketing authorisation holder**	**Therapeutic area** ▪ Target species ▪ Summary of indication	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	European Commission ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ ProMeris Duo ▪ COMBINATION-METAFLUMIZONE, AMITRAZ ▪ Part B	▪ Fort Dodge Animal Health	▪ Dogs	▪ 12/07/2005 ▪ 12/10/2006 ▪ 210 ▪ 252	▪ 12/10/2006 ▪ 19/12/2006 ▪ ▪
▪ Cortavance ▪ hydrocortisone aceponate ▪ Part B	▪ Virbac	▪ Dogs	▪ 15/11/2005 ▪ 08/11/2006 ▪ 210 ▪ 154	▪ 09/11/2006 ▪ 09/01/2007 ▪ ▪
▪ Meloxidyl ▪ MELOXICAM ▪ Generic	▪ CEVA	▪ Dogs	▪ 21/02/2006 ▪ 08/11/2006 ▪ 210 ▪ 50	▪ 17/11/2006 ▪ 15/01/2007 ▪ ▪
▪ Ypozane ▪ osaterone acetate	▪ Virbac	▪ Dogs	▪ 21/12/2005 ▪ 08/11/2006 ▪ 210 ▪ 113	▪ 11/12/2006 ▪ 11/01/2007 ▪ ▪

Centralised applications – Negative opinions

Product ▪ Brand name ▪ INN ▪ Part A or B	**Marketing authorisation holder**	**Therapeutic area** ▪ Target species ▪ Summary of indication	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ Veraflox ▪ Pradofloxacin ▪ Part B	▪ Bayer	▪ Cats & dogs	▪ 12/07/2004 ▪ 14/09/2006	▪ ▪ 11/12/2006 ▪ ▪

Withdrawals prior to opinion (since 20 November 2005)

Product ▪ Brand name ▪ INN ▪ Part A or B	**Marketing authorisation holder**	**Therapeutic area** ▪ Target species ▪ Summary of indication	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of decision ▪ Notification ▪ Official Journal
▪ N/A	N/A	▪ N/A	▪ N/A	▪ N/A

Establishment of maximum residue limits for new substances

Substance INN	**Therapeutic area** ▪ Target species	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of regulation ▪ Official Journal

Substance INN	**Therapeutic area** ▪ Target species	**EMEA/CVMP** ▪ Validation ▪ Opinion ▪ Active time ▪ Clock stop	**European Commission** ▪ Opinion received ▪ Date of regulation ▪ Official Journal
▪ Peforelin	▪ Porcine	▪ 19.01.2006 ▪ 19.04.2006 ▪ 90 days ▪ 0 days	▪ 19.05.2006 ▪ 29.09.2006 ▪ OJ L 271, ▪ 30.09.2005, p 37
▪ Sodium nitrite	▪ Bovine	▪ 19.01.2006 ▪ 19.04.2006 ▪ 90 days ▪ 0 days	▪ 19.05.06 ▪ 29.09.06 ▪ OJ L 271, ▪ 30.09.2005, p 37
▪ Fluazuron	▪ Bovine	▪ 09.12.2004 ▪ 19.04.2006 ▪ 90 days ▪ 0 days	▪ 19.05.2006 ▪ 29.09.2006 ▪ OJ L 271, ▪ 30.09.2005, p 37
▪ Fenvalerate	▪ Bovine	▪ 16.02.2006 ▪ 17.05.2006 ▪ 90 days ▪ 0 days	▪ 15.06.2006 ▪ 07.12.2006 ▪ OJ L 343, ▪ 08.12.2006, p 66
▪ Firocoxib	▪ Equidae	▪ 13.07.2006 ▪ 11.10.2006 ▪ 90 days ▪ 0 days	▪ 07.11.2006 ▪ ▪
▪ Lasalocid (extension)	▪ Poultry (eggs)	▪ 07.07.2005 ▪ 15.02.2006 ▪ 120 days ▪ 223 days	▪ 10.03.2006 ▪ 12.07.2006 ▪ OJ L 192, ▪ 13.07.2006, p 3
▪ Ceftiofur (extension)	▪ Sheep (with extrapolation to all mammalian food producing species)	▪ 16.12.2005 ▪ 15.03.2006 ▪ 90 days ▪ 0 days	▪ 05.04.2006 ▪ 16.08.2006 ▪ OJ L 225, ▪ 17.08.2006, p 3
▪ Doramectin (extension)	▪ All mammalian food producing species	▪ 19.01.2006 ▪ 19.07.2006 ▪ 119 days ▪ 62 days	▪ 31.07.2006 ▪ 13.12.2006 ▪ OJ L 354, ▪ 14.12.2006, p 5
▪ Oxytetracycline (extension)	▪ All food producing species	▪ 17.03.2005 ▪ 19.04.2006 ▪ 120 days ▪ 278 days	▪ 19.05.2006 ▪ ▪
▪ Thiamphenicol	▪ All food producing species	▪ 16.02.2006 ▪ 17.05.2006 ▪ 90 days ▪ 0 days	▪ 15.06.2006 ▪ 07.12.2006 ▪ OJ L 343, ▪ 08.12.2006, p 66
▪ Ginseng	▪ All food producing species	▪ 05.06.2006 ▪ 13.09.2006 ▪ 90 days ▪ 0 days	▪ 09.10.2006 ▪ ▪
▪ Amoxicillin (NEGATIVE)	▪ Poultry (eggs)	▪ 19.01.2006 ▪ 13.09.2006 ▪ 90 days ▪ 117 days	▪ 09.10.2006 ▪ ▪

Annex 11 COMP opinions in 2006 on designation of orphan medicinal products

Positive COMP designation opinions

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ 4-amino-5-oxo-4 (pyridinium-1-ylmethyl) proline	▪ Prodimed S.A. - Spain	▪ Treatment of renal cell carcinoma	▪ 30/09/2005 ▪ 14/11/2005 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ Alpha-1 proteinase inhibitor	▪ Octapharma (IP) Limited - UK	▪ Treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency	▪ 25/10/2005 ▪ 14/11/2005 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ 2'-O-methyl-phosphorothioate oligonucleotide	▪ Prosensa B.V. - The Netherlands	▪ Treatment of Duchenne muscular dystrophy	▪ 26/10/2005 ▪ 14/11/2005 ▪ 11/01/2006/ ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ 26-base single-stranded phosphodiester DNA oligonucleotide	▪ Antisoma Research Limited - United Kingdom	▪ Treatment of renal cell carcinoma	▪ 26/10/2005 ▪ 14/11/2006 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ 26-base single-stranded phosphodiester DNA oligonucleotide	▪ Antisoma Research Limited - United Kingdom	▪ Treatment of pancreatic cancer	▪ 26/10/2005 ▪ 14/11/2006 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ Apomorphine hydrochloride (inhalation use)	▪ Vectura Group plc - UK	▪ Treatment of off-periods in Parkinson's disease not responding to oral treatment	▪ 04/10/2005 ▪ 17/10/2006 ▪ 11/01/2006 ▪ 86 days	▪ 25/01/2006 ▪ 16/02/2006
▪ Miglustat (INN)	▪ Actelion Registration Limited - United Kingdom	▪ Treatment of Niemann-Pick disease, type C	▪ 04/10/2005 ▪ 14/11/2006 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 16/02/2006
▪ Oxalobacter formigenes strain HC-1	▪ OxThera AB - Sweden	▪ Treatment of primary hyperoxaluria	▪ 26/10/2005 ▪ 14/11/2006 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 17/02/2006
▪ Zosuquidar trihydrochloride	▪ Kanisa Europe Limited - UK	▪ Treatment of acute myeloid leukaemia	▪ 27/10/2005 ▪ 14/11/2006 ▪ 11/01/2006 ▪ 58 days	▪ 25/01/2006 ▪ 17/02/2006
Human monoclonal antibody against HLA-DR	▪ GPC Biotech AG - Germany	▪ Treatment of multiple myeloma	▪ 26/10/2005 ▪ 14/11/2006 ▪ 07/02/2006 ▪ 85 days	▪ 15/02/2006 ▪ 28/02/2006
▪ Ciclosporin	▪ Novagali Pharma - France	▪ Treatment of vernal keratoconjunctivitis	▪ 14/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 06/04/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Adeno-associated viral vector containing the human calpain 3 gene	▪ Généthon - France	▪ Treatment of calpainopathy	▪ 19/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 06/04/2006
▪ Temsirolimus	▪ Wyeth Europa Limited - United Kingdom	▪ Treatment of renal cell carcinoma	▪ 25/11/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 06/04/2006
▪ Human heterologous liver cells (for infusion)	▪ Cytonet GmbH & Co. KG - Germany	▪ Treatment of acute liver failure	▪ 26/05/2005 ▪ 12/12/2005 ▪ 08/03/2006 ▪ 86 days	▪ 23/03/2006 ▪ 11/04/2006
▪ Parathyroid hormone (1-34) transglutaminase fusion protein fibrin matrix complex	▪ Kuros Biosurgery International AG - Liechtenstein	▪ Treatment of solitary bone cysts	▪ 15/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 11/04/2006
▪ Sorafenib tosylate	▪ Bayer HealthCare AG - Germany	▪ Treatment of hepatocellular carcinoma	▪ 15/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 11/04/2006
▪ Glutathione	▪ Mukoviszidose e.V. - Germany	▪ Treatment of cystic fibrosis	▪ 19/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 11/04/2006
▪ 4-[131I] iodo-L-phenylalanine	▪ Dr Andreas Kluge - Germany	▪ Treatment of glioma	▪ 16/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 11/04/2006
▪ Tobramycin (liposomal)	▪ EUCRO GmbH & Co. KG - Germany	▪ Treatment of Pseudomonas aeruginosa lung infection in cystic fibrosis	▪ 16/12/2005 ▪ 09/01/2006 ▪ 08/03/2006 ▪ 58 days	▪ 23/03/2006 ▪ 11/04/2006
▪ Mecasermin	▪ Tercica Europe Limited - Ireland	▪ Treatment of primary insulin-like growth factor-1 deficiency due to molecular or genetic defects	▪ 02/12/2005 ▪ 09/01/2006 ▪ 06/05/2006 ▪ 117 days	▪ 24/04/2006 ▪ 22/05/2006
▪ 1-deoxygalactonojirimycin hydrochloride	▪ Amicus Therapeutics UK Ltd - United Kingdom	▪ Treatment of Fabry disease	▪ 02/12/2005 ▪ 09/01/2006 ▪ 05/04/2006 ▪ 86 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Hydrocortisone (modified release tablet)	▪ DuoCort AB - Sweden	▪ Treatment of adrenal insufficiency	▪ 15/12/2005 ▪ 09/01/2006 ▪ 05/04/2006 ▪ 86 days	▪ 24/04/2006 ▪ 22/05/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix	▪ Cellerix SL - Spain	▪ Treatment of epidermolysis bullosa	▪ 16/12/2005 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Heparin sodium	▪ Ockham Biotech Limited - United Kingdom	▪ Treatment of cystic fibrosis	▪ 10/01/2006 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Nilotinib	▪ Novartis Europharm Limited - UK	▪ Treatment of chronic myeloid leukaemia	▪ 02/02/2006 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Recombinant P-selectin glycoprotein immunoglobulin	▪ RJM Consultancy Ltd - United Kingdom	▪ Prevention of post transplantation graft dysfunction	▪ 06/02/2006 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Methoxsalen	▪ Johnson & Johnson Medical Ltd - United Kingdom	▪ Treatment of Graft-Versus-Host disease	▪ 06/02/2006 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days	▪ 24/04/2006 ▪ 22/05/2006
▪ Decitabine	▪ MGI Pharma Ltd - United Kingdom	▪ Treatment of acute myeloid leukaemia	▪ 03/02/2006 ▪ 20/02/2006 ▪ 05/04/2006 ▪ 44 days ▪	▪ 24/04/2006 ▪ 08/06/2006
▪ Mecasermin rinfabate	▪ Insmed Europe Ltd - UK	▪ Treatment of patients with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH	▪ 04/04/2006 ▪ 18/04/2006 ▪ 16/05/2006 ▪ 28 days	▪ 01/06/2006 ▪ 20/06/2006
▪ Mecasermin rinfabate	▪ Insmed Europe Ltd - UK	▪ Treatment of primary insulin-like growth factor-1 deficiency due to molecular or genetic defects	▪ 04/04/2006 ▪ 18/04/2006 ▪ 16/05/2006 ▪ 28 days	▪ 01/06/2006 ▪ 20/06/2006
▪ Diphenylcyclopropenone	▪ Orfagen - France	▪ Treatment of alopecia totalis	▪ 01/02/2006 ▪ 20/02/2006 ▪ 16/05/2006 ▪ 85 days	▪ 06/06/2006 ▪ 29/06/2006
▪ Siplizumab	▪ MedImmune Oncology, Inc. - The Netherlands	▪ Treatment of T-cell and NK-cell neoplasms	▪ 02/03/2006 ▪ 20/03/2006 ▪ 16/05/2006 ▪ 57 days	▪ 06/06/2006 ▪ 29/06/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Diphenylcyclopropenone	▪ Orfagen - France	▪ Treatment of alopecia universalis	▪ 01/02/2006 ▪ 20/02/2006 ▪ 16/05/2006 ▪ 85 days	▪ 06/06/2006 ▪ 29/06/2006
▪ Human monoclonal antibody against Pseudomonas aeruginosa serotype O11	▪ MDS Pharma Services GB Limited - UK	▪ Treatment of pneumonia caused by serotype O11 Pseudomonas aeruginosa	▪ 03/02/2006 ▪ 20/03/2006 ▪ 16/05/2006 ▪ 57 days	▪ 06/06/2006 ▪ 29/06/2006
▪ Pazopanib hydrochloride	▪ GlaxoSmithKline Research & Development Limited - UK	▪ Treatment of renal cell carcinoma	▪ 02/03/2006 ▪ 20/03/2006 ▪ 16/05/2006 ▪ 57 days	▪ 06/06/2006 ▪ 29/06/2006
▪ Becatecarin	▪ Helsinn Birex Pharmaceuticals Ltd - Ireland	▪ Treatment of cancers of the biliary tree	▪ 31/03/2006 ▪ 18/04/2006 ▪ 15/06/2006 ▪ 58 days	▪ 28/06/2006 ▪ 25/07/2006
▪ Amikacin sulfate (liposomal)	▪ Morgan Lewis & Bockius - UK	▪ Treatment of Pseudomonas aeruginosa lung infection in cystic fibrosis	▪ 31/03/2006 ▪ 18/04/2006 ▪ 15/06/2006 ▪ 58 days	▪ 28/06/2006 ▪ 25/07/2006
▪ Lestaurtinib	▪ Cephalon UK Limited - United Kingdom	▪ Treatment of acute myeloid leukaemia	▪ 29/03/2006 ▪ 18/04/2006 ▪ 15/06/2006 ▪ 58 days	▪ 28/06/2006 ▪ 25/07/2006
▪ 4-[123I] iodo-L-phenylalanine	▪ Dr Andreas Kluge - Germany	▪ Diagnosis of glioma	▪ 03/03/2006 ▪ 20/03/2006 ▪ 15/06/2006 ▪ 87 days	▪ 28/06/2006 ▪ 25/07/2006
▪ 2-(4-(diethylamino) phenyl)-6-methyl-2H-benzo[d][1,2,3] triazol-5-amine	▪ VASTox Plc - UK	▪ Treatment of Duchenne muscular dystrophy	▪ 31/03/2006 ▪ 18/04/2006 ▪ 15/06/2006 ▪ 58 days	▪ 28/06/2006 ▪ 25/07/2006
▪ Human telomerase reverse transcriptase peptide (611-626)	▪ Pharmexa A/S - Denmark	▪ Treatment of pancreatic cancer	▪ 03/04/2006 ▪ 18/04/2006 ▪ 15/06/2006 ▪ 58 days	▪ 28/06/2006 ▪ 25/07/2006
▪ Metastable technetium 99 [99mTc] Demogastrin 2	▪ Biomedica Life Sciences SA - Greece	▪ Diagnosis of medullary thyroid carcinoma	▪ 03/03/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Mecasermin rinfabate	▪ ROP Pharma AB - Sweden	▪ Prevention of retinopathy of prematurity in neonates of less than 32 weeks of gestational age	▪ 22/05/2006 ▪ 12/06/2006 ▪ 24/07/2006 ▪ 42 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Cholest-4-en-3-one, oxime	▪ Trophos SA - France	▪ Treatment of amyotrophic lateral sclerosis	▪ 18/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ N-methyl D-(2,3,4,5,6-pentahydroxy-hexyl)-ammonium; 2-(3,5-dichloro-phenyl)-benzoxazole-6-carboxylate	▪ ICON Clinical Research (UK) Limited - UK	▪ Treatment of familial amyloid polyneuropathy	▪ 24/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ H-Val-Ile-Val-Lys-Leu-Ile-Pro-Ser-Thr-Ser-Ser-Ala-Val-Asp-Thr-Pro-Tyr-Leu-Asp-Ile-Thr-Tyr-His-Phe-Val-Ala-Gln-Arg-Leu-Pro-Leu-OH	▪ Debioclinic SA - France	▪ Treatment of myasthenia gravis	▪ 26/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Human monoclonal antibody against inhibitory killer cell lg-like receptors (1-7 F9)	▪ Novo Nordisk A/S - Denmark	▪ Treatment of acute myeloid leukemia	▪ 28/03/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin	▪ Analytica International GmbH - Germany	▪ Treatment of follicular lymphoma	▪ 26/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Autologous CD34+ cells transduced with retroviral vector containing the human gp91 (phox) gene	▪ Vision 7 GmbH - Germany	▪ Treatment of chronic granulomatous disease	▪ 27/03/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ 4-amino-(6R,S)-5,6,7,8-tetrahydro-L-biopterin dihydrochloride	▪ vasopharm BIOTECH GmbH - Germany	▪ Treatment of moderate and severe traumatic brain injury	▪ 23/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Aviptadil	▪ mondoBIOTECH Laboratories Anstalt - Liechtenstein	▪ Treatment of acute lung injury	▪ 31/03/2006 ▪ 18/04/2006 ▪ 13/07/2006 ▪ 86 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Amphotericin B (for inhalation use)	▪ Nektar Therapeutics UK Ltd - United Kingdom	▪ Prevention of pulmonary fungal infection in patients deemed at risk	▪ 31/03/2006 ▪ 18/04/2006 ▪ 12/07/2006 ▪ 85 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Opebacan	▪ XOMA Ireland Ltd - Ireland	▪ Treatment of meningococcal disease	▪ 16/11/2005 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Cardiotrophin-1	▪ Digna Biotech S.L. - Spain	▪ Prevention of the ischemia/reperfus-ion injury associated with solid organ transplantation	▪ 25/05/2006 ▪ 12/06/2006 ▪ 12/07/2006 ▪ 30 days	▪ 28/07/2006 ▪ 28/08/2006
▪ Genetically modified allogenic (human) tumor cells for the expression of IL-7, GM-CSF, CD80 and CD154, in fixed combination with a DNA-based double stem loop immunomodulato r (dSLIM)	▪ Mologen AG - Germany	▪ Treatment of renal cell carcinoma	▪ 31/03/2006 ▪ 12/06/2006 ▪ 06/09/2006 ▪ 86 days	▪ 25/09/2006 ▪ 23/10/2006
▪ 5-(2,6-Difluoro-phenoxy)-3(R,S)-{2(S)-[2(S)-(3-methoxycarbonyl-2(S)-{3-methyl-2(S)-[(quinoline-2-carbonyl)-amino]-butyrylamino}-propionylamino)-3-methyl-butyrylamino]-propionylamino}-4-oxo-pentanoic acid methyl ester	▪ Theraptosis - France	▪ Treatment of neonatal brain injury	▪ 23/06/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 23/10/2006
▪ Adenoviral vector containing human p53 gene	▪ Gendux Arbiebolag - Sweden	▪ Treatment of Li Fraumeni syndrome	▪ 24/05/2006 ▪ 12/06/2006 ▪ 06/09/2006 ▪ 86 days	▪ 25/09/2006 ▪ 23/10/2006
▪ Arimoclomol	▪ Wainwright Associates Ltd - UK	▪ Treatment of amyotrophic lateral sclerosis	▪ 22/06/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 26/10/2006
▪ Doxorubicin hydrochloride (liposomal)	▪ GP-Pharm S.A. - Spain	▪ Treatment of soft tissue sarcoma	▪ 30/05/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 27/10/2006
▪ Human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use)	▪ Immunservice GmbH - Germany	▪ Treatment of renal cell carcinoma	▪ 22/06/2006 ▪ 10/07/2006 ▪ 04/10/2006 ▪ 86 days	▪ 17/10/2006 ▪ 27/10/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ L-asparaginase encapsulated in erythrocytes	▪ Erytech Pharma S.A. - France	▪ Treatment of acute lymphoblastic leukemia	▪ 23/05/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 27/10/2006
▪ Iodine (^{131}I) anti-tenascin monoclonal antibody 81C6	▪ BCG (Europe) Ltd - United Kingdom	▪ Treatment of glioma	▪ 22/06/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 30/10/2006
▪ Paclitaxel (liposomal)	▪ MediGene AG - Germany	▪ Treatment of pancreatic cancer	▪ 28/07/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 31/10/2006
▪ Recombinant fusion protein consisting of the extracellular portion of CD95 fused to the Fc part of a human IgG1 molecule	▪ Apogenix GmbH - Germany	▪ Prevention of Graft-Versus-Host disease	▪ 23/06/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 31/10/2006
▪ Heparin-binding epidermal growth factor-like growth factor (HB-EGF), amino acids 74-148	▪ Dr Michael Moore - UK	▪ Prevention of necrotizing enterocolitis	▪ 22/06/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 31/10/2006
▪ Human cytomegalovirus immunoglobulin	▪ Biotest Pharma GmbH - Germany	▪ Prevention of congenital cytomegalovirus infection following primary cytomegalovirus infection	▪ 22/06/2006 ▪ 10/07/2006 ▪ 06/09/2006 ▪ 58 days	▪ 25/09/2006 ▪ 31/10/2006
▪ Catumaxomab	▪ Fresenius Biotech GmbH - Germany	▪ Treatment of gastric cancer	▪ 20/06/2006 ▪ 10/07/2006 ▪ 04/10/2006 ▪ 86 days	▪ 17/10/2006 ▪ 03/11/2006
▪ 4,7,10,13,16,19-docosahexaenoic acid	▪ Jose Manuel Cela Lopez - Spain	▪ Treatment of retinitis pigmentosa	▪ 25/07/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 03/11/2006
▪ Budesonide (oral use)	▪ Dr Falk Pharma GmbH - Germany	▪ Treatment of Graft-Versus-Host disease	▪ 22/06/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 03/11/2006
▪ Ciclosporin (implant)	▪ Dr Manfred Zoltobrocki - Germany	▪ Prevention of rejection for corneal transplant	▪ 28/07/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 03/11/2006

▪ **Product INN**	**Sponsor**	**Summary of indication**	**EMEA/COMP** ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Antisense oligonucleotide 5'-d[P-Thio] (CCCTG CTCCC CCCTG GCTCC)-3' (see comments box for cenersen sodium)	▪ CanReg Europe Ltd - Ireland	▪ Treatment of acute myeloid leukemia	▪ 26/06/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 03/11/2006
▪ Temsirolimus	▪ Wyeth Europa Limited - United Kingdom	▪ Treatment of mantle-cell lymphoma	▪ 25/07/2006 ▪ 14/08/2006 ▪ 04/10/2006 ▪ 51 days	▪ 17/10/2006 ▪ 06/11/2006
▪ Paclitaxel (micellar)	▪ Oasmia Pharmaceutical AB - Sweden	▪ Treatment of ovarian cancer	▪ 28/07/2006 ▪ 14/08/2006 ▪ 09/11/2006 ▪ 87 days	▪ 20/11/2006 ▪ 18/12/2006
▪ Forodesine hydrochloride	▪ Napp Pharmaceuticals Research Limited - UK	▪ Treatment of acute lymphoblastic leukaemia	▪ 25/08/2006 ▪ 11/09/2006 ▪ 09/11/2006 ▪ 59 days	▪ 20/11/2006 ▪ 18/12/2006
▪ Tazarotene	▪ Orfagen - France	▪ Treatment of congenital ichthyoses	▪ 25/08/2006 ▪ 11/09/2006 ▪ 16/11/2006 ▪ 66 days	▪ 20/11/2006 ▪ 18/12/2006 ▪
▪ Fenretinide	▪ Cancer Research UK - UK	▪ Treatment of soft tissue sarcomas	▪ 28/09/2006 ▪ 13/10/2006 ▪ 06/12/2006 ▪ 54 days	▪ 29/12/2006 ▪ 30/01/2007
▪ Fenretinide	▪ Cancer Research UK - UK	▪ Treatment of primary malignant bone tumours	▪ 28/09/2006 ▪ 13/10/2006 ▪ 06/12/2006 ▪ 54 days	▪ 21/12/2006 ▪ 26/01/2007
▪ Forodesine hydrochloride	▪ Napp Pharmaceuticals Research Limited - UK	▪ Treatment of cutaneous T-cell lymphoma	▪ 25/08/2006 ▪ 11/09/2006 ▪ 06/12/2006 ▪ 52 days	▪ 21/12/2006 ▪ 29/01/2007
▪ Complement factor H	▪ Laboratoire française du Fractionnement et des Biotechnologies (LFB) - France	▪ Treatment of atypical haemolytic uraemic syndrome (aHUS) associated with an inherited abnormality of the complement system	▪ 26/09/2006 ▪ 13/10/2006 ▪ 06/12/2006 ▪ 54 days	▪ 21/12/2006 ▪ 26/01/2007
▪ Thiotepa	▪ Adienne S.r.l - Italy	▪ Conditioning treatment prior to haematopoietic progenitor cell transplantation	▪ 27/07/2006 ▪ 11/09/2006 ▪ 06/12/2006 ▪ 52 days	▪ 21/12/2006 ▪ 29/01/2007
▪ Recombinant modified vaccinia Ankara expressing human 5T4	▪ Oxford Biomedica (UK) Ltd - UK	▪ Treatment renal cell carcinoma	▪ 28/09/2006 ▪ 13/10/2006 ▪ 06/12/2006 ▪ 54 days	▪ 21/12/2006 ▪ 26/01/2007

Negative COMP designation opinions

Product INN	Sponsor	Summary of indication	EMEA/COMP ▪ Submission ▪ Start date ▪ Opinion ▪ Active time	European Commission ▪ Opinion received ▪ Date of decision
▪ Tramadol hydrochloride	▪ TheraQuest Ltd - United Kingdom	▪ Treatment of painful HIV-associated neuropathy	▪ 19/12/2005 ▪ 09/01/2006 ▪ 05/04/2006 ▪ 86 days	▪ 10/08/2006 ▪ 21/09/2006
▪ Capsaicin	▪ TheraQuest Ltd - United Kingdom	▪ Treatment of painful HIV-associated neuropathy	▪ 19/12/2005 ▪ 09/01/2006 ▪ 05/04/2006 ▪ 86 days	▪ 10/08/2006 ▪ 21/09/2006

Annex 12A HMPC Community herbal monographs

Reference number	Document title	Status
EMEA/HMPC/340719/2005	Community herbal monograph on Valerianae radix (valerian root)	Adopted in July 2006
EMEA/HMPC/340849/2005	Community herbal monograph on Lini semen (linseed)	Adopted in July 2006
EMEA/HMPC/340857/2005	Community herbal monograph on Plantaginis ovatae seminis tegumentum (ispaghula husk)	Adopted in July 2006
EMEA/HMPC/340861/2005	Community herbal monograph on Plantaginis ovatae semen (ispaghula seed)	Adopted in July 2006
EMEA/HMPC/340865/2005	Community herbal monograph on Psyllii semen (psyllium seed)	Adopted in July 2006
EMEA/HMPC/51871/2006	Community herbal monograph on Sennae fructus (senna pods)	Adopted in September 2006
EMEA/HMPC/51869/2006	Community herbal monograph on Sennae folium (senna leaf)	Adopted in September 2006
EMEA/HMPC/76307/2006	Community herbal monograph on Frangulae cortex (frangula bark)	Adopted in September 2006
EMEA/HMPC/76310/2006	Community herbal monograph on Aloe (barbados aloes; cape aloes)	Adopted in September 2006
EMEA/HMPC/137423/2006	Community herbal monograph on Anisi fructus (aniseed)	Draft released for public consultation in September 2006
EMEA/HMPC/263273/2006	Community herbal monograph on Anisi aetheroleum (anise oil)	Draft released for public consultation in September 2006
EMEA/HMPC/137428/2006	Community herbal monograph on Foeniculi amari fructus (bitter-fennel fruit)	Draft released for public consultation in October 2006
EMEA/HMPC/263293/2006	Community herbal monograph on Foeniculi dulcis fructus (sweet-fennel fruit)	Draft released for public consultation in October 2006
EMEA/HMPC/263292/2006	Community herbal monograph on Foeniculi amari fructus aetheroleum (bitter-fennel fruit oil)	Draft released for public consultation in October 2006

Annex 12B Entry to 'List of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products'

Reference number	Document title	Status
EMEA/HMPC/428817/2006	Community list entry on Foeniculi amari fructus (bitter-fennel fruit)	Draft released for public consultation in October 2006
EMEA/HMPC/428963/2006	Community list entry on Foeniculi dulcis fructus (sweet-fennel fruit)	Draft released for public consultation in October 2006

Annex 13 Guidelines and working documents in 2006

Committee for Medicinal Products fro Human Use (CHMP)

Working Party/Group	Total number of adopted guidelines/ documents for which working party/group is responsible	Number of concept papers/ guidelines/ documents initiated in 2006	Number of concept papers/ guidelines/ documents in progress during 2006	Number of guidelines/ documents adopted in 2006
CHMP Biologics Working Party	57	4	38	6
CHMP Blood Products Working Party	26	3	7	2
CHMP Efficacy Working Party	227	14	42	21
CHMP Gene Therapy Working Party	6	4	6	3
CHMP Paediatrics Working Party	19	10	8	9
CHMP Pharmacogenetics Working Party	10	4	6	6
CHMP Pharmacovigilance Working Party	23	2	0	15
CHMP Safety Working Party	30	1	12	8
CHMP Similar Biological (Biosimilar) Medicinal Products Working Party	19	8	14	12
CHMP Vaccine Working Party	8	3	3	3
CHMP Working Party on Cell-based Products	1	0	1	1
EMEA Human Scientific Committees Working Party with Patients and Consumers' Organisations (replaced the POWG)	4	3	1	2
CHMP Working Group with Health-Care Professionals' Organisations	Not applicable. Working Group convened for the first time in November 2006.			
CHMP Invented Name Review Group	1	0	1	0
Joint CHMP/CVMP Quality Working Party	77	4	11	19

Working Party/Group	Subject of concept papers/guidelines/documents of significant scientific/therapeutic interest	
	Initiated	**Adopted**
CHMP Biologics Working Party	Plasma derived medicinal products (Concept paper for revision of guideline) Cell-based medicinal products (Quality part of guideline) Quality aspects of gene therapy medicinal products (Concept paper on development of technical guidance) Process analytical technology in manufacture of biological active substances (Guidance development)	Quality aspects of similar biological medicinal products containing biotechnology derived proteins as active substance (Guideline) Scientific requirements for plasma master file (PMF) (Revised guideline) Validation of immunoassays for detection of Hepatitis-B surface antigen (HBsAg) and antibody to human immunodeficiency virus (anti-HIV) in plasma pools (Guidelines) Environmental risk assessments for medicinal products containing, or consisting of, genetically modified organisms (GMOs) (Guidance)
CHMP Blood Products Working Party	Factor VIII inhibitors (International expert workshop report) Intravenous immunoglobulin (Expert workshop report)	
CHMP Efficacy Working Party		Postmenopausal osteoporosis in women (Revised guideline) Clinical Trials in Small Populations (Guideline) Clinical investigation of medicinal products for the treatment of multiple sclerosis (Revised guideline)
CHMP Gene Therapy Working Party	Clinical monitoring and follow up of patients exposed to gene therapy/gene transfer medicinal products (Concept paper) Gene transfer vaccines (Concept paper) Medicinal products containing genetically-modified cells (Concept paper)	Guideline on non-clinical testing for inadvertent germline transmission of gene transfer vectors ICH Considerations: General Principles to Address the Risk of Inadvertent Germline Integration of Gene Therapy Vectors
CHMP Paediatrics Working Party	Investigating medicinal products intended for neonatal use (Guideline)	Off-patent medicinal products for paediatric studies (Priority list) Formulations of choice for the paediatric population (Reflection paper)
CHMP Pharmacogenetics Working Party	Pharmacogenomic biomarkers validation process	Use of pharmacogenetics in the pharmacokinetic evaluation of medicinal products (Reflection paper) Pharmacogenetics briefing

Working Party/Group	Subject of concept papers/guidelines/documents of significant scientific/therapeutic interest	
	Initiated	**Adopted**
		meetings (Guideline) Joint FDA/EMEA VGDS general principle document
CHMP Pharmacovigilance Working Party	Pharmacovigilance (i.e. safety surveillance) for vaccines (Guideline) Crisis Managament Plan for medicinal products authorised through national procedures	Major revision of EudraLex Volume 9 (now EudraLex Volume 9A) on pharmacovigilance (i.e. safety surveillance) for human medicinal products Procedures for the communication of safety information to healthcare professionals (New guideline in Volume 9A) Pharmacovigilance for medicines used in children (Guideline)
CHMP Safety Working Party	Non-clinical requirements to support early phase I clinical trials with pharmaceutical compounds (Concept paper)	
CHMP Similar Biological (Biosimilar) Medicinal Products Working Party	Immunological assessment of therapeutic proteins (Guideline)	Similar biological medicinal products: non-clinical and clinical issues (Guideline) Immunological assessment of therapeutic proteins (Guideline) Comparability after changes in the manufacturing procedure: non-clinical and clinical issues (Guideline)
CHMP Vaccine Working Party	Co-administration of vaccines (Conclusions from 2006 Workshop)	Clinical evaluation of new vaccines (Guideline and Annex – SPC requirements) Influenza vaccines prepared from viruses with a potential to cause a pandemic and intended for use outside of the core dossier context (Guideline) Explanatory note on immunomodulators (For guideline on adjuvants in vaccines for human use)
CHMP Working Party on Cell-based Products		Cell-based medicinal products (Guideline)
EMEA Human Scientific Committees Working Party with Patients and Consumers' Organisations (having replaced the POWG)	Completion of declaration of interest, confidentiality undertaking and expert nomination form for patients and consumers involved in committees' activities (Guidance) Procedure for review of information on products by patients'/ consumers' organisations	EMEA Performance Indicators for the Interaction with Patients' and Consumers' Organisations

Working Party/Group	Subject of concept papers/guidelines/documents of significant scientific/therapeutic interest	
	Initiated	**Adopted**
CHMP Working Group with Health-Care Professionals' Organisations	N/A	N/A
CHMP Invented Name Review Group	N/A	N/A
Joint CHMP/CVMP Quality Working Party	Use of near infrared spectroscopy (Revision of guideline) Radiopharmaceuticals (Revision of guideline) Quality of combination herbal medicinal products (Guideline)	Quality of investigational medicinal products (CHMP guideline) Quality of inhalation and nasal products (CHMP guideline) Quality data for veterinary medicinal products intended for minor species minor use (MUMS) (CVMP guideline) Quality of herbal medicinal product/traditional herbal medicinal product (CPMP guideline)

Committee for Medicinal Products for Veterinary Use (CVMP)

CVMP Efficacy Working Party

Reference number	Document title	Status
EMEA/CVMP/EWP/170208/2005-CONSULTATION	Guideline on the SPC for anthelmintics	Adopted for consultation June 2006 (end of consultation Decenber 2006)
EMEA/CVMP/EWP/117899/2004	Guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species	Adopted July 2006 for implementation by February 2007
EMEA/CVMP/EWP/005//00-CONSULTATION	Guideline on "Testing and evaluation of the efficacy of antiparasitic substances for the treatment of tick and flea infestations in dogs and cats"(	Adopted for consultation October 2006 (end of consultation February 2007)
EMEA/CVMP/EWP/295306/2006-CONSULTATION	Concept paper for a revision of the Guideline for the conduct of Bioequivalence studies for veterinary medicinal products	Adopted for consultation December 2006 (end of consultation March 2007)
EMEA/CVMP/83804/2005	Guideline on pharmaceutical fixed combination products	Adopted December 2006 for implementation by July 2007

CVMP Environmental Risk Assessment (ERA) Working Party

Reference number	Document title	Status
EMEA/CVMP/ERA/418282/2005-CONSULTATION	Guideline on environmental impact assessment for veterinary medicinal products – In support of the VICH Guidelines GL6 and GL38	Adopted for consultation January 2006 (end of consultation 31 July 2006)

CVMP Immunologicals Working Party

Reference number	Document title	Status
EMEA/CVMP/IWP/46853/2006	Reflection paper: minimum data requirements for an authorisation under exceptional circumstances for vaccines for emergency use in birds against H5 and/or H7 highly pathogenic avian influenza virus	Adopted February 2006
EMEA/CVMP/IWP/54533/2006-CONSULTATION	User Safety for Immunological Veterinary Medicinal Products	Adopted for consultation March 2006 (end of consultation September 2006
EMEA/CVMP/123846/2006-CONSULTATION	Concurrent administration of immunological veterinary medicinal products (IVMPs) in view of determining day X to be 14 days and consequent revision of the summary of product characteristics (SPC) guideline for immunologicals	Adopted for consultation April 2006 (end of consultation July 2006
EMEA/CVMP/86063/2006-CONSULTATION	Requirements for Vaccines for Use in Birds Against Avian Influenza Virus	Adopted for consultation April 2006 (end of consultation May 2006)
EMEA/CVMP/168467/2006	Public Statement (Need for sterility testing at the end of the proposed shelf-life for Immunological Veterinary Medicinal Products)	Adopted May 2006
EMEA/CVMP/IWP/222624/2006-CONSULTATION	Guideline on requirements for an authorisation under exceptional circumstances for vaccines for use in birds against avian influenza	Adopted for consultation July 2006 (end of consultation September 2006)
EMEA/CVMP/IWP/205712/2006-CONSULTATION	New master seeds to replace established master seeds already used in authorised immunological veterinary medicinal products (IVMPs)	Adopted for consultation July 2006 (end of consultation October 2006)
EMEA/CVMP/IWP/219089/2006-CONSULTATION	Data requirements to support in-use stability claims for IVMPs	Adopted for consultation July 2006 (end of consultation October 2006)
EMEA/CVMP/IWP/123243/2006-CONSULTATION	Guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species	Adopted for consultation July 2006 (end of consultation January 2007)

CVMP Pharmacovigilance Working Party (PhVWP-V)

Reference number	Document title	Status
EMEA/CVMP/68614/2006-CONSULTATION	Concept paper (for a guideline on use of data in EudraVigilance veterinary)	Adopted for consultation June 2006 (end of consultation October 2006
EMEA/CVMP/PhVWP/110607/2005	Simple guide to veterinary pharmacovigilance in the EU	Adopted June 2006

Joint CHMP/CVMP Quality Working Party

Reference number	Document title	Status
EMEA/CVMP/814/00-Rev.1	Guideline on Quality of Herbal Medicinal Products/Traditional Herbal Medicinal Products	Adopted March 2006
EMEA/CVMP/815/00-Rev.1	Guideline on Specifications: Test Procedures and Acceptance Criteria for Herbal Substances, Herbal Preparations and Herbal Medicinal Products/Traditional Herbal Medicinal Products	Adopted March 2006
EMEA/CVMP/QWP/339588/2005-CONSULTATION	Guideline on Parametric Release	Adopted October 2006
EMEA/CVMP/QWP/134/02-Rev.2-CONSULTATION	Active Substance Master File (revision)	Adopted for consultation April 2006 (end of consultation August 2006)
EMEA/HMPC/287539/2005-CONSULTATION	Guideline on the declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products in the SPC	Adopted for consultation May 2006 (end of consultation November 2006)
EMEA/HMPC/58222/2006-CONSULTATION	Concept paper (for the development of a guideline on the quality of combination herbal medicinal products/traditional herbal medicinal products)	Adopted for consultation May 2006 (end of consultation August 2006)
EMEA/CHMP/QWP/173698/2006-CONSULTATION	Guideline on the use of near-infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations	Adopted for consultation May 2006 (end of consultation August 2006)
EMEA/CVMP/QWP/128710/2004	Guideline on the quality data requirements for veterinary medicinal products intended for minor uses or minor species	Adopted July 2006 for implementation by February 2007
EMEA/CVMP/QWP/434665/2006-CONSULTATION	Concept paper for the development of a Guideline on the quality aspects of single-dose veterinary spot-on product	Adopted for consultation December 2006 (end of consultation March 2007)

CVMP Safety Working Party

Reference number	Document title	Status
EMEA/CVMP/66781/2005	Guideline on safety and residue data requirements for veterinary medicinal products intended for minor uses or minor species	Adopted July 2006 for implementation by February 2007
EMEA/CVMP/VICH/393388/2006-CONSULTATION	Guideline on Target Animal Safety for Pharmaceuticals at step 4 of the VICH procedure	Adopted November 2006 (end of consultation May 2007)

CVMP Scientific Advisory Group on Antimicrobials

Reference number	Document title	Status
EMEA/CVMP/SAGAM/184651/2005-CONSULTATION	Reflection paper on the use of fluoroquinolones in food-producing animals in the European Union: development of resistance and impact on human and animal health	Released for consultation January 2006 (end of consultation May 2006)

CVMP General

Reference number	Document title	Status
EMEA/CVMP/32995/2006-Rev.1	Guideline on the procedure for accelerated assessment pursuant to Article 39 (8) of Regulation (EC) No 726/2004	Adopted Mai 2006
EMEA/CVMP/064/05	Guidelines on the Summary of Product Characteristics for pharmaceutical veterinary medicinal products	Adopted April 2006
EMEA/CVMP/065/05	Guidelines on the Summary of Product Characteristics for pharmaceutical veterinary medicinal products	Adopted April 2006
EMEA/CVMP/120559/2006-CONSULTATION	Questions and answers document regarding application of the so-called ‘sunset clause’ to centrally authorised veterinary medicinal products	Adopted for consultation December 2006 (end of consultation March 2007)
EMEA/CVMP/482393/2006-CONSULTATION	Guideline on procedures for re-examination of CVMP opinions	Adopted for consultation December 2006 (end of consultation February 2007)
EMEA/CVMP/425558/2006-CONSULTATION	Reflection paper Withdrawals of marketing authorisation applications in the centralised procedure	Adopted for consultation December 2006 (end of consultation February 2007)

EMEA/CVMP/459912/2006-CONSULTATION	Reflection paper Refusals of marketing authorisation applications in the centralised procedure	Adopted for consultation December 2006 (end of consultation February 2007)

Committee for Orphan Medicinal Products (COMP)

Scientific Committee	Total number of adopted guidelines/ documents for which committee is responsible	Number of concept papers/ guidelines/ documents initiated in 2006	Number of concept papers/ guidelines/ documents in progress during 2006	Number of guidelines/ documents adopted in 2006
Committee for Orphan Medicinal Products	5	1	1	1

Scientific Committee	Subject of concept papers/guidelines/documents of significant scientific/therapeutic interest	
	Initiated	Adopted
Committee for Orphan Medicinal Products		Five-year review of sufficient profitability of orphan medicines (Commission Guideline)

Committee on Herbal Medicinal Products (HMPC) *[*]

Reference number	Document title	Status
EMEA/HMPC/166326/2005	Guideline on the clinical assessment of fixed combinations of herbal substances/herbal preparations'	Adopted in January 2006
EMEA/HMPC/138139/2005	Public statement on the allergenic potency of herbal medicinal products containing soya or peanut protein	Adopted in January 2006
EMEA/HMPC/138309/2005	Public statement on Chamomilla containing herbal medicinal products	Adopted in March 2006
EMEA/HMPC/32116/2005	Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed	Draft released for consultation in January 2006 Adopted in July 2006

[*] Including documents prepared by the former HMPC Safety & Efficacy Drafting Group replaced by the HMPC Working Party on Community monographs and Community list (MLWP)

Reference number	Document title	Status
	applications) and in applications for simplified registration	
EMEA/269259/2006	Public statement on herbal medicinal products containing Cimicifugae racemosae rhizoma (black cohosh, root)	Adopted in July 2006
EMEA/HMPC/104613/2005	Guideline on the assessment of clinical safety and efficacy in the preparation of Community herbal monographs for well-established and of Community herbal monographs/entries to the Community list for traditional herbal medicinal products/substances/preparations	Draft released for consultation in May 2006 Adopted in September 2006
EMEA/HMPC/413271/2006	Concept paper on the development of a guideline on the assessment of genotoxic constituents in herbal substances/preparations	Draft released for consultation in October 2006

HMPC Quality Drafting Group

Reference number	Document title	Status
EMEA/HMPC/246816/2005	Guideline on good agricultural and collection practice for starting materials of herbal origin	Adopted in January 2006
	Contribution to the revision of the Annex 7 to GMP guide - Manufacture of Herbal Medicinal Products (published in March 2006 by the European Commission)	January 2006
CPMP/QWP/2819/00 Rev.1 and EMEA/CVMP/814/00 Rev.1	Guideline on quality of herbal medicinal products/traditional herbal medicinal products	Adopted in March 2006
CPMP/QWP2820/00 Rev.1 and EMEA/CVMP/815/00 Rev.1	Guideline on specifications: test procedures and acceptance criteria for herbal substances, and herbal medicinal products/traditional herbal medicinal products	Adopted in March 2006
EMEA/HMPC/151144/2006	Overview of Questions and Answers relating to technical/scientific issues	Adopted in May 2006
EMEA/HMPC/CHMP/CVMP/ 287539/2005	Guideline on the declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products in the SPC	Draft released for public consultation in June 2006

Reference number	Document title	Status
EMEA/HMPC/CHMP/CVMP/ 5822/2006	Concept paper on quality of combination herbal medicinal products/traditional herbal medicinal products	Draft released for public consultation in June 2006
EMEA/HMPC/125562/2006	Reflection paper on the use of fumigants	Draft released for public consultation in July 2006

HMPC Organisational Matters Drafting Group

Reference number	Document title	Status
EMEA/HMPC/261344/2005	Concept paper on CTD for traditional herbal medicinal products	Adopted in March 2006
EMEA/HMPC/31897/2006	Public statement on the interpretation of the term "external use" for use in the field of traditional herbal medicinal products	Adopted in May 2006
EMEA/HMPC/418902/2005	Assessment report template for the development of Community monographs and for inclusion of herbal substance(s), preparation(s) or combinations thereof in the list	Draft released for consultation in May 2006
EMEA/HMPC/182320/2005 Rev.1	Procedure for the preparation of Community monographs for herbal medicinal products with well-established medicinal use	Revision adopted in July 2006
EMEA/HMPC/182352/2005 Rev.1	Procedure for the preparation of Community monographs for traditional herbal medicinal products	Revision adopted in July 2006
EMEA/HMPC/107436/2005 Rev.2	Template for a Community herbal monograph	Revision adopted in July 2006
EMEA/HMPC/100824/2005 Rev.1	Structure of the list of herbal substances, preparations and combinations thereof	Revision adopted in July 2006
EMEA/HMPC/431129/2005	Guidance on documentation to be provided by Member States and applicants/MAHs in support of a simplified registration referral under Articles 16c(1)(c) and 16c(4)	Draft released for public consultation in March 2006 Adopted in September 2006
EMEA/HMPC/1004/2006	Procedure for calls for scientific data for use in HMPC assessment work	Draft released for public consultation in May 2006 Adopted in October 2006

Annex 14 Arbitration and Community referrals overview 2006

Referrals made to the CHMP

Procedures started

Type of referral	Date of CHMP start of procedure	International non-proprietary name (INN)
Article 29(4) of Directive 2001/83/EC	23/03/2006	doxazosin
Article 29(4) of Directive 2001/83/EC	27/04/2006	alendronic acid, glucosamine HCl
Article 29(4) of Directive 2001/83/EC	01/06/2006	doxazosin, ciprofloxacin, felodipine/metoprolol tartrate
Article 29(4) of Directive 2001/83/EC	29/06/2006	ciprofloxacin hydrogen sulphate
Article 29(4) of Directive 2001/83/EC	27/07/2006	ciprofloxacin lactate, alendronate
Article 29(4) of Directive 2001/83/EC	18/10/2006	alteplase, fexofenadine hydrochloride
Article 29(4) of Directive 2001/83/EC	14/12/2006	lansoprazole
Article 30 of Directive 2001/83/EC	02/06/2006	lornoxicam
Article 31 of Directive 2001/83/EC	27/07/2006	bicilutamide
Article 31(2) Of Commission Regulation (EC) N. 1084/2003	21/09/2006	piroxicam, veralipride
Article 36 of Directive 2001/83/EC	27/04/2006	cetirizine dihydrochloride
Article 36 of Directive 2001/83/EC	01/06/2006	gadobutrolum
Article 36 of Directive 2001/83/EC	21/09/2006	simvastatin

Procedures finalised

Type of referral	Date of CHMP opinion	International non-proprietary name (INN)
Article 6(12) Of Commission Regulation (EC) N. 1084/2003	March 2006	atorvastatin
Article 6(12) Of Commission Regulation (EC) N. 1084/2003	May 2006	fluoxetine
Article 6(13) Of Commission Regulation (EC) N. 1084/2003	April 2006	salmeterol/fluticasone proprionate
ARTICLE 29(2) OF DIRECTIVE 2001/83/EC	January 2006	nifedipine
Article 29(2) of Directive 2001/83/EC	May 2006	ceftriaxone
Article 29(4) of Directive 2001/83/EC	June 2006	doxazosin
Article 29(4) of Directive 2001/83/EC	September 2006	glucosamine HCl
Article 29(4) of Directive	October 2006	alendronate sodium

Type of referral	Date of CHMP opinion	International non-proprietary name (INN)
2001/83/EC		trihydricum
Article 29(4) of Directive 2001/83/EC	November 2006	ciprofloxacin, ciprofloxacin hydrogen sulphate
Article 29(4) of Directive 2001/83/EC	December 2006	felodipine/metoprolol tartrate
Article 30 of Directive 2001/83/EC	January 2006	tacrolimus
Article 30 of Directive 2001/83/EC	April 2006	live yellow fever vaccine
Article 30 of Directive 2001/83/EC	May 2006	gabapentin
Article 30 of Directive 2001/83/EC	September 2006	lansoprazole
Article 31 of Directive 2001/83/EC	March 2006	pimecrolimus
Article 36 of Directive 2001/83/EC	May 2006	cetirizine dihydrochloride
Article 36 of Directive 2001/83/EC	October 2006	simvastatin
Article 36 of Directive 2001/83/EC	December 2006	gadobutrolum
Article 20 of Council Regulation (EC) No 726/2004	March 2006	tacrolimus
Article 20 of Council Regulation (EC) No 726/2004	April 2006	hepatitis B (recombinant) vaccine, haemophilus b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccine, perflutren

Referrals made to the CVMP

Procedures started

Type of referral	Date of CVMP opinion	International non-proprietary name (INN)
Article 33(4) of Directive 2001/82/EC	17.05.2006	Ivermectin (Equimectin 12mg/g)
Article 33(4) of Directive 2001/82/EC	21.06.06	Doxycycline base as hyclate (Doxyprex 100 mg/g)
Article 33(4) of Directive 2001/82/EC	08.11.2006	Inactivated antigen of cytopathic BVD virus strain C-86 (Bovilis BVD)
Article 33(4) of Directive 2001/82/EC	13.12.2006	Ephedrine hydrochloride (Enurace 50, 50 mg)
Article 34(1) of Directive 2001/82/EC	12.09.2006	Trimethoprim and sulfamethoxazole (Methoxasol-T)
Article 40 of Directive 2001/82/EC	19.07.06	Inactivated porcine parvovirus, strain S-80, Inactivated Erysipelothrix rhusiopathiae, strain B-7 (serotype 2)) –

Type of referral	Date of CVMP opinion	International non-proprietary name (INN)
		(Suvaxyn Parvo/E)
Article 40 of Directive 2001/82/EC	19.07.06	Inactivated Erysipelothrix rhusiopathiae, strain B-7 (serotype 2) – (Suvaxyn Ery)

Procedures finalised

Article 33(4) of Directive 2001/82/EC	17.05.2006	Cefquinome (Cobactan IV 4.5%)
Article 33(4) of Directive 2001/82/EC	09.11.2006	Ketoprofen (Dolovet / Rifen)
Article 6(13) of Regulation (EC) no 1084/2003	20.07.2006	Cefquinome (Cobactan DC and associated names)

Annex 15 EMEA contact points

Pharmacovigilance and product defect reporting

The constant monitoring of the safety of medicines after authorisation ('pharmacovigilance') is an important part of the work of the national competent authorities and the EMEA. The EMEA receives safety reports from within the EU and outside concerning centrally authorised medicinal products and coordinates action relating to the safety and quality of medicinal products.

For matters relating to pharmacovigilance for medicinal products for human use:	Panos TSINTIS Direct telephone: (44-20) 75 23 71 08 E-mail: panos.tsintis@emea.europa.eu
For matters relating to pharmacovigilance for medicinal products for veterinary use:	Barbara FREISCHEM Direct telephone: (44-20) 74 18 85 81 E-mail: barbara.freischem@emea.europa.eu
For product defect and other quality-related matters:	E-mail: qualitydefects@emea.europa.eu Fax: (44-20) 74 18 85 90 Out of hours telephone: (44-7880) 55 06 97

Certificates of a medicinal product

The EMEA issues certificates of a medicinal product in conformity with the arrangements laid down by the World Health Organization. These certify the marketing authorisation and good manufacturing status of medicinal products in the EU and are intended for use in support of marketing authorisation applications in and export to non-EU countries.

For enquiries concerning certificates for centrally authorised medicines for human or veterinary use:	E-mail: certificate@emea.europa.eu Fax: (44-20) 74 18 85 95

EMEA PMF/VAMF certificates

The EMEA issues plasma master file (PMF) and vaccine antigen master file (VAMF) certificates of a medicinal product in conformity with the arrangements laid down by Community legislation. The EMEA PMF/VAMF certification process is an assessment of the PMF/VAMF application dossier. The certificate of compliance is valid throughout the European Community.

For enquiries concerning PMF certificates:	Silvia DOMINGO Direct telephone: (44-20) 74 18 85 52 Fax: (44-20) 74 18 85 45 E-mail: silvia.domingo@emea.europa.eu
For enquiries concerning VAMF certificates:	Ragini SHIVJI Direct telephone: (44-20) 75 23 71 47 Fax: (44-20) 74 18 85 45 E-mail: ragini.shivji@emea.europa.eu

Documentation services

A wide range of documents has now been published by the EMEA, including press releases, general information documents, annual reports and work programmes.

These and other documents are available:

- on the Internet at: www.emea.europa.eu
- by e-mail request to: info@emea.europa.eu
- by fax to: (44-20) 74 18 86 70
- by writing to:

  EMEA Documentation service

  European Medicines Agency

  7 Westferry Circus

  Canary Wharf

  UK – London E14 4HB

European experts list

Approximately 3 500 European experts are used by the EMEA in its scientific evaluation work. The list of these experts is available for examination on request at the EMEA offices.

Requests should be sent in writing to the EMEA or by e-mail to: europeanexperts@emea.europa.eu

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