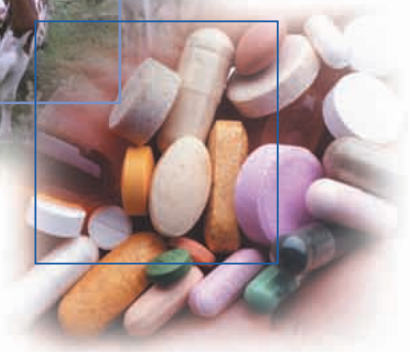
The European Agency for the Evaluation of Medicinal Products

Ninth Annual Report
2003

Presented to the Management Board on 11 March 2004



The annual report for 2003 is presented to the Management Board by the Executive Director in accordance with Article 55(3) of Council Regulation (EEC) No 2309/93. It is forwarded to the European Parliament, Council, Commission and Member States. It is available in all official EU languages.

Previous annual reports and other reference documents are available from the EMEA web site **www.emea.eu.int**

This report covers activities of the EMEA in 2003. 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 and Article 42(1) of Council Directive 2001/82/EC.

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A great deal of additional information on the European Union is available on the Internet. It can be accessed through the Europa server (http://europa.eu.int)

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EMEA mission statement

EMEA mission statement

To contribute to the protection and promotion of public and animal health by:

- Mobilising scientific resources from throughout the European Union to provide high quality evaluation of medicinal products, to advise on research and development programmes and to provide useful and clear information to users and health professionals
- Developing efficient and transparent procedures to allow timely access by users to innovative 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

The European system offers two routes for authorisation of medicinal products. The EMEA plays a role in both procedures:

- The centralised procedure is compulsory for medicinal products derived from biotechnology and available at the request of companies for other innovative new products. 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 applying to the whole European Union
- The decentralised procedure (or mutual recognition procedure) applies to the majority of conventional medicinal products and is based upon the principle of mutual recognition of national authorisations. It 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.

Foreword by the Chairman of the Management Board
Philippe Duneton

This ninth annual report gives a detailed and precise account of the work and efforts devoted by the Agency to achieve the goals of the 2003 work programme.

The primary objective achieved by the Agency was to guarantee a high level evaluation and control of the safety, quality and efficacy of medicines for human and veterinary use in Europe. It also took up other challenges and in particular prepared for the enlargement of the European Union with the ten new Member States, contributed in an active way to the review of pharmaceutical regulation, continued to further improve its operation and that of its scientific committees, and developed the corresponding information systems. The Agency also reinforced the close links established with the national competent authorities, an essential condition in achieving our mission of public health.

This report shows the great diversity of the work undertaken by the EMEA within its three scientific committees, working groups and ad hoc groups, in fields as varied as paediatric drugs, gene therapy, pharmacogenomics, pandemic influenza vaccine, and herbal medicinal products. This reflects the actions engaged by the Agency to support the delivery of scientific opinions and consideration of pharmacovigilance aspects in the early stages of the development of new pharmaceutical products.

Actions taken in 2003 by the EMEA and heads of the national agencies in regard to pharmacovigilance are an example of our capacity to join forces in pursuing the same objective of public health. This work constitutes remarkable progress in the setting up of a European risk management strategy aimed at reinforcing the safety of all pharmaceutical products being put on the European market, whether or not through the centralised procedure. In the same way, the work carried out in the field of pharmacovigilance for veterinary medicinal products allowed implementation of several specific actions to consolidate progress already made.

The Management Board examined with satisfaction the report on the first three years of operation of the European policy on orphan drugs. It encouraged work on veterinary medicinal products and resistance to antibiotics, and it adopted proposals in favour of the development of scientific opinions on veterinary medicinal products for minor use and minor species.

The Board also supported the good corporate governance conducted in 2003 that aimed at reinforcing the quality and safety of work carried out by the Agency, particularly the first external audit of the Committee for Proprietary Medicinal Products, creation of a new internal audit structure and new measures in support of the Agency's policy on transparency.

The EMEA took an active part in the final phase of the PERF III programme, and invited the national authorities of accession countries to participate in the work of the scientific committees, working groups and Management Board as observers in order to familiarise themselves with European procedures. These preparatory actions for the enlargement of the Community have ensured that our system remains as effective and reactive as possible.

I wish to underline once again the quality of the commitment and competence of the EMEA staff, under the authority of the Executive Director, as well as that of the members and experts of the scientific committees, and the network of competent authorities. Finally, I wish to thank the colleagues of the Management Board for their advice and their judicious and constructive remarks that enable us to contribute efficiently to the development of the EMEA and of our system for evaluating the safety, quality and efficacy of pharmaceuticals in Europe.

Introduction by the Executive Director
Thomas Lönngren

My introduction to the work programme for 2003 emphasised that the year would be a mix of challenges resulting from preparations for the '2001 review' and EU enlargement, managing a changing workload, while at the same time trying to fulfil new public health tasks. This annual report shows that the Agency met these challenges and did so with success contributing both to public and animal health and also to the competitiveness of the European pharmaceutical industry. It is important to recognise that such achievements are the result of combined efforts of the Agency's staff, the European experts and the national competent authorities.

The EMEA and European Commission have both been concerned to identify the underlying reasons for the shortfall of applications from the pharmaceutical industry in 2002. I invited senior industry representatives to the Agency in June 2003 to explore the factors behind the shortfall. The EMEA also undertook benchmarking exercises with EU and international authorities and concluded that the shortfall is a global issue for which the regulators are not primarily responsible. Instead we found a number of sectorial, commercial and other factors were the main contributors to the shortfall. We did however have a critical look at our own processes and an audit of the CPMP was performed in 2003 with an action plan of improvements.

One of the major contributions that the EMEA can make to help the development of new medicines is the provision of scientific advice in the R&D process. This was one of my priorities for 2003. More and more companies are realising the benefit of coming to the EMEA for scientific advice during their development of new medicines. An analysis of scientific advice over the past years has shown that companies that come for advice have both a higher success rate and a faster review time when they come to apply for marketing authorisation.

The Agency made progress in its part of the European risk management strategy for medicines. One of the most important elements in this strategy is the early involvement of pharmacovigilance experts in the assessment of new medicines – this is part of the EMEA move towards to a more life-cycle approach to the supervision of medicines.

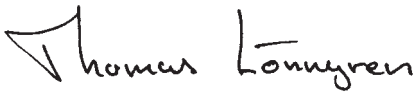
In terms of the public health outcome, the Agency's scientific committees dealt with a number of important new medicines, particularly in the field of HIV/AIDS, cancer, diabetes, Alzheimer's disease, rare and severe cardiovascular, pulmonary and congenital conditions. The CPMP adopted 24 positive opinions, of which 7 were for orphan medicines for rare diseases and conditions, with an average review and processing time of some 8 months.

Activities in the veterinary field were marked in particular by a strong number of applications for new medicines. We also made good progress in our initiatives on pharmacovigilance for veterinary medicines and on improving availability of medicines for minor uses and minor species.

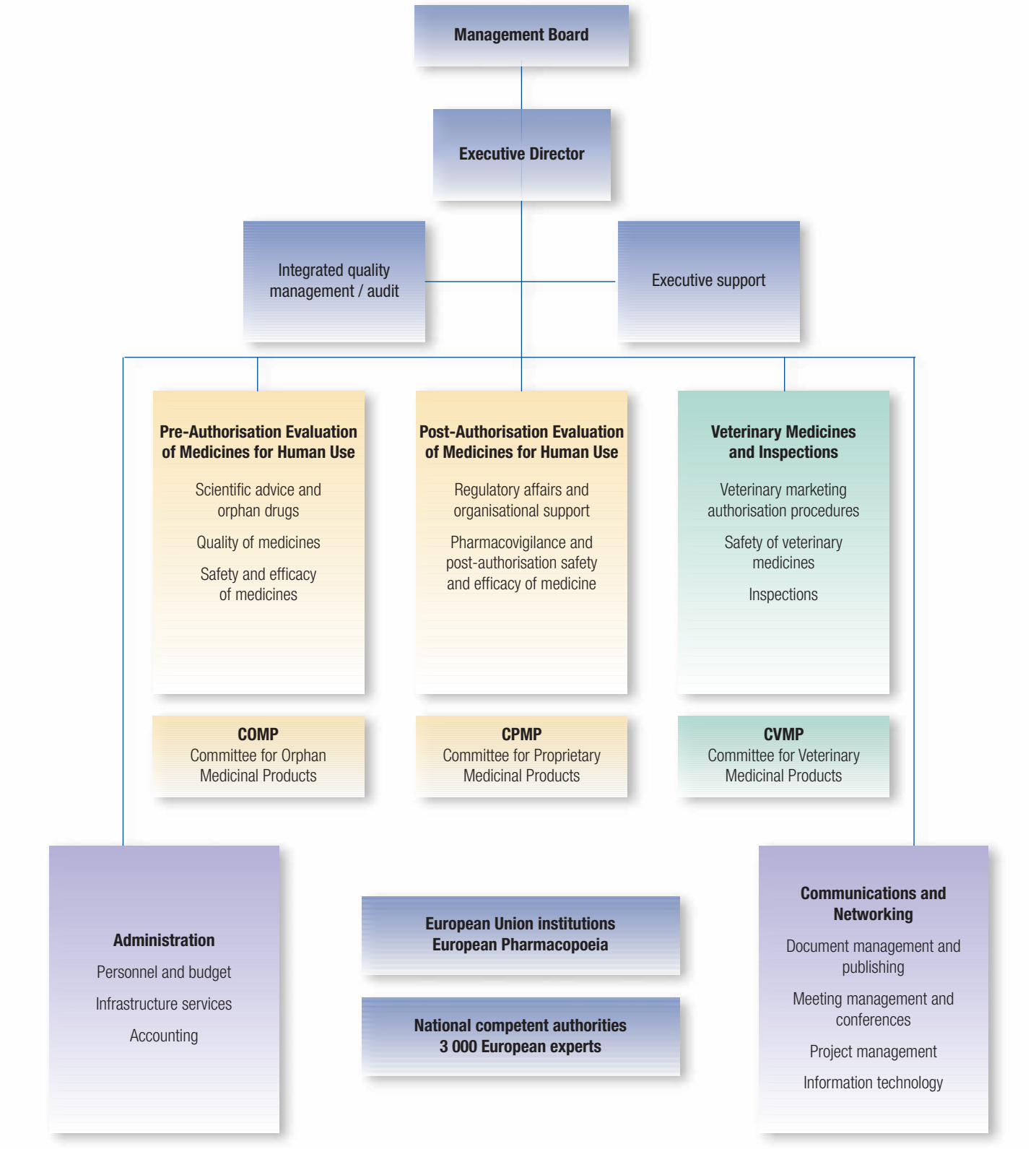
This was also the first year when the EMEA had responsibility for implementation of the EU telematics strategy for pharmaceuticals. We have worked closely with the Member States and the European Commission to achieve the milestones in the strategy. We were able to deliver the first prototype of the European database of medicines (EuroPharm), launch the initial version of the European viewing tool for electronic submissions. The telematics strategy continued to expand in scope and number of projects with the addition of a new database for reporting suspected unexpected serious adverse reactions (SUSARs) and the clinical trials database (EudraCT) in 2003.

Recognising the increasing international context within which both the pharmaceutical industry and regulators operate, the European Commission and EMEA concluded a confidentiality arrangement with the US Food and Drug Administration in 2003. This arrangement will not only help the two agencies work better together, but it will also help industry, particularly in allowing us to give parallel scientific advice to companies as they develop new medicines.

These issues were in the background to what will certainly be one of the more important events in the recent history of the European Union – enlargement in May 2004. The 5-year Pan-European Regulatory Forum (PERF) programme came to an end in 2003 and represents a considerable effort on the part of the EMEA and all national competent authorities to prepare ourselves and assist colleagues in the accession countries to ensure a smooth transition into the European family.



Structure of the EMEA



Chapter 1
EMEA in the European system

1.1 Management Board

Chairman of the Management Board
Philippe DUNETON

Vice-chairman of the Management Board
Jytte LYNGVIG

The Management Board meet four times in 2003.

20 February 2003

- Management Board began a new mandate
- Elected Keith Jones and Philippe Duneton as chairman and vice-chairman Adopted 2003 draft work programme and preliminary draft budget totalling € 84 224 000

5 June 2003

- Observers from EU accession countries began attending Management Board on a regular basis
- New EMEA financial regulation and implementing rules were provisionally adopted
- Decision taken to create an Audit Advisory Committee

2 October 2003

- Board adopted 23 recommendations aimed at improving EMEA transparency
- Pilot project approved for free scientific advice for new veterinary medicines for minor uses and minor species

18 December 2003

- Election of Philippe Duneton and Jytte Lyngvig as chairman and vice-chairman
- Adopted 2004 work programme and budget totalling € 96 619 000

The Board heard regular reports during the year on both preparations for enlargement and the implementation by the EMEA of the EU telematics strategy projects.

1.2 Relations with competent authorities

Useful web sites:

Heads of agencies for medicines for human medicines
http://heads.medagencies.org

Heads of European veterinary regulatory authorities for medicinal products
http://www.hevra.org/

Mutual recognition product index
http://mri.medagencies.org

The Agency participated in all meetings of the heads of national competent authorities for human and veterinary medicines in 2003. Topics included resource planning, the European telematics strategy, risk management strategies, pharmacovigilance and training. The Agency also worked closely with the European Commission and national authorities through the telematics management structure and implementation groups.

The heads of human and veterinary medicines agencies of the EU accession countries met at the Agency in September and October as part of the preparations for future membership. A delegation from the Romanian national inspection service visited the Agency in June 2003.

The EMEA was please to welcome the Italian Minister of Health, Prof. Girolamo Sirchia, as part of the preparations for the Italian EU presidency. There were also delegations from the Greek, Swedish and UK national authorities during the course of 2003. The Agency also received representatives from the German, French and British national parliaments.

The EMEA paid € 30 075 000 in 2003 to national competent authorities for scientific services provided for the evaluation of medicines for human and veterinary use. This represents 31 % of the EMEA budget.

1.3 EU enlargement

Useful web sites:

Pan-European Regulatory Forum
http://perf.eudra.org

Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries
http://www.cadreac.org

Collaboration Agreement between Veterinary Drug Registration Institutions
http://www.cavdri.info

Web sites for national authorities of the accession countries:

Cyprus
Ministry of Health, Ministry of Agriculture
http://www.pio.gov.cy

Czech Republic
State Institute for Drug Control
http://www.sukl.cz

Institute for the State Control of Veterinary Biologicals and Medicaments
http://www.uskvbl.cz

Estonia
State Agency of Medicines
http://www.sam.ee

Hungary
National Institute of Pharmacy, Institute for Veterinary Medicinal Products
http://www.ogyi.hu

Latvia
Food and Veterinary Service
http://zaale.vza.gov.lv

Lithuania
State Medicines Control Agency
http://www.vvkt.lt

State Food and Veterinary Service
http://www.vet.lt

Malta
Medicines Regulatory Unit
http://www.health.gov.mt/mru

Poland
Office for Medicinal Products
http://www.urpl.gov.pl

Slovak Republic
State Institute for Drug Control
Institute for State Control of Veterinary Biologicals and Medicaments
http://www.sukl.sk

Slovenia
Agency for Medicinal Products (Ministry of Health), Ministry of Agriculture, Forestry and Food
http://www2.gov.si/mz/mz-splet.nsf

Following signature of the accession treaties, the national authorities of the accession candidate countries were invited to send observers to EMEA scientific committees and working parties with effect from April 2003.

The Agency continued to participate actively in the third and final phase of the Pan-European Regulatory Forum for Pharmaceuticals (PERF III), which was successfully concluded in December 2003. The forum is funded by the European Commission PHARE programme. Part of the efforts in this last part of the PERF activities were aimed at informing representatives of patient and health care professional associations about the implications of EU enlargement.

Other areas of activity included preparations for the availability of information on centrally authorised medicines in all the 9 new official EU languages. This was done in cooperation with the national authorities of the accession countries. The EMEA also worked towards ensuring that all the new authorities were linked to the EudraNet communications network. Efforts were also made to recruit interims, new staff members and national experts on secondment from the accession countries.

While Bulgaria and Romania are not part of the accession on 1 May 2004, they continued to participate in the work of the EMEA through their CADREAC and CAVDRI representatives.

1.4 Transparency

EMEA general information service:
emearequests@emea.eu.int

On a proposal from the Executive Director, the Management Board adopted a series of 23 recommendations in October 2003 following a public consultation exercise. The recommendations aim both at improving existing transparency and public access initiatives and introduce new proposals. The scope of the recommendations was intended to complement the measures under discussion by the European Parliament and Council as part of the review of pharmaceutical legislation.

The EMEA founding regulation was amended in June 2003 bringing the Agency within the scope of EU legislation on access to documents (Regulation (EC) No 1049/2001). This change came into force in October 2003. Preparations were made to adapt the existing rules on access to documents to the requirements of the Regulation with a view to their adoption by the Management Board at the beginning of 2004.

The three scientific committees continued their work in maximising relations with interested parties. The CPMP established a working group with patient representatives, which met in May, September and December 2003.

The EMEA web site underwent a number of changes during the year. More than 10 000 documents were either published or revised in 2003. A new part of the web site was launched relating to inspections to increase the visibility and access to procedural documents, guidance and inspection-related news. Work on a new web site progressed in 2003 and takes into account comments made by contributors to the transparency public consultation exercise, including the development of a new search tool.

1.5 Preparation for the review of the European system

The EMEA contributed actively to the review of pharmaceutical legislation. At the invitation of both the Greek and Italian presidencies, the Agency participated at all Council of Ministers working party meetings in 2003.

Council reached its common position on the texts at the Health Council of 2-3 June 2003 and the European Parliament gave its second reading on 17 December 2003.

Work on preparation for the implementation of the revised legislation became more important as it was realised that at least part of the new Regulation would come into force in early 2004.

1.6 Revision of EMEA fees

The level of fees payable to the EMEA by applicants for and holders of Community marketing authorisations were revised by Commission Regulation (EC) No 494/2003 in March 2003.

As part of efforts to simplify administrative arrangements, the Management Board adopted a decision in June 2003 consolidating all implementing rules for the fee regulation. This was published on the EMEA web site. The consolidated decision was amended in October and December 2003.

An internal EMEA task force began work on the future financing of the Agency, in parallel to the review of EU pharmaceutical legislation. The Agency has been working together with the Management Board/European Commission in preparing for new fee structure to take into account the implications of the legislation.

1.7 International partners

Useful web sites:

International Conference on Harmonisation
http://www.ich.org

Veterinary International Conference on Harmonisation
http://vich.eudra.org

World Health Organisation
http://www.who.int

The Agency continued its commitment to and active participation in the two international conferences on harmonisation for human and veterinary medicines. Both the ICH and VICH processes made good progress in 2003 and this is described in Chapters 2 and 3.

The EMEA provided technical support to the European Commission delegation to the Codex Alimentarius, in particular to the 13th Codex Alimentarius Committee for Residues of Veterinary Drugs in Food in Washington, DC.

The EMEA continued its collaboration with WHO in particular on INNs, in preparation of the scientific opinion in the framework of the EU legislation and on pharmacovigilance aspects. WHO experts have participated to EMEA Scientific Committees meetings on various Public Health issues or for products under review.

EMEA has also participated on a regular basis to meetings organised by CIOMS.

The EMEA welcomed delegations from a number of non-EU countries in 2003, including from Australia, Canada, China, Japan, New Zealand, Taiwan, Vietnam and the US. The Agency was pleased to host a meeting of the VICH Steering Committee in May 2003.

The EMEA hosted the annual EU-US Food and Drug Administration bilateral for the first time. An exchange of letters on a confidentiality arrangement was concluded between the FDA, European Commission and EMEA on 12 September 2003. A detailed implementation plan is under discussion between the FDA and EMEA.

1.8 Corporate governance: integrated quality management and financial control

A programme of benchmarking visits to the national authorities in the accession countries, including Bulgaria and Romania, was launched in April 2003. The visits are intended to enhance the implementation of an integrated quality management system to ensure good regulatory practices in the EU. The visits also intended to provide targeted audit training for participating quality professionals in the EU and accession country agencies. The audit teams were composed of representatives from national authorities of existing and future Member States and from the European Directorate of the Quality of Medicines (EDQM).

The annual programme of internal audits continued, including a number of integrated management audits conducted together with the Agency's financial controller. Work also progressed on the drafting of a risk register for the Agency. The results of the risk analysis were shared with the European Commission Internal Audit Service (IAS), which will use this information in preparation for the first IAS audit of the EMEA.

An audit of the CPMP was conducted in June 2003. This was the first audit outside of the secretariat and involved two auditors from national inspection services.

The Management Board endorsed a proposal from the Executive Director in June 2003 to establish an Audit Advisory Committee. The Committee will advise the Director on an annual audit programme and be composed of external and internal members.

As part of the introduction of new financial regulations for the European Commission and all EU bodies, the post of financial controller was abolished at the EMEA during 2003. A new system of *ex ante* and *ex post* controls and internal audits was introduced.

Chapter 2
Medicines for human use

Overview

Unit for the Pre-authorisation evaluation of medicines for human use

Head of Unit
Patrick LE COURTOIS

Head of Sector for scientific advice and orphan drugs
Agnès SAINT RAYMOND

Head of Sector for quality of medicines
John PURVES

Head of Sector for safety and efficacy of medicines
Isabelle MOULON

Deputy Head of Sector for safety and efficacy of medicines
Marisa PAPALUCA AMATI

Unit for the Post-authorisation evaluation of medicines for human use

Head of Unit
Noël WATHION

Head of Sector for regulatory affairs and organisational support
Tony HUMPHREYS

Head of Sector for pharmacovigilance and post-authorisation safety and efficacy of medicines
Panos TSINTIS

Deputy Head of Sector for pharmacovigilance and post-authorisation safety and efficacy of medicines
Sabine BROSCH

See Annex 2 and 4 for Committee members, working parties and ad hoc groups.

Priorities for medicines for human use in 2003 – progress report

- The total number of new applications for marketing authorisation received in 2003 has been higher than initially planned following the drop seen in 2002, particularly for non-orphan products. The EMEA adhered to timelines for all completed procedures. Summaries of opinion were published for all applications at the time of opinion and EPARS were made public in the 2 weeks period after the European Commission decision
- There has been a steady progress in the further development of the EudraVigilance database and dataprocessing network following release of version 6.0 of the system. Development of the SUSAR module of EudraVigilance has started and will be implemented during 2004, hence leading to the electronic receipt of adverse reaction reports from clinical trials. Delays have, however, occurred as regards the implementation of the EudraVigilance project, due to a delay in the electronic reporting by national competent authorities and pharmaceutical industry
- 2003 has seen a sharp increase in Type II Variations relating to clinical safety, efficacy and quality aspects. The new Variation Regulation entered into force in the autumn. Relevant post-authorisation guidance was developed and published on the Agency website. A new type of minor variations has to be directly managed by the Agency
- Discussions continued at Heads of Agencies level, with the participation of the Agency, on the further development of a EU Risk Management Strategy. As part of the Agency's strategy the CPMP agreed on a revised procedure for the handling of safety concerns for centrally processed applications, both pre- and post-authorisation. Such revised procedure, which contributes to the concept of life-cycle management of medicines, will be implemented in 2004
- A new procedure for scientific advice and protocol assistance has been implemented early 2003 allowing for additional meeting days for the Scientific Advice Working Group outside of the CPMP week. The composition of the group has been modified, more expertise is involved and the rate of face-to-face meetings has increased. The mean duration of the procedure has been reduced while the number of applications increased substantially. A survey performed in 2003 shows a high level of satisfaction with the new procedures from users while the positive outcome, at the time of marketing authorisation phase, is now evidenced

- Applications for obtaining EU orphan status for products aiming at treating rare diseases remain stable and the duration of the procedure is constantly below the official time frame. Post designation activities are rapidly increasing in relation with the number of products designated and getting a marketing authorisation but have been nevertheless managed within time frames

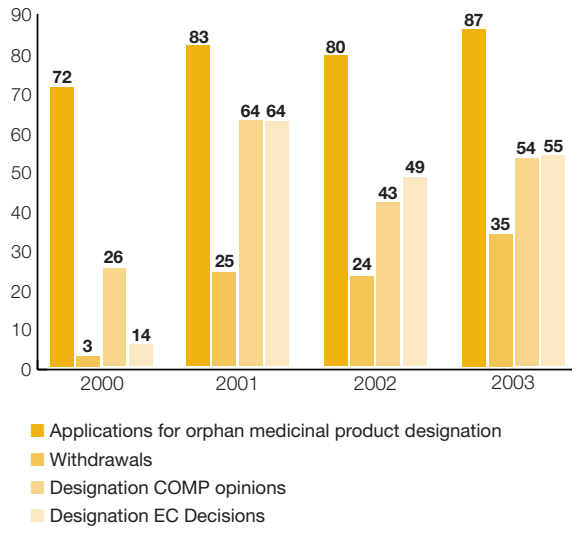
2.1 Orphan medicinal products

Management and organisation of the COMP

The Committee for Orphan Medicinal Products (COMP) is responsible for making recommendations to the European Commission for the designation of orphan medicinal products intended for rare diseases. The COMP has also responsibilities for advising the European Commission on the development of an orphan drug policy and for providing assistance in liaison with international partners and patient organisations.

The COMP met 11 times in 2003. Membership of the Committee is given in Annex 4.

Orphan medicinal product procedures 2000-2003



The second 3-year mandate of the COMP started in May 2003. Since July 2003, non-voting members from Norway, Iceland and Liechtenstein can participate in the COMP as their countries have now transposed into their national laws the orphan regulation.

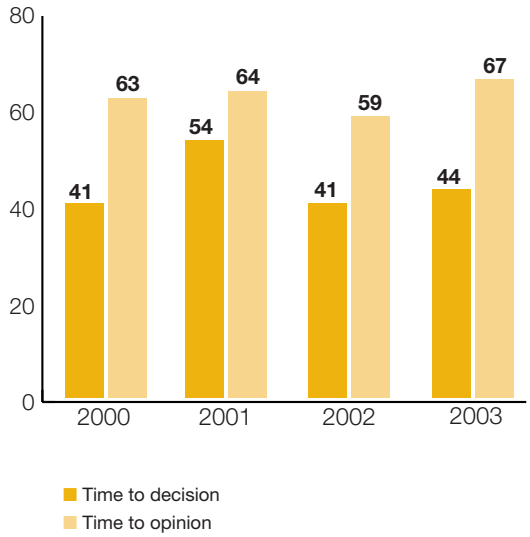
The level of applications for designation of orphan medicines remained high, with 15 % more applications than forecast. There have now been more than 300 applications since the implementation of the orphan medicines Regulation (EC) No 141/2000. This indicates a continuing interest on the part of sponsors to benefit from the incentives of the Regulation.

Pre-submission meetings were held for 87 % of applications. The quality of applications improved over time, particularly when there was a pre-submission meeting and this is shown in the decreased time to validation that was 33 days while the average time for an application for which a pre-submission meeting was not held was 67 days.

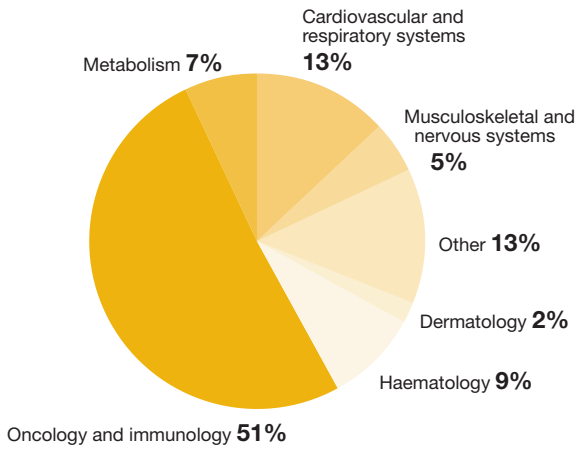
A total of 35 applications for designation were withdrawn in 2003 since the sponsors were not able to fully justify their requests.

The average time taken by the COMP to adopt recommendations on the designation of orphan medicines in 2003 was 67 days in average, below the target 90 days. The time taken to transform opinions on designation into European Commission decision has been improved and the overall process for designation remains to a large extend below the 120-day timeframe (average 44 days).

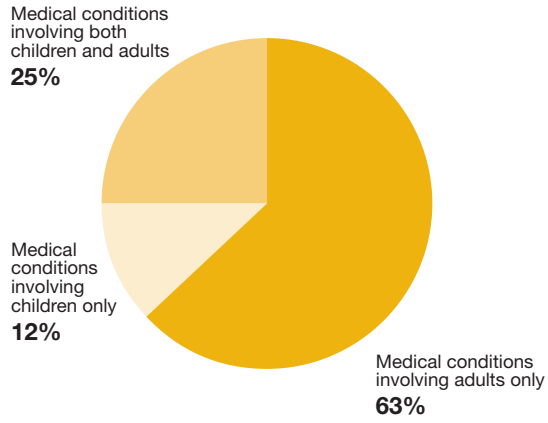
Time for Orphan medicines procedures (days)



COMP opinions by therapeutic area 2003



Orphan medical products for the treatment of children 2003



More than half of the medicinal products that received a COMP opinion in 2003 were developed for the treatment of cancers, diseases of immunological origin and metabolic diseases, of which a number are related to enzyme deficiencies. Details of designation opinions in 2003 are given in Annex 9.

In 2003 summaries of COMP opinions were regularly published on the EMEA web site and now include translation of the rare disease's name and the product's in all languages. These documents provide brief information in lay terms on the expected mode of action of the products and a description of the orphan condition. Summaries of COMP opinions are published in English, following the decision on orphan designation made by the European Commission.

The regular review of annual reports for designated orphan medicinal products provides an update on the development of designated orphan products up to the granting of a marketing authorisation. One hundred twenty seven annual reports were reviewed in 2003, a 27% increase of the planned activities.

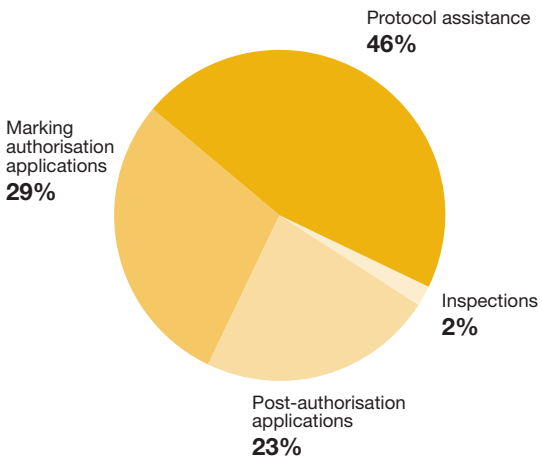
Of the medicinal products that received an opinion from the COMP in 2003, 12 % are aimed at treating conditions that only affect children and 25 % are aimed at diseases that affect both adults and children.

The COMP created an ad-hoc group on significant benefit to provide clearer advice to sponsors on this criterion for designation and reviewed a number of guidance documents to facilitate the preparation of applications and annual reports by sponsors. Details of these documents are given in Annex 9.

The EMEA information brochure on orphan medicinal products was updated in 2003. A workshop with academia and health professionals was held in October 2003 to address the issues of rare diseases which prevalence is either increasing or decreasing over time.

Designated orphan medicinal products are entitled to receive reductions on fees levied by the EMEA when applications are made for protocol assistance, marketing authorisation or other regulatory actions. A special contribution voted each year by the Council and the European Parliament is allocated for these reductions. Fee reductions in 2003 were mainly used for applications for marketing authorisation and protocol assistance.

Use of EU special contribution for Orphan medicines 2003



2.2 Scientific advice and protocol assistance

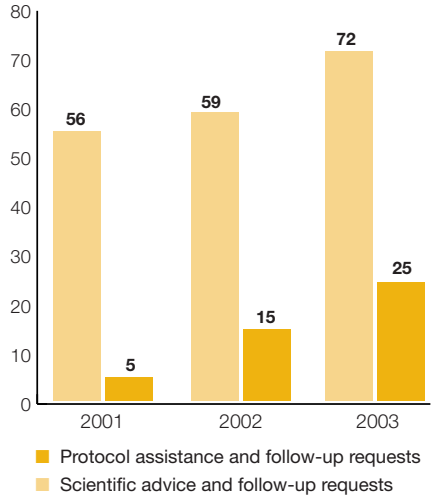
Beginning of January 2003, a new group and a new procedure for scientific advice or protocol assistances were set up. The Scientific Advice Working Group (SAWG) of the CPMP is responsible for providing advice to sponsors on quality, safety or efficacy related aspects of medicinal products. Designated orphan medicinal products are entitled to receive scientific advice in the form of protocol assistance on the same issues and on significant benefit as one of the criteria for orphan designation. The Group met 11 times in 2003.

The meetings of the SAWG take place in between CPMP meetings and last for 2 full days. The number of face-to-face meetings with sponsors and the group has increased considerably as the time available for such meetings was previously missing. The duration of the procedure has been shortened by nearly one week. In addition an exceptional 100-day procedure for complex issues and 40-day fast procedure for simple requests have been set up.

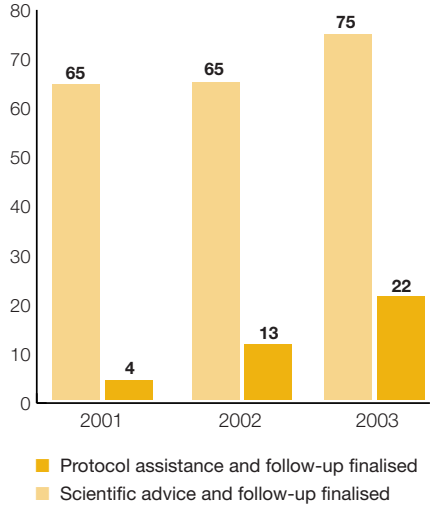
The composition of the SAWG is based on expertise and comprises 18 members, two being COMP members.

The number of scientific advice activities in 2003 has increased both for the number of requests received and advice finalised, exceeding expectations by 10-15 %. Protocol assistance increased by nearly 50 %. This increase shows the high interest of companies developing medicines for rare diseases in receiving help along the development of their orphan product. Oral explanation meetings with sponsor companies were held in the majority of cases were advice was given in 2003 and for all protocol assistance procedures. Pre-submission meetings increased dramatically by about 100 % as compared to 2002. Overall the workload increased by more than 20 %.

Scientific advice and protocol assistance requests (received)

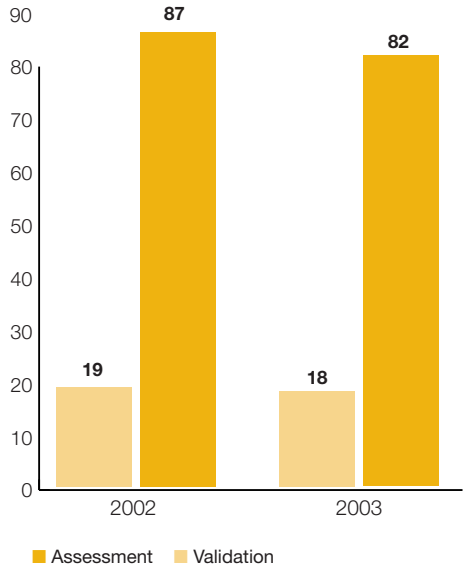


Scientific advice and protocol assistance requests (finalised)



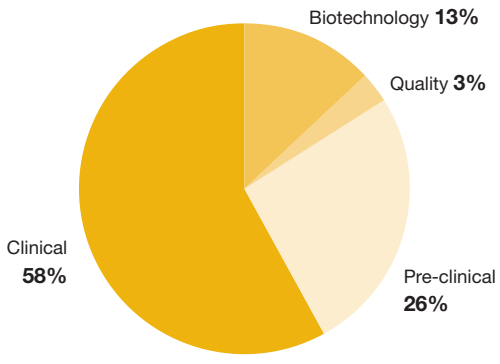
The mean duration of the procedures was about 82 days, an improvement related to the new procedure. Including validation time the overall procedure took 100 days.

Mean duration of Scientific Advice procedures (days)

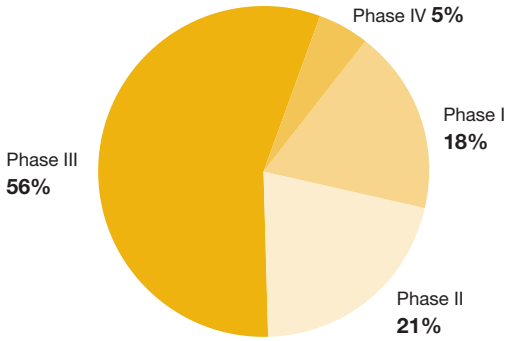


Of the requests for scientific advice and protocol assistance finalised in 2003, two-thirds related to the clinical aspects of the development of medicinal products. Early consultation of the group was observed with phase I trials representing 18 % compared to 2 % in 2002. 56 % of requests related to phase III clinical trials.

Scientific advice requests by topic 2003

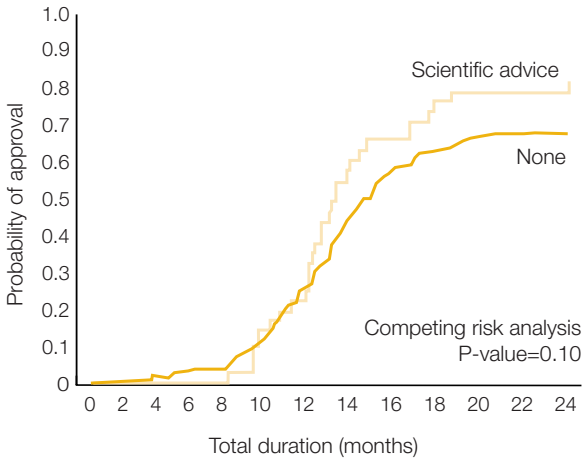


Clinical trial phases of scientific advice requests 2003



The impact of scientific advice on the outcome of the scientific evaluation at the stage of marketing authorisation was assessed. In 2003 up to 45 % of applicants for marketing authorisation have received scientific advice. The chances of favourable outcome at the time of the opinion of the Committee for Proprietary Medicinal Products are increased for products having received scientific advice or protocol assistance.

Impact of Scientific Advice (n=41) on proportion of approvals over time



2.3 Initial evaluation

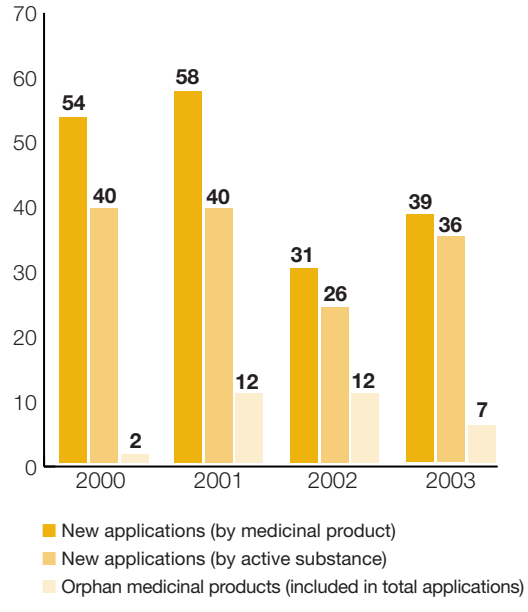
Initial applications for marketing authorisation were above target for new drugs (non-orphan), with 32 applications received out of the 22 forecast for the entire year.

The number of marketing authorisation applications for designated orphan medicines was below target, with 7 applications received out of the total 16 forecast for 2003.

There were 24 positive opinions (including 7 orphan drugs), 2 negative opinions for orphan medicines, which after appeal got further negative opinions and 4 withdrawals (including 3 orphan drugs). This brings to 13 the number of orphan medicinal products available to patients in the EU.

A total of 69 applications were under review within the year.

Initial evaluation applications 2000-2003

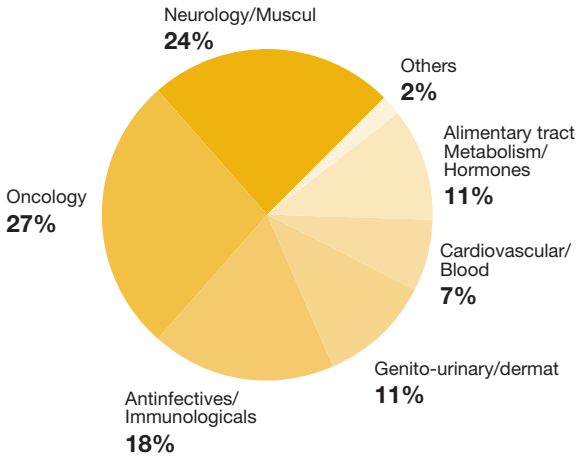


This indicates that the number of medicinal products reaching the stage of marketing applications reverted to the figures reached in 2000 and 2001 and increased slightly compared to the previous year when a significant drop was observed. A small number of products submitted in 2003 had been planned initially for submission in 2002 but were delayed. There were fewer multiple applications than in 2000 and 2001, and a lower proportion of products aimed at treating rare diseases.

A total of 11 marketing authorisations were issued for designated orphan medicinal products, out of which 4 were in 2003. 13 more applications for designated orphan medicinal products are ongoing.

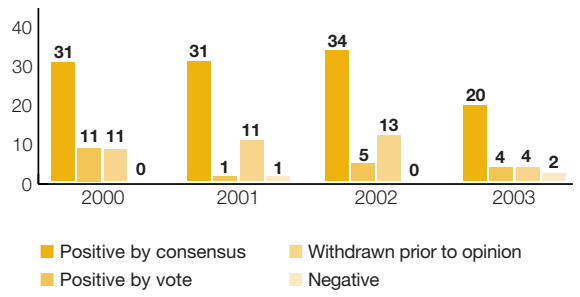
A large number of the applications were submitted either fully or partially using the new international common technical document (CTD) format, which became a mandatory requirement in the EU from mid-2003. The first electronic CTD was submitted late 2003.

Initial marketing authorisation applications per therapeutic area



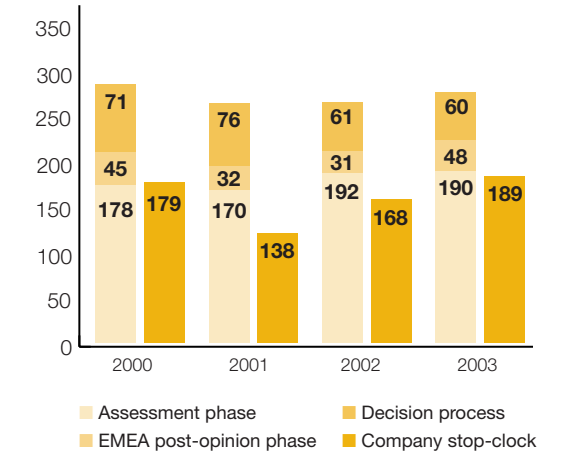
Three therapeutic areas (Oncology, anti-infectives and neurology) represented in 2003 70 % of the applications received.

Initial evaluation opinions and withdrawals 2000-2003



Performance indicators show that timelines were adhered to for all completed procedures (range = 139 to 210 days, with 5 procedures finalised in less than 180 days), with an average of 190 days well bellow the 210 days target time.

Average number of days for centralised procedures 2000-2003



The average time from opinion to decision (108 days) is still below the target of 120 days. A new procedure was introduced in 2003 at the request of the pharmaceutical industry to facilitate the process for applicants to provide translations of the product information documents necessary for health professionals and patients in all official EU languages. As a result of this the post-opinion phase increased by 17 days compared to 2002.

Similarly, some flexibility has been introduced concerning clock stop during the procedure, allowing in particular cases, on the request of applicants, to extend the period for preparation of additional information or data. This increase in clock stop time has also to be compared to the lower rate of withdrawals during the same period of time.

Summaries of opinions were published, for all applications, at the time of the opinion given by the CPMP in all cases. European Public Assessment Reports (EPARs) were published within 2 weeks of the Commission decision in most cases. However, delays were experienced because of disagreement between the companies and EMEA and the CPMP rapporteurs on the content of the EPAR. Procedures in this respect have been reviewed.

Overall these medicinal products will benefit patients affected by diseases such as infections, AIDS cancer, diabetes, Alzheimer's disease, rare and severe cardiovascular and pulmonary conditions or rare congenital deficiencies. Details of all CPMP opinions are given in Annex 7.

Committee for Proprietary Medicinal Products

The CPMP held twelve plenary meetings in 2003. An extraordinary meeting was held in April 2003 to examine safety concerns for centrally authorised hexavalent vaccines. This reflects the growing workload of the Committee in post-authorisation activities. The membership of the CPMP is provided in Annex 2.

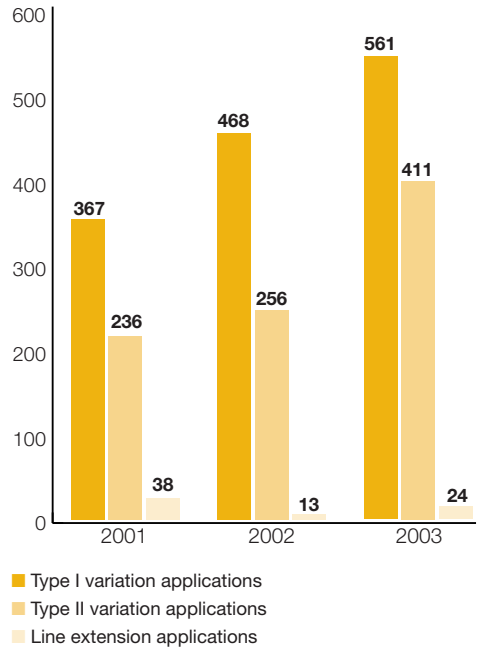
As planned, the CPMP, through its Organisational Matters Group (ORGAM), kept its working practices under close review and introduced any necessary changes to improve the functioning and operation of the Committee and the centralised procedure. In addition, as part of the Agency's ongoing integrated quality management initiatives, an audit of the CPMP was performed in June 2003. This led to a number of initiatives, resulting in an EMEA action plan to further improve its processes in relation to medicines for human use.

The Committee established three therapeutic advisory groups in 2003 in the fields of oncology, anti-infectives and diagnostics. Further to a first joint meeting of the three therapeutic advisory groups held in June 2003, further separate meetings were organised during the remainder of 2003.

2.4 Post-authorisation activities

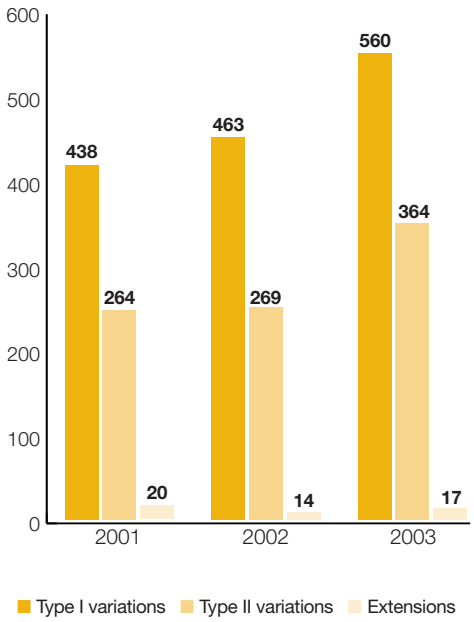
The number of variations to marketing authorisations increased significantly in 2003. The number of minor (type I) variations was 12 % over target. Also major (type II) variations were running over target with a 67 % increase over planned figures. Such increase related to efficacy/clinical safety aspects as well as quality aspects. With respect to procedures finalised in 2003 the results were as an average 32% over projections for minor and major changes.

Applications received (Input)

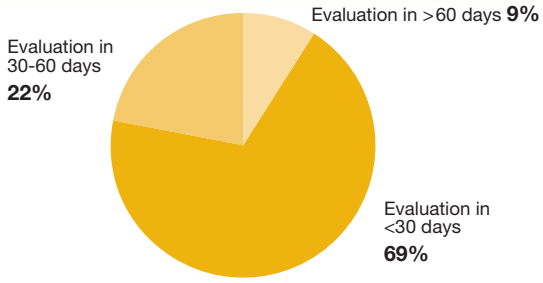


Following the entry into force of new Community legislation on variations in October 2003, the procedures for processing the new type IA and type IB variations were established and implemented. The impact of this change to the legislation will be assessed in 2004.

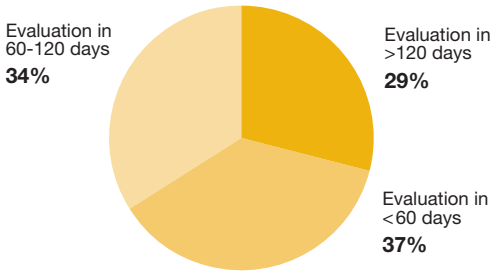
Post-authorisation opinions 2001-2003



Evaluation time for type I variations 2003



Evaluation time for type II variations 2003



As planned, adherence to regulatory timelines for active review time by the CPMP was achieved. The evaluation times given in the above charts show that the majority of Type I variations are managed in less than 30 days while an extension of the time frame is necessary for the rest. In terms of processing Type II variations, 71 % are processed in less than 120 days, whilst 29 % required an extension of that time frame.

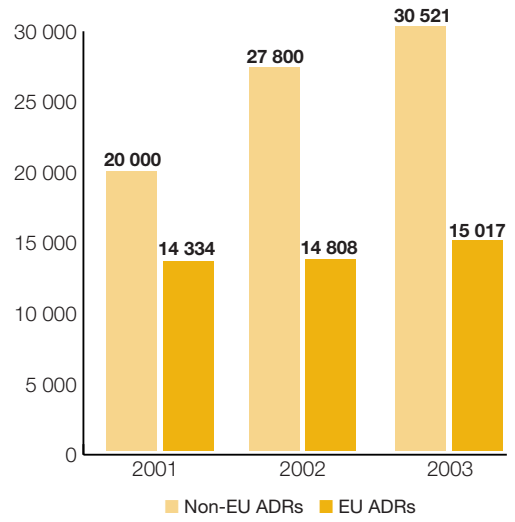
Although it was planned to increase the Agency's transparency in the post-authorisation phase, further discussion on this issue before implementation was necessary. As a consequence, a consultation with the Agency's stakeholders on its transparency policy took place in 2003. It resulted in the adoption by the Management Board in October 2003 of recommendations in different fields including the post-authorisation area.

2.5 Pharmacovigilance and maintenance activities

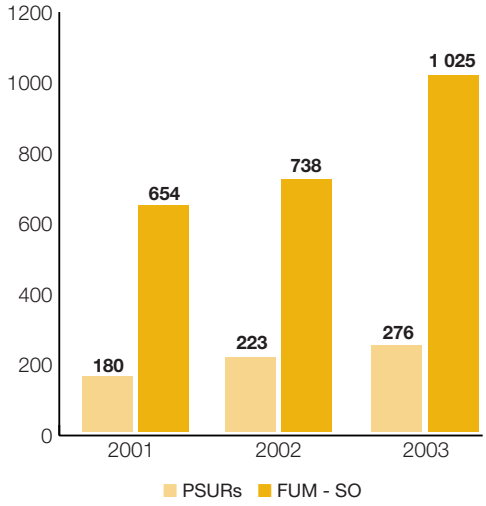
Useful website:

EudraVigilance
http://eudravigilance.emea.eu.int

EU and non-EU adverse drug reaction reports 2001-2003



PSURs, specific obligations and follow-up measures 2001-2003



A total of 45 538 adverse drug reaction reports[1] were received by the Agency during 2003 for centrally authorised medicinal products. This represents an overall 11 % increase in the level of reporting over 2002, which was in line with the forecast. 15 017 reports were from EU sources and 30 521 from outside the EU. There has been a workload increase of 66 % in specific obligations and follow-up measures handled by the EMEA and CPMP.

In terms of periodic safety updates, work throughput continued to increase in 2003 compared with 2002. These increased workloads mirror the increases in new medicinal products, authorised in 2003, being subject to follow-up activities and 6-monthly PSUR cycle. A total of 21 annual reassessments were handled by EMEA.

Three urgent safety restrictions were completed during 2003 introducing important new product information to support safe use of the medicines concerned. Appropriate communication to healthcare professionals and the public accompanied these activities.

1 This figure refers to all reports received either on paper or electronically by the Agency.

2.6 EudraVigilance

Further development of the EudraVigilance project proceeded as planned. However progress with the implementation of the EudraVigilance project was hampered in particular due to delayed implementation at the level of national competent authorities and pharmaceutical companies.

In 2003, the implementation of the electronic transmission of individual case safety reports (ICSRs) to EudraVigilance was achieved with an additional 2 Member State authorities and 13 pharmaceutical companies. In total, three national competent authorities and 18 pharmaceutical companies were in production at the end of 2003.

In total, ICSRs referring to 25 190 individual cases were reported electronically to EudraVigilance during 2003. This figure refers to reports for centrally authorised medicinal products as well as those authorised through the mutual recognition and national procedure.

In parallel a further 4 national competent authorities and 27 pharmaceutical companies entered into the testing phase. Five national competent authorities have opted or are in a process of evaluating to use a copy of the EudraVigilance system at national level. Three national competent authorities have installed and tested EudraVigilance version 6.0 locally in 2003.

Version 6.0 of the EudraVigilance system was launched in spring 2003. In addition, a special web-based tool was designed to support the electronic reporting by small and medium sized enterprises and is due to be released early in 2004 following appropriate training. A full training programme for EudraVigilance users was elaborated.

Some 23 meetings were held with national competent authorities and pharmaceutical industry in order to further support the implementation phase of EudraVigilance. Added functionality is planned for data analysis by the application of a 'data warehouse' concept allowing for the implementation of standard signal detection and data mining methodologies.

Preparations for future interaction with healthcare professionals and patient groups were begun as part of the Agency's transparency initiatives.

EMEA continued active participation at ICH concerning the E2B-M2 topics by leading the Expert Working Group on implementation in the 3 regions.

2.7 EMEA Risk Management Strategy

Heads of national agencies in cooperation with the Agency agreed on the establishment of a European risk management strategy. The Agency proceeded as planned with regard to the development of the EMEA component of this risk management strategy. As part of this strategy, the mandate of the CPMP Pharmacovigilance Working party was reviewed. This resulted in an increase in frequency of meetings of the working party from 8 to 11 per year and the meeting schedule of the meetings was changed to coincide with the CPMP week of each month.

As part of the Agency's component of the European risk management strategy the CPMP agreed on a revised handling of safety concerns for centrally processed applications, both pre- and post-authorisation. Once implemented, this procedure will allow for a pro-active conduct of pharmacovigilance, contributing to the concept of life-cycle management of medicinal products.

An important component is the involvement of specialised expertise in the CPMP activities. The CPMP endorsed nominations of some 92 experts at its November 2003 meeting who will form a pool to provide scientific support to the CPMP and rapporteurs. Areas of expertise include pharmacovigilance, epidemiology, biostatistics, methodology, clinical safety, vaccinology, advanced therapies and risk communication. Where appropriate, pharmaceutical companies will be encouraged to provide risk management plans addressing specific safety issues.

2.8 Arbitration and Community referrals

There was a significant increase in arbitration and Community referrals in 2003.

Referrals fall into 3 main categories:

- Referrals arising from the mutual recognition procedure for both initial applications (under Article 29 of the Community Code on medicines for human use) and post-authorisation variations (under Article 7(5) of Commission Regulation (EC) No 542/95) where there are disagreements between Member States
- Community interest referrals for safety-related issues (under Articles 31 and 36 of the Community Code)
- Referrals to harmonise within the European Union the conditions for medicines that are already authorised in the Member States, in particular with regard to their therapeutic indications (under Article 30 of the Community Code)

Details of all referrals are given in Annex 11.

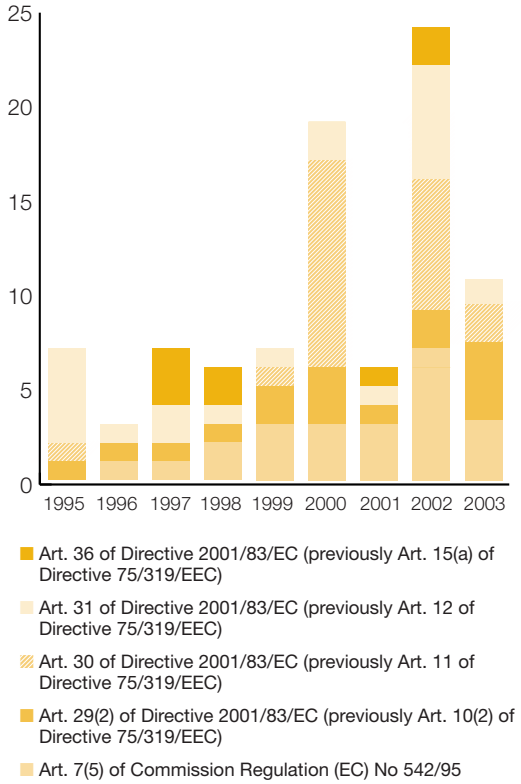
Referrals to the CPMP now constitute a significant allocation of the Agency's resources both in terms of scientific evaluation and discussion during CPMP plenary meetings. Approximately one-third of CPMP meeting time in 2003 was dedicated to consideration of arbitration and referral procedures.

Referral workload remained significant throughout 2003 with 2 ongoing referrals under Article 30 and 1 referral under Article 29 of Council Directive 2001/83/EC evaluated during the year. The CPMP issued 3 opinions for Article 30 procedures and 3 opinions for Article 29 procedures.

With respect to Community referrals under Article 31 of Council Directive 2001/83/EC the workload remained very high mainly due to the number of companies and marketing authorisations involved. The CPMP issued opinions for 4 Article 31 referral procedures.

The Agency managed the increasing workload in relation to these procedures, whilst adhering to the regulatory timeframes. Public information was made available once Commission Decisions were issued. In addition, internal working groups have reviewed the different aspects relating to arbitration and referral procedures, resulting in specific proposals to improve various aspects related to the management of such procedures. These proposals will be converted in 2004 in publicly available guidance documents.

Arbitration and Community referrals made 1995 - 2003



2.9 Regulatory guidance

EMEA Post-Authorisation Guidance document

A first version of the EMEA post-authorisation guidance for centrally processed applications was developed. Once completed, this guidance document will provide companies with clarification on the interpretation of Community legislation on post-authorisation activities including the new variation legislation. It provides an overview of the EMEA position on issues, which are typically addressed in discussions or meetings with marketing authorisation holders in the post-authorisation phase. This guidance document currently addresses requirements on variations (type IA/IB and II) and extension applications.

EMEA policy on handling of conflicts of interests

As part of the Agency's continuous efforts to further improve its processes, a revision of the current handling of conflicts of interests for scientific committee members and experts was undertaken by the EMEA. This resulted in a revised policy that, with the agreement of the Management Board in December 2003, will enter into force as a pilot phase during the first quarter of 2004.

Plasma master files (PMFs) and vaccine antigen master files (VAMFs)

Guidelines on the data requirements and the proposed procedures for the processing of these new master files were developed in consultation with interested parties, including the European Commission and pharmaceutical industry. As a result of the consultation exercises, the guidelines and procedures were refined to allow implementation of the new facility afforded by the modifications to the legislation.

Provision of CPMP scientific opinions to WHO

Work begun on preparation of a procedure to provide CPMP scientific opinions in the context of cooperation with WHO, as foreseen in the ongoing review of pharmaceutical legislation. Draft guidelines on the data requirements and the proposed procedure will be put to interested parties for consultation and agreement, prior to implementation.

Guideline on submission of marketing authorisation applications for pandemic influenza vaccines through the centralised procedure

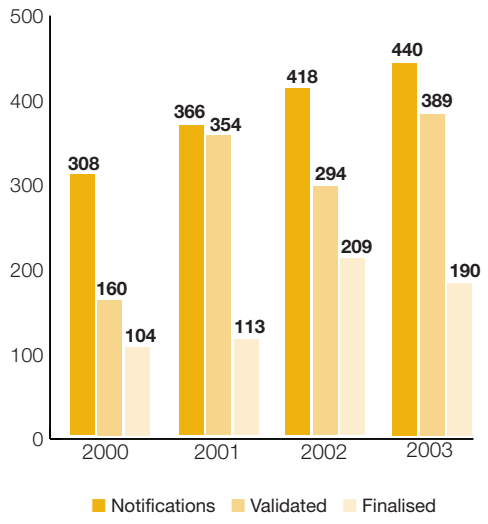
A guideline on a proposed procedure for the processing of marketing authorisation applications for pandemic influenza vaccines was developed in consultation with interested parties, including the European Commission and pharmaceutical industry. As a result of this consultation exercise and a workshop organised by the European Commission in November 2003, the guidelines and procedures were refined to allow implementation of the new facility afforded by the modifications to the legislation.

2.10 Parallel distribution

The number of parallel distribution notifications was on target for 2003 with 389 initial notifications validated and 144 notifications of a change validated. The EMEA met with the Regulatory Affairs Sub-Group of the European Association of EuroPharmaceutical Companies (EAEPC) in July 2003 to develop process improvements, e.g. conduct of quality checks, labelling change notification process etc.

A further interested parties meeting was held with EAEPC in November 2003.

Parallel distribution notifications 2000 - 2003



2.11 Working parties and ad hoc groups

Biotechnology Working Party (BWP)

The BWP met on nine occasions in 2003. In addition to the plenary meetings, it held a number of drafting groups to facilitate the development of positions papers on topics such as TSE, blood products, viral safety of biological/biotech products. The objectives are to provide on request of the CPMP a forum for discussion and harmonisation amongst quality and other experts to maintain and reinforce a uniform approach to the understanding of biotechnology and biological issues and to avoid and eliminate divergences in assessing biotechnology issues and interpreting biotechnology guidelines. The forum of the BWP facilitates the efficient use of European expertise on products, the provision of scientific advice and the generation of guidelines.

Efficacy Working Party (EWP)

The Efficacy Working Party met four times in 2003. Four therapeutic drafting groups have met as planned to support the Efficacy Working Party with very positive impact on the preparation of guidelines in cardiovascular, anti-infectives, CNS and pharmacokinetics.

The working party was responsible for preparing 26 guidelines of which four were new and 11 were published.

Safety Working Party (SWP)

The Safety Working Party met 3 times in 2003 and was in charge of 9 guidelines of which 4 were published and 5 are under discussion.

Two drafting groups supported the work of the Safety Working Party in the following areas: environmental risk assessment and risk assessment of medicinal products on human reproductive and developmental toxicities: from data to labelling.

Pharmacovigilance Working Party (PhVWP)

The PhVWP held 11 meetings in 2003 in the same weeks as the CPMP was holding its meetings, and herewith introduced their new meeting schedule that provided the opportunity for increased interaction between the CPMP and the PhVWP. In addition to the plenary, on average 5 drafting groups were held at the margins of each meeting on product-related issues, guidelines or organisational matters. Overall, 56 product-related issues were discussed at the request of the CPMP and 92 at the request of Member States.

Other activities of the PhVWP related to ongoing work on guidelines, contributions to the Notice to Applicants and to ICH. The PhVWP also held joint meetings with other working groups with regard to EudraVigilance and the implementation of the Clinical Trials Directive. Discussions were held with MRFG in relation to initiatives for improved interaction between the MRFG and the PhVWP and work sharing between Member States. In relation to organisational matters, the PhVWP initiated in particular a review of new tools for Regulators for the purpose of information exchange and tracking of implementation and follow-up action. Moreover, the PhVWP provided contribution to the ongoing discussion on the EU risk management strategy. Part of this strategy was the revision of the PhVWP Mandate in September 2003, now reflecting in more detail their mission to provide advice on safety of medicinal products, investigate adverse drug reactions and to enable risk identification, assessment and management at any phase of the product life cycle.

Herbal Medicinal Products Working Party (HMPWP)

The Herbal Medicinal Products Working Party met 3 times in 2003 and welcomed the participation of additional observers from the Accession Countries. The Working Party adopted 3 core-data and prepared 4 new core-data after review of the corresponding monographs from ESCOP (European Scientific Cooperative on Phytotherapy). They also prepared 5 position papers concerning the use of herbal medicinal products containing various herbal substances (see Annex 10). A draft position paper on the biopharmaceutical characterisation of herbal medicinal products was prepared and the SOP on the recording of core-data was revised.

The working party also closely monitored the progress made at European Parliament, Council and Commission level on the proposal for a Directive on traditional herbal medicinal products, started preparatory discussions regarding Community herbal monographs and developed a draft structure for the future list of herbal substances, preparations and combinations with traditional indications.

Organisational Matters Group (ORGAM)

The ORGAM met 11 times in 2003 and addressed a wide variety of organisational topics aiming at further improving the EMEA processes in relation to human medicines as well as the functioning of the CPMP. The topics related to CPMP meeting

organisation (e.g. preparation for enlargement and improvement of the use of IT tools), the centralised procedure (e.g. establishment of therapeutic advisory groups, training of assessors, follow-up to the CPMP audit), pharmacovigilance-related issues (e.g. the handling of safety concerns by the CPMP, the revised mandate of the PhVWP, the implementation of EudraVigilance), and transparency and communication (e.g. establishment of the EMEA/CPMP Working Group with Patients Organisations, the 2003 performance indicators survey).

As part of a wider effort to streamline CPMP plenary meetings, the scope of the discussions within ORGAM has been extended since September 2003 to systematically include discussion on CPMP working party topics, mainly in the area of guideline development.

EMEA/CPMP Working Group with patients' organisations

The EMEA/CPMP working group with patients' organisations has been created as a result of the EMEA/CPMP workshop with patients' organisations organised in 2002. The mandate of the group is to make proposals for action in the following areas in the context of the EMEA activities: pharmacovigilance, product information, dissemination of information/transparency and interaction between the EMEA/CPMP and patients organisations. This group, which met three times in 2003, involves 8 European patients organisations.

Invented name Review Group (NRG)

The Invented Name Review Group (NRG) met 11 times in 2003 to review whether invented name(s) proposed by applicants for medicinal products would create public health concerns and more particularly potential safety risks. Collaboration with WHO in this field was increased resulting in a systematic participation by WHO in the review process. An interested parties meeting was held with EFPIA in April 2003 to review implementation of the revised guideline adopted in 2002 and process performance aspects. The NRG also welcomed observers from the accession countries to its meeting. In addition a retrospective review of invented names of centrally authorised products versus nationally authorised products in the accession countries was performed as part of the preparation for the EU enlargement.

A new tracking database became operational in 2003 to allow better monitoring of the review process.

The percentage acceptance rate for 2003 is 63 %, based on a total of 107 names reviewed, 67 names accepted, 40 names rejected and 13 names justified by applicants. The average timeframe to complete an invented name review was 39 days, which is in accordance with the guideline.

Ad hoc Working group on (pre-) clinical comparability of biotechnology products

This group met twice in 2003 and finalised an annex to the note for guidance on comparability of medicinal products containing biotechnology-derived proteins as drug substance.

Paediatric Expert Group (PEG)

The Paediatric Expert Group met five times in 2003 and issued two concept papers on renal system and immune system in the context of development of medicinal products for children. The group contributed to guidelines of the CPMP efficacy and quality working parties. The group was consulted by the EC on its proposals for a future paediatric regulation and was requested to prepare a preliminary list of priorities for studies on medicines for children's use to be funded. The PEG liaised with EU paediatric learned societies in order to foster the necessary networking, particularly for clinical trials developments.

Vaccine Expert Group (VEG)

The VEG met on five occasions in 2003 including one meeting devoted to influenza pandemic. Plenary sessions are complemented by drafting groups addressing specific issues in a more focussed manner and generating positions papers on topics such as TSE, blood products, viral safety of biological or biotech products. The VEG prepared guidelines on the data and dossier requirements necessary in the event of influenza pandemic in consultation with the European Commission and vaccine manufacturers.

Blood Products Working Group (BPWG)

The BPWG met on four occasions in 2003 including two times as specialist drafting groups.

Ad hoc Expert group on cell therapy

The group met twice in 2003. In consultation with the other CPMP and CVMP working parties, the ad hoc group completed the revision of a concept paper on xenogeneic cell therapy that was adopted by the CPMP and CVMP in December 2003.

Ad hoc Group on gene therapy

During its two meetings in 2003, the group contributed to a BWP position paper related to lenti-viral sectors and discussed topics including insertional mutagenesis and oncogenesis, gonadal signalling and germ-line integration study in order to prepare for the second ICH workshop on gene therapy held in November 2003 as a satellite session of the of the ICH 6 Conference, in Japan. The two scientific meeting reports and the ICH gene therapy workshop communication paper were published by the EMEA.

Ad hoc Group on pharmacogenetics

This group met three times in 2003. The group finalised the English version of the CPMP position paper on terminology in pharmacogenetics in lay language, ahead of its translation into all official EU languages. The Pharmacogenetics expert group finalised a concept paper on Pharmacogenetics briefing sessions, published in January 2003 and participated to three briefing session with companies where pharmacogenetics-specific issues were discussed under the 'safe harbour' concept.

Ad hoc groups on Chemical Threats

At the request of the European Commission, in the framework of action Programme of Cooperation on Preparedness and Response to Biological and Chemical attacks (BITCHAT), the EMEA established a CPMP expert group responsible for drafting a guidance document on medicinal products to be used in the framework of chemical threats. The EMEA guideline was released on 13 May 2003.

2.12 Enlargement and international activities

Major efforts were made in 2003 to allow for a smooth transition for the new Members States in May 2004. Considerable resources were allocated into the PERF III programme and specific training was provided to assessors from accessing countries in order to allow familiarisation with the European procedures.

International activities focussed on involvement in ICH and collaboration with non-EU national competent authorities. The EMEA contributed to the ICH process through the provision of technical coordination and scientific support through its scientific committee and working parties. In 2003 three meetings were organised, one in Europe and two in Japan, the last meeting being followed by the ICH-6 conference and satellite sessions. The EMEA contributed directly to such activities.

The EU and the US Food and Drug Administration (FDA) concluded a confidentiality arrangement that provides a framework for regulatory cooperation. Preparations for an implementation plan were begun. Cooperation with the FDA in 2003 mainly focussed on regular videoconferences in the field of pharmacovigilance.

In addition, considerable progress was made in the field of scientific advice. The CPMP Scientific Advice Working Group held a first videoconference with the FDA as a pilot phase for parallel advice given by the Agency and the US FDA authorities on an orphan medicinal product.

Other examples of international cooperation related to visiting expert programmes with the Canadian and Chinese Health Authorities.

2.13 Mutual recognition facilitation group

Web Sites:

Heads of Agencies for human medicines
http://heads.medagencies.com

European product index
http://mri.medagencies.com/prodidx

EMEA/MRFG secretariat
mrp@emea.eu.int

The Mutual Recognition Facilitation Group (MRFG) reports to the heads of national authorities for human medicines.

The MRFG is made up of delegates from the EU, Iceland and Norway who meet at the EMEA to coordinate Member States' positions on topics related to the mutual recognition procedure. Observers from the accession countries and European Commission also participate in the monthly meetings.

The MRFG provides procedural and regulatory advice on request and develops general guidance papers, which are published on the MRFG website.

The MRFG met eleven times in 2003. Julia Yotaki chaired the meetings during the Greek presidency in the first half of 2003 and Silvia Fabiani during the Italian presidency in the second half of the year. Press releases with statistics and adopted documents are published monthly on the Heads of Agencies website. Two informal meetings were held in 2003, in Athens and Rome.

The future enlargement of the European Union was a permanent item on the MRFG agenda. In addition, the MRFG continued to answer questions from the pharmaceutical industry and develop new guidance papers to assist marketing authorisation holders and national competent authorities. Existing guidance documents were updated in accordance with new Community legislation.

A number of MRFG subgroups met in 2003. The Joint CPMP/MRFG working group on harmonisation of SPCs, created in 2001 under a mandate given by the Heads of Agencies, met 4 times in 2003. The CTS/Eudratrack subgroup, dealing with the mutual recognition procedures' tracking system, met 5 times in 2003. On 1 October 2003, after the new variations regulation entered into force, a new CTS/Eudratrack client was released, taking into account the new type IA and IB variations. The group is now working in close contact with DIMDI/BfArM to test and improve the client in view of the final reengineering, foreseen in May 2004.

The joint Pharmacovigilance Working Party/MRFG working group met 3 times in 2003, the main aims of this group being to improve cooperation between the Pharmacovigilance Working Party and MRFG in risk management, to harmonise the birthdates of PSURs, to share work in the field of PSUR assessment and to improve the format and quality of PSURs.

The EMEA supported the chairpersons, the MRFG and the subgroups in their activities. This support included the organisation of two preparatory meetings for the hand-over of the presidency.

The subgroup looking at preparations for implementation of new Community legislation, in particular concerning the establishment of the Coordination Group, met twice in September and October 2003, in Lisbon and Rome respectively. A document was drafted and submitted to Heads of Agencies for consideration at their meeting in November 2003. This document addresses the function and the role of the future coordination group, and the support the EMEA should provide to such coordination group.

The number of new applications finalised in 2003 increased compared to 2002. In addition, there was an increase in the number of arbitrations compared to previous years. Statistical information on applications under the mutual recognition procedure is provided by the EMEA and presented in the monthly MRFG press releases.

Mutual recognition procedure	Total submitted in 2003*	Under evaluation in 2003*	Ended positively in 2003*	Referrals started in 2003
New applications	620	135	529	5
Type I variations	2 326	107	2 473	N/A
Type IA variations	434	92	230	N/A
Type IB variations	257	93	94	N/A
Type II variations	1 091	232	754	3

**The numbers include multiple procedures as stated at 31 December 2003.*

Chapter 3
Veterinary medicines

Overview

Unit for the Veterinary medicines and inspections

Head of Unit
Peter JONES

Head of Sector for veterinary marketing authorisation procedures
Jill ASHLEY-SMITH

Deputy Head of Sector for veterinary marketing authorisation procedures
Melanie LEIVERS

Head of Sector for safety of veterinary medicines
Kornelia GREIN

Head of Sector for inspections
Emer COOKE

The annual report for inspection activities is given in Chapter 4.

For Committee members, working parties and ad hoc groups, see Annex 3.

Priorities for veterinary medicines in 2003 – progress report

- The definition of EU standards for electronic reporting has been progressed and preparation of all the elements to bring EudraVigilance to full operational release and implementation is close to being finalised
- The Agency and CVMP have made further significant progress in advancing initiatives to facilitate better provision of medicines for minor uses and minor species. In particular, further extrapolation of major species MRLs to minor species has been achieved and the CVMP issued a landmark consultation paper in June 2003 setting out its strategy for a minor uses and minor species (MUMS) policy
- The Pharmacovigilance Working Party succeeded in meeting some of the goals agreed to by the Committee in promoting veterinary pharmacovigilance in the EU, by having finalised a common reporting form and drafted guidelines on, mechanisms to trigger investigations on safety of medicines and on causality assessment
- In response to requests from heads of veterinary medicines agencies, the EMEA developed a concept paper to be completed by working parties, subsequently adopted by CVMP, to set out a business case/impact analysis prior to work on any new guideline/ position paper being initiated; this enables consultation by interested parties and Member States on the guidelines in question
- Considerable effort in supporting the accession countries in their preparation for enlargement has met with particular success in the veterinary sectors within the PERF programme. A number of workshops on various disciplines resulted in many of the outstanding issues being addressed and the PERF III veterinary mini-conference held in Warsaw was very successful in meeting the objectives set
- Despite encouragement to prospective applicants through the centralised procedure to request scientific advice from the CVMP in the pre-development phase, the uptake of this service continued to be slow in the veterinary area and discussions are ongoing with industry to clarify where difficulties may exist
- The Immunologicals Working Party addressed two critical issues in 2003. The first was an annex was prepared to the Note for guidance on requirements and controls applied to Bovine Serum to aim to control contamination with Bovine Viral diarrhoea virus. The second was a paper on data requirements for removing target animal batch safety test as final product testing in the EU

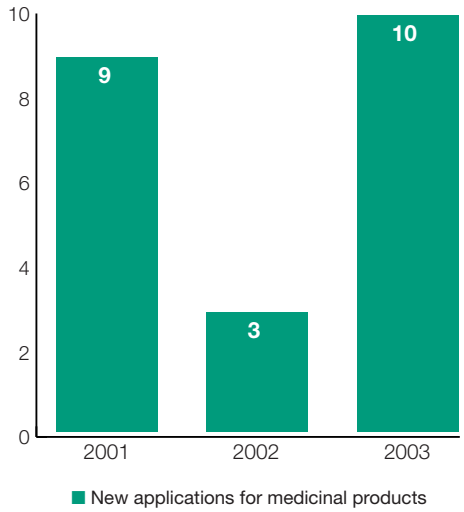
3.1 Scientific advice

Even though applicants are more aware of this provision, the growth in submissions requesting such advice was slower than expected. Industry have reported that some elements in the procedure are discouraging potential applicants and discussions are ongoing on these issues to try and address the matters of concern.

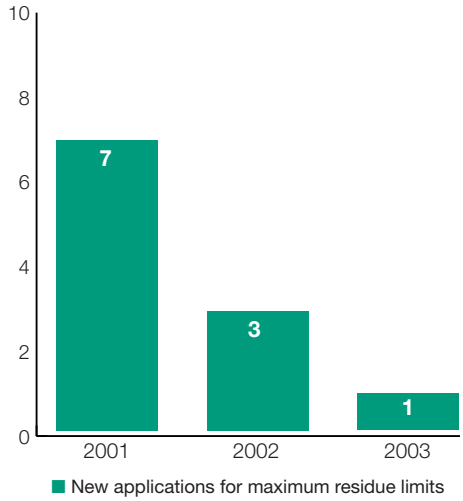
3.2 Initial evaluation

The total of 10 centralised applications were received in 2003, in line with forecasts. A significant number of letters of intent for applications to be submitted in the first half of 2004 were also received in the last quarter of 2003. The number of applications to establish new maximum residue limit fell short of forecasts.

New centralised applications 2001-2003

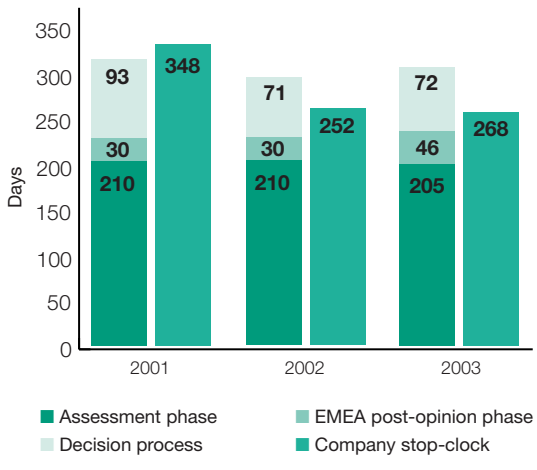


New applications for maximum residue limits 2001-2003



All applications were processed within the regulatory deadlines. Most EPARs were also published in a timely manner following publication of the Commission marketing authorisation decision.

Average number of days for centralised procedures 2001-2003



The third report of the joint EMEA-industry survey of the centralised procedure for veterinary medicinal products covering 12 applications was published in 2003.

As the number of applications continues to grow there is a greater familiarity with procedures, which was reflected in the results showing a high level of satisfaction with the procedure overall with some clear improvements evident since the last survey.

The survey indicated that rapporteurs and co-rapporteurs continued to have concerns about the quality of the safety and efficacy dossiers in some of the submissions reflecting that a number of the applications might have been submitted somewhat prematurely. The results of the survey were presented at the Infoday with interested parties on 14 November 2003.

Management and organisation of the CVMP

The CVMP elected a new chairman and vice-chairman at the beginning of the year, Gérard Moulin and Johannes Hoogland. The Committee met 11 times and no extraordinary meetings were held.

The Strategic Planning Group has met five times under the chairmanship of the CVMP vice-chairman, Johannes Hoogland. Topics considered included:

- Consideration of additional initiatives for improving the transparency of its activities to be included in an updated EMEA transparency policy
- The group considered the options for further progress to be achieved by the Committee in minimising development of antimicrobial resistance following the use of antibiotics in veterinary medicine. A summary of discussions at the informal CVMP meeting in Athens in May under the Greek presidency was published on the EMEA website (CVMP/558/03)
- The group took an active role in providing ideas to CVMP on topics for assessor training which are then finally agreed upon in conjunction with the heads of veterinary regulatory agencies
- Draft programmes for working parties are reviewed, analysed and approved by the Strategic Planning Group prior to adoption by the CVMP
- The Strategic Planning Group was given presentations by leading pharmaceutical industry executives on the current status of research and development into new veterinary medicines, to assist in the discussion on business trends and forecasting for applications in the centralised procedure
- The group continues to monitor the operating efficiency of the Committee's activities focussing in particular on:
  - Participation of all members
  - Improvements in communication
  - Interpretation in CVMP meetings
  - Consistency in procedures and documentation

3.3 Availability of medicines

The ongoing concern regarding the provision of sufficient veterinary medicinal products for use by practitioners in minor uses and minor species has again stimulated considerable effort by EMEA and CVMP in this reporting year to achieve further progress to try and find solutions to the problem with regular and detailed consultation with Member States and interested parties.

Continued progress was achieved in extrapolating major species MRLs to minor uses particularly for those substances in cattle, to goats and sheep (10 substances), especially for milk-producing animals. In addition, extensions were made for four substances in Annex II to all food producing species (acetylsalicylic acid, sodium acetylsalicylate, acetyl acid DL-lysine and carbasalte calcium) and for one substance in Annex I (emamectin) from salmonidae to fin fish.

All parties agreed that a piecemeal approach to this problem will not provide the answers and with this in mind, the Committee at its June meeting adopted for consultation a position paper detailing a strategy for a minor uses and minor species policy, taking a holistic approach to the subject for both biologicals and pharmaceuticals and detailing proposals for the short, medium and long-term.

The commitment of the Agency to support and drive this programme forward is underpinned by the decision of the Management Board, at its October 2003 meeting, to approve one of the key short-term recommendations in the paper to

grant free scientific advice, under a 12-month pilot project, to any sponsor seeking to develop a veterinary product for minor uses and minor species according to criteria to be adopted by CVMP.

3.4 Establishment of maximum residue limits for old substances

Of the 8 old substances that were remaining in Annex II of Council Regulation (EC) No 2377/90, CVMP has concluded the evaluation of 5 of them following the receipt of additional data from applicants, 4 of which have been proposed for inclusion in Annex I of Council Regulation (EC) No 2377/90 and one for Annex II. These include:

- Alphacypermethrin
- Cypermethrin
- Kanamycin
- Metamizole
- Morantel

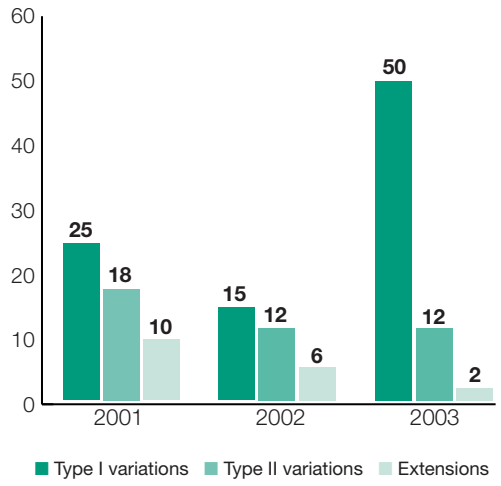
Responses are awaited from the sponsor in respect of the substance altrenogest, and two substances flugesterone acetate and norgestomet, although recommended for inclusion by CVMP in Annex II, have been given provisional status in Annex III with expiry in 2008.

3.5 Post-authorisation activities

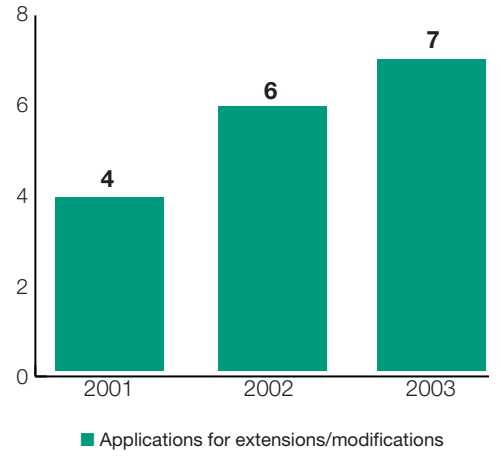
Post-authorisation activities in respect of centrally approved veterinary medicines were much as forecasted with the exception that the number of extensions to market authorisations (2) were fewer than expected (8). The trends were similar to previous years compatible with the growth in products authorised.

Extensions and modifications to existing MRLs were below the forecast.

Post-authorisation applications for centrally authorised medicinal products 2001-2003



Applications for extension/modification of maximum residue limits 2001-2003

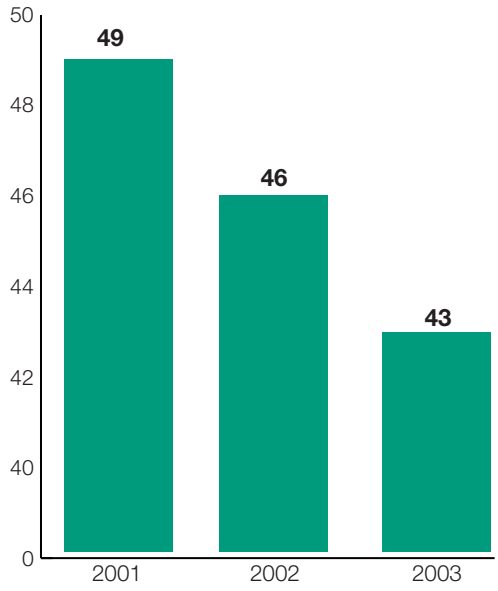


3.6 Pharmacovigilance and maintenance activities

Considerable progress has been achieved in meeting the challenges identified at the beginning of the reporting period as key issues needing to be addressed during 2003. They include:

- EudraVigilance in the veterinary sector was advanced with the release of EudraVigilance Veterinary 2.0, as well as the adoption of the CVMP guideline on data elements for electronic submission of adverse reaction reports (CVMP/065/03), which includes message and transmission specification. Testing of the web-based reporting tool is well underway with good collaboration from Member State competent authorities and marketing authorisation holders. Significant progress was also made to complete the controlled terminology required for EudraVigilance Veterinary
- Further efforts have continued to resolve differences between the parties at VICH on harmonisation of pharmacovigilance reporting, but a successful outcome has yet to be achieved and some significant hurdles remain
- In support of various initiatives supported by CVMP to promote pharmacovigilance in EU, a number of guidelines on topics agreed to by the Committee and its interested parties have been finalised and released for consultation (see report under Pharmacovigilance Working Party) and preparation is well underway to publish pharmacovigilance bulletin reports on products having a Community authorisation. Significant progress was made on the update and revision of the general guideline on pharmacovigilance of veterinary medicinal products on (EMEA/CVMP/183/96) and a new guideline on mechanisms to trigger investigations of the safety of veterinary medicinal products was also progressed
- A total of 43 periodic safety update reports were received – the majority on time, and subsequently processed in a timely manner. No change to the risk benefit of any product was called for
- It is worthy of note that, with one exception, for no centrally authorised product was it considered necessary to change the risk benefit summary underpinning the scientific opinion with consequent changes to the SPC and label

Periodic safety update reports 2001-2003



3.7 Arbitration and Community referrals

There was no significant increase in this activity, with one referral received on the grounds of safety related to potential inadequacy of the withdrawal period of Eprinex Pour-on (eprinomectin).

3.8 Regulatory guidance

Interested parties

The EMEA has continued to build on its relationship with the interested parties to the CVMP with numerous opportunities for dialogue and exchange of views being organised during the year which include:

- Focus groups with industry technical experts between CVMP chair and vice-chair, EMEA secretariat and chairs of CVMP working parties to review the work programmes in 2003 for the CVMP working parties and to receive industry comments on the issues being addressed under the various initiatives
- Regular bilateral meetings were held between the European industry federation, IFAH-Europe, and the secretariat of the Agency to exchange views on matters of current topical interest

The EMEA continues to jointly organise Infodays with the interested parties, the last one being in November, where the two major topics, availability of medicines – MUMS policy and antimicrobial resistance were the subjects for discussion.

Working parties and ad hoc groups

Each working party had undertaken a review of its mandate and continues to plan its activities so that once again the extensive work plans for 2004 were considered in some detail and adopted by CVMP.

The CVMP is reflecting on its next moves in continuing its risk management strategic plan to minimise antimicrobial resistance in the veterinary sector has agreed to create a scientific advisory group to advice the Committee on its future activities in this context and to undertake evaluation of technical issues and questions as they arise.

3.9 Enlargement and international activities

The EMEA and CVMP continue its active involvement in international affairs on various issues.

Continued coordination of the scientific input of the EU regulatory authorities into VICH, where four guidelines have been progressed to the consultation step or finalised.

Scientific expertise in support of 13th CCRVDF meeting of Codex Alimentarius and input into the CCRVDF working parties on antimicrobial resistance and on risk management methodologies in respect to residues from veterinary drugs in food.

Support to FAO/IAEA workshop on strengthening capacities for implementing Codex standards regarding veterinary medicines in developing countries.

The EMEA and IFAH jointly chaired the first global International Animal Health Conference held in Nice, which addressed a wide variety of topics in relation to veterinary medicine. The conference attracted participation from many countries throughout the world and was considered to have been a considerable success by speakers and participants alike.

The culmination of another 18 months work undertaken in 6 workshops on a wide variety of topics under the third phase of the PERF programme was the PERF veterinary conference held in Warsaw. This conference for producers and users of veterinary medicines in the accession countries provided a forum for addressing many of the outstanding issues and planned activities prior to enlargement of the European Union on 1 May 2004.

The Veterinary medicines unit secretariat continues to work with heads of national veterinary medicines agencies through the HEVRA forum.

3.10 Veterinary mutual recognition facilitation group

Useful web site:

Heads of agencies for medicines for veterinary use
http://www.hevra.org

The Veterinary Mutual Recognition Facilitation Group (VMRFG) met once a month (except August) in 2003, at the EMEA under the Chairmanship of the Greek and the Italian presidencies respectively. The group changed their meeting days to Thursdays and Fridays of the CVMP week from June 2003, moving from one day to a two-day meeting. The EMEA provided secretariat and administrative support to the group. Observers from veterinary authorities of central and eastern European countries (CAVDRI) as well as the three EEA-EFTA countries participated in plenary sessions. Two informal meetings were held in 2003 – one in Athens in May under the Greek presidency and one in Rome in November under the Italian Presidency.

The number of mutual recognition procedures completed in 2003 was 88. Nine Member States acted as the reference Member State in mutual recognition procedures in 2003, compared to ten in 2002. During this year, some of the central and eastern European countries (CAVDRI) have been involved in the simplified mutual recognition procedures (9 % of the procedures).

In 2003, VMRFG provided answers to a wide range of questions from both Member States and industry on a number of different issues. The group also adopted a number of documents related to the management of procedures. The summary report of the reasons for withdrawals in 2002 was published on the HEVRA website.

The VMRFG interested parties liaison group met three times (January, June and October) during 2003. The group consisted of representatives from VMRFG, IFAH Europe and from the European Generic Association (EGGVP). The joint VMRFG-IFAH Europe survey of the mutual recognition procedure in 2002 was published on the HEVRA website and was continued in 2003. A report on the activities of the VMRFG was provided at each CVMP meeting in 2003. The chairperson provided a report both to HEVRA (Athens, Rome) and to the Veterinary Pharmaceutical Committee (Brussels) during their meetings.

Chapter 4
Inspections

Overview

Head of Sector
Emer COOKE

Working parties and ad hoc groups

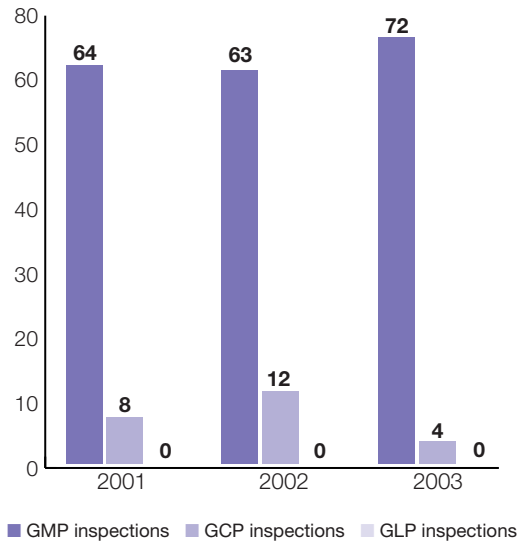
ad hoc Meeting of GMP inspection services
Emer Cooke (chair)

ad hoc Meeting of GCP inspection services
Fergus Sweeney (chair)

Of the priorities identified for 2003, the sector's contribution to the PERF III programme was particularly successful.

- Three GMP workshops were held as part of the PERF III programme, focussing on quality systems, tabletting and practical inspection aspects respectively. Eight joint inspections involving EU inspectors and inspectors from accession countries were also organised
- An important seminar to review progress and experience with the sampling and testing programme was held in EMEA in September 2003, providing important input into improving efficiency of future programmes
- The EU-Canada agreement entered into force on 1 February 2003. The MRA with Japan could not be completed by June 2003 as originally anticipated and preparatory work continued throughout the year. No progress was made on the MRA with the USA during 2003. All other MRAs are operating successful and being closely monitored
- Progress on implementation aspects of the EU clinical trials directive accelerated, with the finalisation of guidance documents foreseen in the directive. Implementation of this has also begun with particular focus on the establishment of a simpler clinical trial database (EudraCT) than originally planned and the integration of the database on suspected unexpected serious adverse reactions (SUSAR) into the Eudravigilance database
- Processing of all inspections proceeded efficiently and within the legal timeframe with those for GMP exceeding the forecasted number and those for good clinical practice (GCP) falling below. The certificate scheme for centrally approved products continued successfully and efficiently in response to over 700 requests for certificates from marketing authorisation holders
- A total of 20 quality defects were successfully coordinated by the EMEA during 2003, resulting in 4 recalls of affected batches of centrally authorised products
- Representatives of accession countries participated actively in the harmonisation work of the EMEA on GMP and GCP through participation in the meetings of the ad hoc group of inspectors on good manufacturing practice (GMP) and good clinical practice (GCP)

Inspections performed 2000-2002



4.1 Inspections

Good manufacturing practice activities

Requests for good manufacturing practice (GMP) inspections exceeded forecasts, mainly due to an increasing focus on the organisation of inspections, providing an important contribution to both the pre- and post-approval monitoring of medicinal products in the human and veterinary medicines fields.

The ad hoc group of GMP inspection services met four times in 2003, and finalised a revision to Annex 1 to the EU GMP guide. Annex 13 of the GMP Guide was published in July. Significant progress was made on several proposed new additions to the GMP guide and a position statement agreed on the professional discretion used by qualified persons releasing products that are not in full compliance with the marketing authorisation. In addition a guideline for inspectors on quality systems was completed. Significant efforts to integrate accession country representatives into the GMP related activities of EMEA were made.

Two joint sessions with the CPMP/CVMP Quality Working Party were held in order to address inspection and assessment implications of aspects of process analytical technology techniques as well as ways of improving the monitoring of ongoing quality of marketed medicinal products.

Significant input into the ICH initiative on GMP and quality systems was also provided, building on FDA initiative for “Good manufacturing practices for the 21st century”.

The year 2003 saw the successful completion of the pilot phase of a joint audit programme to assess the GMP compliance system of Member States in view of harmonising and improving the performance of European inspection services. The experience gained has allowed the development of a simplified scheme making the best use of other similar activities underway.

An apparent decrease in a number of quality related defects for centrally authorised products was noted in the first quarter of 2002 with only two quality defects received by the EMEA, resulting in the recall of affected batches of one centrally authorised product. A total of 15 defect reports were handled during the second quarter leading to three recalls of affected batches. The majority of the quality defects observer were classified as class III (minor) and related to packaging material defects (rubber particles, broken vials, leakages, etc) and labelling problems (e.g. wrong strength, wrong bar code, etc).

Progress on the GMP database developed by the EMEA in 1999 continued during 2003, in particular extending its application to other good practices, including data from GCP, GLP and pharmacovigilance inspections.

This database was originally developed to provide a management tool for GMP Inspections of centrally authorised products. In 2003, it was made accessible through the web to all EEA Member States and is now being extended to a multi-user application, allowing write-access.

Good laboratory practice activities

No good laboratory practice (GLP) inspections were requested in 2003.

Agreement was reached on a number of procedural documents at the final meeting of the ad hoc GLP working group held in October 2003.

- Procedure/SOP for requesting and reporting GLP inspections under the centralised procedure
- Format for GLP reports under the centralised procedure
- Contract between EMEA and inspecting authority for GLP inspections

Good clinical practice activities

The number of good clinical practice (GCP) inspections for human medicinal products requested, decreased significantly in 2003. This decrease reflects resource constraints at Member State level as authorities focus their resources on implementing the clinical trials directive nationally, in addition to the effect of the lower number of centralised applications received last year.

About half of the inspections requested were conducted post-authorisation on pharmacovigilance activities. This reflects the growing emphasis of European regulators on ensuring compliance of marketing authorisation holders with their pharmacovigilance obligations.

The ad hoc group of GCP inspection services met five times in 2003, one of these meetings taking the form of an off-site training session for new and experienced GCP inspectors, including inspectors from accession countries as well as EU, EEA and Switzerland. The majority of its work in 2003 has been focussed on further harmonisation activities in relation to the conduct of inspections and interpretation of GCP and pharmacovigilance data.

In addition the group has worked closely with the Mutual Recognition Facilitation Group on approaches to the assessment and inspection of the clinical investigation of bioequivalence studies of generic products. This collaboration is an important element to assure the quality of these studies.

Work has been initiated on the preparation of guidance on the use of computers in clinical trials, on inspection of phase I trials, as well as continued development of clinical trial product safety/post-marketing pharmacovigilance inspection guidance.

Procedures developed for the GCP of clinical trials in the centralised procedure applications include those for:

- Coordination of inspections
- Preparation of inspections
- Reporting of inspection
- Inspection records
- Sponsor/CRO, investigator, laboratory inspections, which were reviewed and updated during the year.

No GCP inspections for veterinary medicinal products have yet taken place.

4.2 Mutual recognition agreements

The European Commission – Canada agreement entered into force on 1 February 2003 following successful completion of all outstanding tasks. The operational phase started with an exchange of certificates of GMP compliance of a manufacturer between the Canadian and EU authorities.

The preparatory phase of the mutual recognition agreements (MRA) with Japan encountered some delays and was not completed by June 2003 as originally anticipated. Mutual visits and preparation of documents continued throughout 2003 to progress the work.

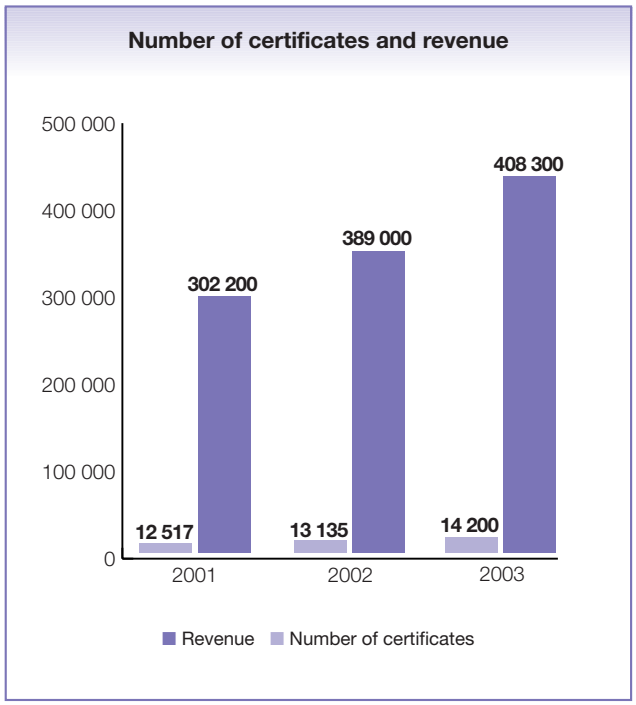
Preparation for enlargement also included the area of MRA. The European Commission – Australia, New Zealand, Switzerland MRAs will automatically extend to the new Member States. For the Canadian agreement, a new round of evaluation visits will be carried out by Health Canada and preparation of GMP inspectorates of accession countries for these visits began at the end of the year.

Mutual recognition agreement (MRA) implementation status and coverage

MRA	Implementation status	Coverage
European Commission – Australia	Human medicinal products: 1 January 1999 Veterinary medicinal products: 1 June 2001	Human and veterinary medicinal products Official batch release excluded
European Commission – Canada	Operational since 1 February 2003	Human and veterinary medicinal products Veterinary immunologicals and vaccines excluded
European Commission – Japan	1 January 2002, start of 18 months preparatory phase. Extended indefinitely to allow work to be completed.	Human medicinal products only, Currently excludes active substances, investigational medicinal products, medicinal gases Official batch release excluded
European Commission – New Zealand	Human medicinal products: 1 January 1999 Veterinary medicinal products: 1 June 2002	Human and veterinary medicinal products Official batch release excluded
European Commission – Switzerland	1 June 2002	Human and veterinary medicinal products and recognition of official batch control of biologicals
European Commission – 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 Certificates of a medicinal product

The revision of the administrative charge at the end of 2002 has had the expected effect of encouraging companies to streamline their requests for certificates thus moderating the number of requests and consequently the administrative work on the side of the EMEA. Reflecting the new arrangements, the demand for certificates was unstable during 2003, with higher requests seen in the first half of the year but significantly lower demand during the second half of the year.



4.4 Implementation of the clinical trials directive

Preparations for the implementation of Directive 2001/20/EC on the conduct of clinical trials continued in 2003. The GMP inspectors' group started work on a concept paper for GMP for investigational medicinal products used in gene and cell therapy and prepared modifications to the batch certificate and GMP certificate forms to reflect the possibility of including investigational medicinal products.

The harmonisation and training activities of the GCP inspectors' group are fundamental to the mutual recognition of GCP inspections between member states.

EMEA continued to participate actively in the European Commission working party on the preparation of other documents needed under the Directive, in particular, as rapporteur for the guidance documents on the European database on clinical trials (EudraCT) and on the European database of SUSARs (Eudravigilance clinical trial module). The texts of these guidance documents were finalised and published in July 2003.

In addition EMEA has drafted design and specification documents and begun work on the projects to implement the clinical trial database and the clinical trial part of the EudraVigilance database. As part of this work, the EMEA provided support to the first two Technical Implementation Groups on the EudraCT database, chaired by Spain in the third quarter of 2003.

4.5 Sampling and testing

Monitoring of centrally authorised medicinal products is performed by the Network of Official Medicines Control Laboratories. The activities of the network are coordinated by the European Directorate of the Quality of Medicines (EDQM) and the EMEA. The 2003 testing programme was implemented for 38 centrally authorised products.

A seminar involving all stakeholders in the programme was organised in the EMEA in September 2003. Over 50 participants attended from national competent authorities, official control laboratories, inspectorates, accession countries and industry. This was an important occasion, providing the first opportunity since the launch of the programme in 1999 for all partners to have an open discussion and provide feedback on current processes. The issues raised during discussion will be addressed in an action plan and be reflected as changes to subsequent programmes.

Chapter 5
EU telematics strategy

The direction of the implementation of the EU telematics strategy during 2003 was changed following a meeting of the Telematics Steering Committee in Verona in July 2003. The strategy changed from a sequential approach involving beginning and completing a small number of projects before embarking upon a second wave, to a slower implementation across the whole spectrum of projects.

The achievements during 2003 have been as follows:

Initiatives	Achievements
EudraNet	The EMEA successfully assumed responsibility for the service with effect from 1 January 2003 EudraLink was successfully launched in January 2003. Take-up has been good, and the service now has approximately 1 600 registered users from the regulatory authorities and other stakeholders in the regulatory system A project to define and implement a security infrastructure that meets the requirements of all the stakeholders in the regulatory system and which will be common to all Eudra systems has been initiated. The requirements gathering exercise, together with analysis thereof, has been completed Testing of an IP/VPN infrastructure in comparison with the service using the existing structure has been completed during the year EudraWorkSpace has been installed in pilot form at the Agency. The form and extent of its deployment is currently being reviewed
EuroPharm	Agreement on a pan-European reference data model is nearly complete. The reference data model will need to be extended as work on EuroPharm over its entire scope progresses A limited prototype has been built for demonstration to interested parties over the early part of 2004 A contract for the specification of the system was put in place
EudraVigilance	The principal achievement during the year was to extend the system to include reports relating to medicinal products for veterinary use

Cont...

Initiatives	Achievements
Electronic submission	The first phase of the implementation of the electronic common technical document (eCTD) at the EMEA is complete, and the first full submission using the eCTD (in parallel with the paper submission) has been received and processed. One variation has also been received in eCTD format and processed, again in parallel with the paper submission A contract for a review solution that is available for all competent authorities in the EU is in place, and the system is installed at the EMEA and two of the national competent authorities. The system is being used to refine the reviewers' requirements over 2004 The Product Information Management (PIM) proof of concept was completed, and further work on the exchange standard, based on the proof of concept experience, was carried out. A contract for the specification of a system for the Agencies was put in place
Clinical trials databases	Both the clinical trials database and the EudraVigilance clinical trials module were specified, and contractors started work on developing the two databases
Infrastructure	Projects have been accompanied with appropriate infrastructure. Work on defining the architecture underlying, and binding together, the collection of Eudra projects is complete Project management staffing has been increased over 2003 to provide appropriate resources to take the projects forward in 2004. This situation was only achieved in the third and fourth quarters of 2003

Chapter 6
Support activities

6.1 Administration

The following specific objectives were achieved and projects carried out in 2003:

- Introduction of the new financial regulation, with revision of related procedures
- Continuous information to staff on the proposed new staff regulation and participation in preparatory conferences with the European Commission
- Further development of the computer-based personnel data and management system
- Development of an improved activity based budgeting database and budgetary planning
- Participation in the preparation of a concept for a new legislative base for the future financing of the agency
- Preparation for refurbishment of the 4th, 5th and 8th floor to accommodate new staff, the telematics projects and delegates and experts from the new member states; refurbishment of 8th floor was practically accomplished in 2003
- Expansion of the training programme and development of a competence development scheme for all staff
- Preparation of new and modified accounting practices in line with the reform of the EU accounting system

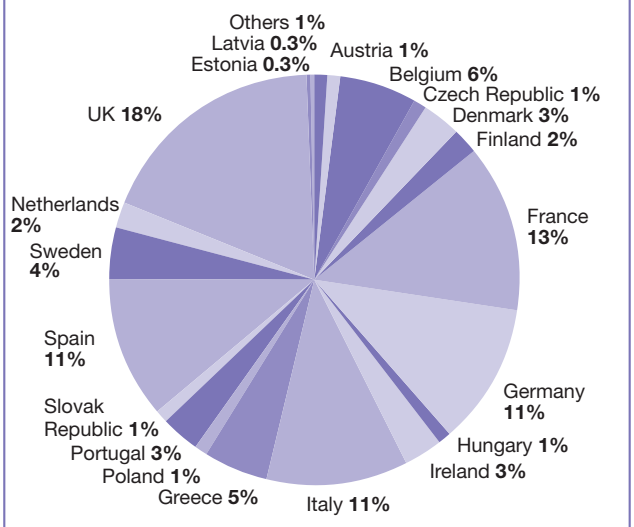
Personnel and budget

The principal objectives of the Personnel and Budget Sector are the development and timely and accurate management of EMEA human and financial resources, including recruitment procedures and professional training, as well as the provision of information to staff and other concerned persons on these matters. All the above objectives were achieved and further developed with a view to the specific projects mentioned below.

Specific Projects

- The new Financial Regulation with revision of procedures and staff training was successfully introduced and implemented
- The system of activity based budgeting was further developed and refined as well as adapted to the specific work environment of the agency
- An expanded professional training programme directed towards a continuous system of competence development was set up and will be put into practice in the coming year
- The 2003 budget was successfully implemented through regular monitoring, regular contacts and meetings with the scientific units and the European Commission and continuous and cautious adaptations through transfers and one amending budget; principles of sound financial management were applied
- The 2004 draft budget was reviewed as compared to the preliminary draft budget of February 2003 and the 2005 preliminary draft budget was prepared
- Contacts were established with the budgetary authority for the 2002 discharge procedure
- Together with the scientific units a harmonised system for the financial processing of fees was set up and successfully introduced
- Following a thorough preparatory phase an internal policy for part-time working was introduced respecting the prerogatives of the staff regulations on the one side and the specific work environment of the EMEA on the other
- The policy for movement between categories was introduced and successfully applied
- A set of guidelines for a ‘family friendly policy’ has been set up and implemented successfully

EMEA staff members by nationality in 2003



Accounts

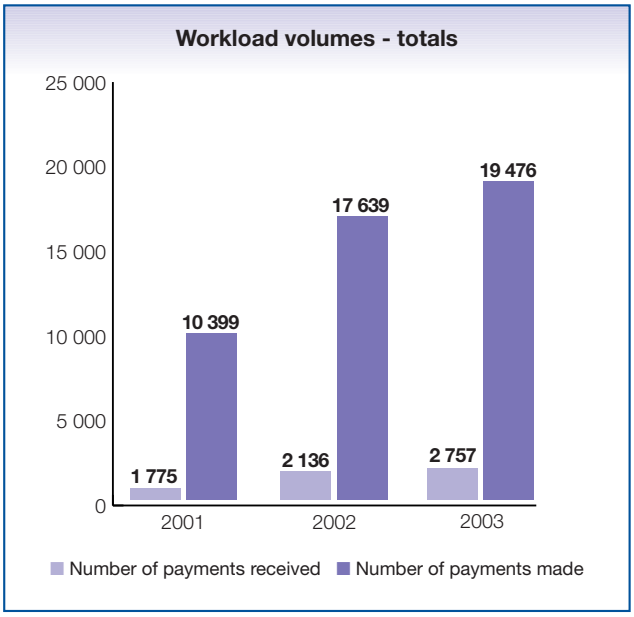
General Objectives

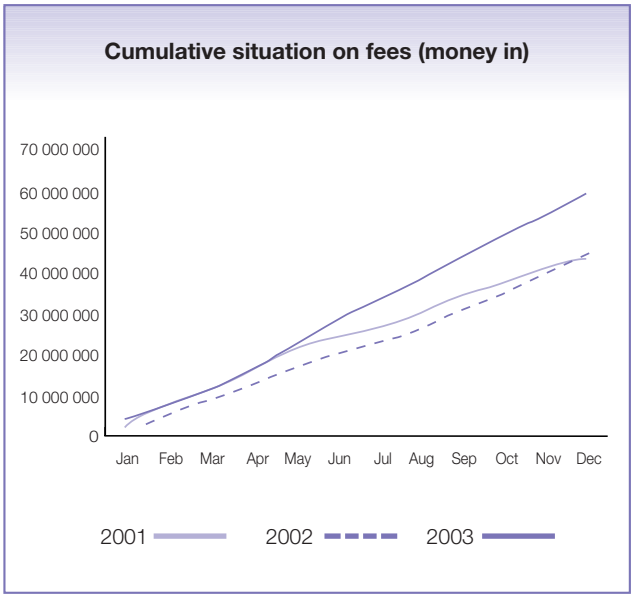
- To maintain the accounts, make payments and collect revenue in accordance with the procedures laid down in the financial regulation
- Overall this objective is achieved and no significant matters have been raised by either internal or external audits
- To manage efficiently the cash resources of the agency including the relationship with the agency's banks
- By use of the forward contract facility Euros were sold forward to purchase pounds whenever the rate was significantly above the budget rate. This activity is carried out in accordance with the approved EMEA policy. The EMEA's Sterling needs are covered through the end of June 2004
- To provide accurate, timely financial information to management
- The timeliness of the budgetary accounting reporting slipped in the earlier months. This has been addressed and specific deadlines have been put in place

Specific Objectives

- Internal procedures were improved with regard to the cooperation with the operational sectors and by external communication with pharmaceutical companies
- The customer accounting module was developed as planned
- Si2/SAGE/Lloydslink integration
- This project has been accelerated on completion of the Si2 upgrade in 2002. The Si2 /Lloydslink Bulkload interface was completed and is fully operational
- The Accounts Sector contributed where appropriate to the drafting of the new financial regulation, which was implemented from 1 July 2003
- The new version of Si2 complying with the new financial regulation was installed in August
- The ActiTrak system for the cost analysis of EMEA staff and activities has been revised and overhauled both to reflect a changed pattern of activity and to support the activity based budgeting as an instrument for planning
- Cooperation with the Court of Auditors for the 2002 budget was successfully conducted

Workload

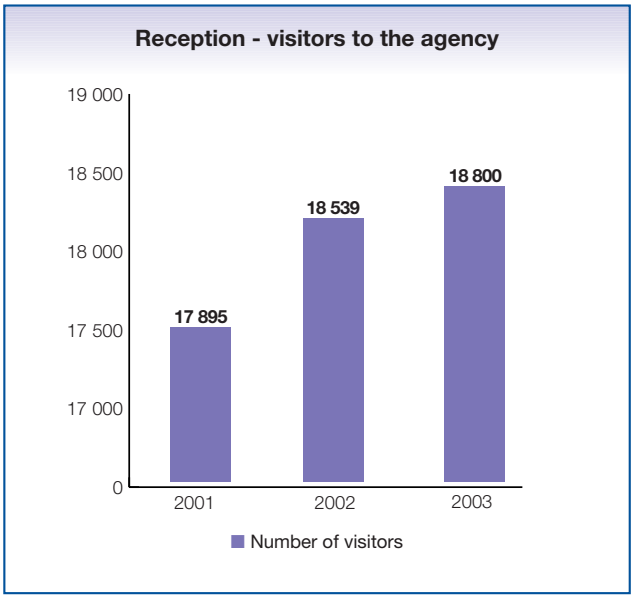




Infrastructure services

Specific Objectives:

- In preparation for the ten new Member States a tender was launched for the refurbishment of the 4th floor to increase the number of offices for the delegations
- Business continuity planning and disaster recovery. The business continuity plan was completed and all Units and Sectors prepared telephone cascades. A tender for a business continuity supplier to provide the EMEA with a disaster recovery site were prepared. A disaster recovery company has been identified to manage the telephone calls to the Agency for contingency purposes
- The function of a contract manager was introduced at the end of 2003. The contract manager will have a horizontal function in that she will be responsible for the supervision, organisation and conclusion of EMEA contracts with third parties
- Acquisition of additional office space. This year has seen the acquisition of the 8th floor of 7 Westferry Circus and the consequent publication of a tender for the fitting out of this floor with offices, IT training room and a computer room
- Award of contract for off-site archiving. A new contract was awarded for off-site archiving and ISERV oversaw the move of all the archive storage boxes to the new location



6.2 IT and project management at the EMEA

IT Sector

Major refurbishments and upgrades to the IT infrastructure were carried out at the EMEA in 2003. A new data storage system and a range of infrastructure facility enhancements were introduced for all delegates to improve the progress of meetings. These facilities include secure remote access to mail systems using Internet browser technology, video streaming and wireless LAN connections in meeting rooms.

The requirements and IT solution for business continuity and disaster recovery were defined and documented. The preparatory stages for the provision of new 8th floor computer room facilities were also completed. These facilities will provide high availability and back-up to the existing services currently made available from the 4th floor computer room. The dual computer room environment will provide appropriate levels of business continuity in the event of failures, which is essential for the EU telematics services being provided to both the EU regulatory authorities and industry. This major undertaking begun in 2003 will eventually lead to the creation of a second off-site IT infrastructure, mirroring mission-critical data and applications.

IT preparation for enlargement has had a major impact on the Sector workload in 2003, as telematics services must be made available to accession countries prior to 1 May 2004. Detailed planning and preparation with all new accession country institutions has taken place through the EudraNet telematics implementation group (TIG) in 2003, which the EMEA chairs.

EMEA core applications

The IT Sector maintained high levels of IT services throughout 2003, with more than 99.5 % service availability. The EMEA help desk handled over 3 000 calls during the year.

The development of core applications continued, including the launch of the second module of the Meetings Management System (MMS) and continuation of the EMEA tracking systems development (SIAMED). Other applications that were further developed included the personnel database, SI2 and ActiTrak.

An area of key importance to the EMEA in 2003 was the implementation of secure communication systems. Several projects were undertaken during the year and remote access facilities were provided to a selected range of internal EMEA and EU Regulatory Authorities users. The Sector also provided support throughout 2003 to the EudraVigilance application. All European initiatives and activities were in line with the EU Telematics strategy (see chapter 5).

The IT Sector took over the coordination and management of EudraNet and was heavily involved in a range of Eudra IT projects in the pharmaceutical sector. The IT Sector provided full helpdesk facilities for EudraNet and maintained high levels of service availability, handling over 100 issues of a detailed technical nature during the year.

In January 2003, the EudraLink application was launched to replace EudraSafe. This application was very successful and allows secure encrypted message delivery between EMEA, Member State Agencies and Industry. The application is based on “open source” products and has had a very large uptake, with over 1 600 users from EMEA, Member State Agencies and Industry using the service in November 2003. The IT Sector also provided full helpdesk, training and account management facilities for EudraLink and maintained high levels of service availability, handling over 2 400 calls during the year.

Project management sector

The project management sector approached its planned staffing levels towards the end of the year. Its workload comprised EU telematics projects (further described in chapter 5), the logistical support for the Pan-European Forum on Pharmaceuticals (PERF), and involvement in the implementation of the electronic document management system in the Agency.

The progress of the project to implement an electronic document management system was evaluated during the year. The business case was examined and enforced, the requirements were assessed with the users, and the focus of the implementation re-oriented. A new roll-out plan has been drawn up for the Agency.

6.3 Meeting management and conferences

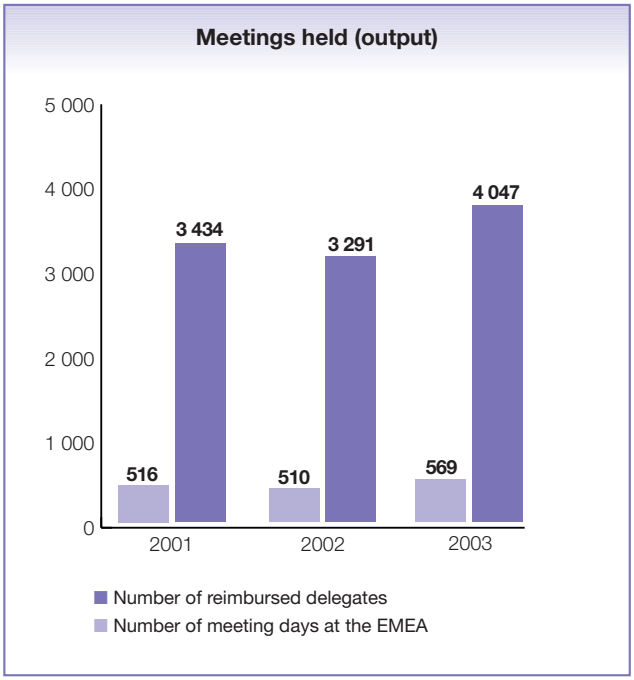
Meeting activities increased compared to 2002, as the number of meetings organised by the EMEA excluding PERF meetings increased by 22 % (from 317 to 386). The number of meeting days also increased by 12 % (from 510 to 569). Interpretation days were reduced by 4 % (239 days in 2003 compared to 251 days in 2002), as interpretation was tailored to meet needs. A service level agreement was signed by the EMEA with the European Commission Joint Interpretation and Conference Service in order to better define interpretation requirements.

The workload of the sector increased by a further 20 % due to the following factors: increased number of delegates using the EMEA travel and hotel services; increased requirement for assistance to delegates; participation by representatives of New Member States in meetings as observers.

To meet the 20 % increase in travel bookings (over 3 000 bookings) expected in 2003, as well as reducing the travel management cost, a travel agency implant was set up at the EMEA premises in mid-2003, in order to streamline the booking process and the billing requirements, especially in preparation for the enlargement.

A total of 4 047 delegate visits were reimbursed, leading to an 11 % increase of expenditure compared to 2002.

Sector Activities



A task force was set up to coordinate the participation of New Member States representatives in meetings as observers since 17 April 2003 and to assess the impact of the enlargement of the European Union in order to ensure that the resulting technical and logistical requirements are taken into account.

Refurbishment of delegate offices began in 2003 to accommodate representatives from the 10 new Member States after enlargement on 1 May 2004. The plans were drawn up after consultation with delegates.

The Sector played a role in facilitating relations with the Agency's partners through the provision of videoconferencing facilities, teleconferencing and a new pilot project to broadcast meetings of scientific committees to national authorities to allow better input from experts. A video streaming/video conferencing feasibility report was prepared and activities were developed according to plan.

6.4 Document management and publishing

Document management

Documentum, the electronic document management system selected for implementation at the Agency, was subject to an external audit during the first half of 2003. As a result a number of activities, such as the review of user specification requirements were carried out in order to clarify and improve the project as a whole. The management of the project was transferred to a full-time project manager recruited in the Project management Sector.

Quality and coherence of regulatory documents

In the context of the enlargement of the European Union, the implications of the automatic extension of European Commission decisions granting marketing authorisations for medicinal products to the 10 new Member States on the date of accession were examined. A major consequence is the volume of translation work implicit in the requirement that product information be available in all the official languages of the European Union. In order to address this burden, it was agreed that such translations would be provided during the next regulatory transaction (e.g. variation or notification procedure) under a process know as the 'common procedure'. Availability of these translated annexes will be an essential requirement to proceed with ongoing regulatory activities for existing centrally approved products and new applications after the accession date.

It was further proposed that pre-accession checks also be carried out in order to avoid peaks of activity both for regulators and industry, thereby enabling a more phased approach. In this way, delays in the supply of affected medicinal products in new Member States after EU enlargement will be avoided, and the circulation of such products with sub-standard product information translations will be prevented, thereby addressing potential public health concerns.

The EMEA therefore set up a 'pre-accession linguistic review process' to coordinate the review of the translations of the product information of the 195 human and 42 veterinary centrally authorised products in the 9 new EU languages. In order to be able to finance this specific exercise, and in particular, in order to support the work of the new Member States, the EMEA has put in place an administrative fee for this work.

Annexes

1. Members of the Management Board
2. Members of the Committee for Proprietary Medicinal Products
3. Members of the Committee for Veterinary Medicinal Products
4. Members of the Committee for Orphan Medicinal Products
5. National competent authority partners
6. EMEA budgets 2001 to 2003
7. CPMP opinions in 2003 on medicinal products for human use
8. CVMP opinions in 2003 on medicinal products for veterinary use
9. COMP opinions in 2003 on designation of orphan medicinal products
10. EMEA guidelines in 2003
11. Arbitration and Community referrals overview 2003
12. EMEA contact points and reference documents

Annex 1

Members of the Management Board

Chairman:	Philippe DUNETON[1]
EMEA contact:	Martin HARVEY ALLCHURCH

Members

European Parliament	Gianmartino BENZI, José-Luis VALVERDE LÓPEZ
	Alternates: Dietrich HENSCHLER, Jean-Pierre REYNIER
European Commission	Jean-Paul MINGASSON, Fernand SAUER
	Alternates: Paul WEISSENBERG, Patricia BRUNKO
Belgium	Johan van CALSTER[2], Lionel LAURIER[3]
Denmark	IB VALSBORG, Jytte LYNGVIG[4] *(vice-chairman)*
Germany	Walter SCHWERDTFEGER[5], Ilse-Dore SCHÜTT[6]
Greece	Charalambos SAVAKIS[7], Thrasyvoulos KEFALAS[8]
Spain	Fernando GARCIA ALONSO, Carlos LENS CABRERA
France	Martin HIRSCH
Ireland	Tom MOONEY, Paddy ROGAN
Italy	Nello MARTINI, Gaetana FERRI
Luxembourg	Mariette BACKES-LIES, Claude A HEMMER
Netherlands	Huib VAN DE DONK[9], Frits PLUIMERS[10]
Austria	Christian KALCHER, Robert SCHLÖGEL
Portugal	Rui dos SANTOS IVO, Manuel NEVES DIAS
Finland	Pekka JÄRVINEN, Hannes WAHLROOS
Sweden	Birgitta BRATTHALL, Anders BROSTRÖM
United Kingdom	Roy ALDER, Steve DEAN

Observers

Iceland	Rannveig GUNNARSDÓTTIR, Ingolf J PETERSEN
Liechtenstein	Brigitte BATLINER, Peter MALIN
Norway	Kai FINSNES , Gro Ramsten WESENBERG

1 Replaced Keith Jones as of December 2003 meeting.
2 Replaced André PAUWELS as of June 2003 meeting.
3 Replaced Frans GOSSELINCKX as of June 2003 meeting.
4 Elected at December 2003 meeting replacing Philippe Duneton as vice-chairman.
5 Replaced Hans-Peter HOFMANN as of October 2003 meeting.
6 Replaced Gerhard Josef KOTHMANN as of February 2003 meeting.
7 Replaced Michalis MARAGOUDAKIS as of June 2003 meeting.
8 Replaced Elias MOSSIALOS as of December 2003 meeting.
9 Resigned as of June 2003 meeting; no replacement nominated.
10 Resigned as of December 2003 meeting; no replacement nominated.

Annex 2

Members of the Committee for Proprietary Medicinal Products

Chair: Daniel BRASSEUR

EMEA contact: Anthony HUMPHREYS

Members

- Eric ABADIE (France) *(vice-chairman)*
- Mark AINSWORTH (Denmark)
- George AISLAITNER (Greece)
- Fernando de ANDRES-TRELLES (Spain)
- Michalis AVGERINOS (Greece)
- Gonzalo CALVO ROJAS (Spain)
- Jens ERSBØLL (Denmark)
- Bruno FLAMION (Belgium)
- Silvio GARATTINI (Italy)
- Jacqueline GENOUX-HAMES (Luxembourg)
- Lars GRAMSTAD (Norway)
- Manfred HAASE (Germany)
- Ian HUDSON[3] (United Kingdom)
- Magnús JÓHANNSSON (Iceland)
- Pekka KURKI (Finland)
- Frits LEKKERKERKER (Netherlands)
- David LYONS (Ireland)
- Pieter NEELS (Belgium)
- Per NILSSON (Sweden)
- Tilmann OTT[1] (Germany)
- Heribert PITTNER (Austria)
- Jean-Louis ROBERT (Luxembourg)
- Pasqualino ROSSI (Italy)
- Frances ROTBLAT[2] (United Kingdom)
- Patrick SALMON (Ireland)
- Tomas SALMONSON (Sweden)
- Cristina SAMPAIO (Portugal)
- Beatriz SILVA LIMA (Portugal)
- Eva SKOVLUND (Norway)
- Josef SUKO (Austria)
- Sigurdur THORSTEINSSON (Iceland)
- Markku TOIVONEN (Finland)
- Jean-Hugues TROUVIN (France)
- Barbara VAN ZWIETEN-BOOT (Netherlands)

1 Replaced Rolf BASS as of September 2003 meeting.
2 Replaced Peter ARLETT as of September 2003 meeting.
3 Replaced Alex NICHOLSON as of November 2003 meeting.

Working parties and ad hoc groups

Biotechnology working party (CPMP BWP)
Chair: Jean-Hugues TROUVIN
EMEA contact: John PURVES

Blood products working group (CPMP BPWP)
Chair: Manfred HAASE
EMEA contact: John PURVES

Efficacy working party (CPMP EWP)
Chair: Barbara VAN ZWIETEN-BOOT
EMEA contact: Isabelle MOULON

Herbal medicinal products working party (CPMP HMPWP)
Chair: Konstantin KELLER
EMEA contact: Anthony HUMPHREYS

Pharmacovigilance working party (CPMP PhVWP)
Chair: Anne CASTOT (acting)
EMEA contact: Panos TSINTIS

Safety working party (CPMP SWP)
Chair: Beatriz SILVA LIMA
EMEA contact: Isabelle MOULON

Joint CPMP/CVMP quality working party (CPMP/CVMP QWP)
Chair: Jean-Louis ROBERT
EMEA contact: Emer COOKE

Scientific advice working group (CPMP SAWG)
Chair: Markku TOIVONEN
EMEA contact: Agnès SAINT RAYMOND

Ad hoc expert group on cell therapy
Chair: Pekka KURKI
EMEA contact: John PURVES

Ad hoc groups on chemical threats
Chair: Thomas SALMONSON
EMEA contact: Isabelle MOULON

Ad hoc working group on (pre) clinical comparability of biotechnology products
Chair: Pekka KURKI
EMEA contact: Isabelle MOULON

Ad hoc expert group on gene therapy (CPMP GTEG)
Chair: Klaus CICHUTEK
EMEA contact: Marisa PAPALUCA AMATI

Paediatric expert group (CPMP PEG)
Chair: Daniel BRASSEUR
EMEA contact: Agnès SAINT RAYMOND

Ad hoc expert group on pharmacogenetics
Chair: Eric ABADIE
EMEA contact: Marisa PAPALUCA AMATI

Vaccine expert group (CPMP VEG)
Chair: Roland DOBBELAER
EMEA contact: John PURVES

Therapeutic advisory group on anti-infectives
Chair: Bjarne ORSKOV LINDHARDT
EMEA contact: Isabelle MOULON

Therapeutic advisory group on diagnostics
Chair: To be appointed
EMEA contact: Panos TSINTIS

Therapeutic advisory group on oncology
Chair: Michel MARTY
EMEA contact: Isabelle MOULON

Working group with patients organisations
Chair: Frits LEKKERKERKER/Noël WATHION
EMEA contact: Isabelle MOULON

Annex 3

Members of the Committee for Veterinary Medicinal Products

Chair: Gérard MOULIN

EMEA contact: Peter JONES

Members

- Margarita ARBOIX (Spain)
- J. Gabriel BEECHINOR (Ireland)
- Hanne BERGENDAHL (Norway)
- Marie-Anne BOTREL (France)
- Rory BREATHNACH (Ireland)
- Ivo CLAASSEN[1] (Netherlands)
- Ricardo de la FUENTE (Spain)
- Johannes DICHTL (Austria)
- Virgilio DONINI (Italy)
- Françoise FALIZE (Belgium)
- Christian FRIIS (Denmark)
- Helle HARTMANN FRIES (Denmark)
- Johannes HOOGLAND (Netherlands), *(vice-chairman)*
- Tonje HØY (Norway)
- Martin ILOTT[2] (United Kingdom)
- Eva FABIANSON-JOHNSSON (Sweden)
- Liisa KAARTINEN (Finland)
- Reinhard KROKER (Germany)
- Jan LUTHMAN (Sweden)
- Agostino MACRI (Italy)
- Ioannis MALEMIS (Greece)
- Eduardo MARQUES FONTES (Portugal)
- Maria Leonor MEISEL (Portugal)
- Manfred MOOS (Germany)
- John O'BRIEN (United Kingdom)
- Eugen OBERMAYR (Austria)
- Sigurdur ÖRN HANSSON (Iceland)
- Orestis PAPADOPOULOS (Greece)
- Halldór RUNÓLFSSON (Iceland)
- Jean-Claude ROUBY (France)
- Liisa SIHVONEN (Finland)
- Bruno URBAIN (Belgium)
- Marc WIRTOR (Luxembourg)

1 Replaced Herman LENSING as of April 2003 meeting

2 Replaced David MACKAY as of December 2003 meeting

Working parties and ad hoc groups

Efficacy working party (CVMP EWP)
Chair: Liisa KAARTINEN
EMEA contact: Jill ASHLEY-SMITH

Immunologicals working party (CVMP IWP)
Chair: Orestis PAPADOPOULOS[1]
EMEA contact: Jill ASHLEY-SMITH

Pharmacovigilance working party (CVMP PhVWP)
Chair: Cornelia IBRAHIM
EMEA contact: Kornelia GREIN

Joint CPMP/CVMP quality working party (CPMP/CVMP QWP)
Chair: Jean-Louis ROBERT
EMEA contact: Emer COOKE

Safety working party (CVMP SWP)
Chair: Christian FRIIS
EMEA contact: Kornelia GREIN

Ad hoc group on antimicrobial resistance (CVMP AGAR)
Chair: Margarita ARBOIX
EMEA contact: Kornelia GREIN

Ad hoc group on environmental risk assessment (CVMP AHGERA)
Chair: Hans HOOGLAND
EMEA contact: Kornelia GREIN

1 Replaced David MACKAY as of December 2003 meeting.

Annex 4

Members of the Committee for Orphan Medicinal Products

Chair: Josep TORRENT i FARNELL

EMEA contact: Agnès SAINT RAYMOND

Members

- Eric ABADIE (EMEA representative)
- Gianmartino BENZI (EMEA representative)
- Heidrun BOSCH-TRABERG (Denmark)
- Birthe BYSKOV HOLM[1] (patient organisation representative)
- Rembert ELBERS (Germany)
- José Manuel GIÃO TOSCANO RICO (Portugal)
- Lars GRAMSTAD[2] (Norway)
- Emmanuel HERON[4] (France)
- Kalle HOPPU (Finland)
- Bernd JILMA (Austria)
- Alastair KENT (patient organisation representative)
- Yann LE CAM (patient organisation representative), *(vice-chairman)*
- André LHOIR (Belgium)
- David LYONS (EMEA representative)
- José Félix OLALLA MARAÑÓN (Spain)
- Henri METZ (Luxembourg)
- Harrie SEEVERENS (The Netherlands)
- Rashmi SHAH (United Kingdom)
- George SHORTEN[3] (Ireland)
- George STATHOPOULOS (Greece)
- Domenica TARUSCIO (Italy)
- Sigurdur THORSTEINSSON (Iceland)
- Kerstin WESTERMARK (Sweden)

Working parties and ad hoc groups

Ad-Hoc biotechnology working group (COMP BWG)

Chair: Harrie SEEVERENS/Jean-Hugues TROUVIN

EMEA contact: Agnès SAINT RAYMOND

Prevalence ad-hoc working group

Chair: Kalle HOPPU

EMEA contact: Agnès SAINT RAYMOND

Working group with interested parties (COMP WGIP)

Chair: Yann LE CAM/Agnès SAINT RAYMOND

EMEA contact: Agnès SAINT RAYMOND

1 Replaced Moisés ABASCAL ALONSO as of May 2003 meeting.
2 Replaced Randi NORDAL as of May 2003 meeting.
3 Replaced Brendan BUCKLEY as of November 2003 meeting.
4 Replaced François MEYER as of May 2003 meeting.

Annex 5

National competent authority partners

Further information on the national competent authorities is also available on the national authorities' Internet sites: *http://heads.medagencies.org* and *http://www.hevra.org*

BELGIUM

Johan van CALSTER

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Annex 6

EMEA budget summaries 2002 – 2004

The summarised comparative budget statements for 2002 to 2004 are as follows: (*Amounts expressed in euro)*

	2002[1] (31.12.2002)		2003[2] (31.12.2003)		2004[3] (18.12.2003)	
Revenue						
Fees	39 000 000	63.61 %	56 742 000	67.41 %	64 800 000	67.08 %
General EU contribution	17 135 000	27.95 %	12 300 000	14.61 %	17 500 000	18.11 %
Special EU contribution for IT telematics strategy	--	-	7 000 000	8.32 %	7 500 000	7.76 %
Special EU contribution for orphan medicinal products	2 750 000	4.49 %	3 100 000	3.68 %	3 500 000	3.62 %
Contribution from EEA	366 000	0.60 %	558 000	0.66 %	573 000	0.59 %
Contribution from EU programmes (PERF)	213 000	0.35 %	1 530 000	1.82 %	p.m.	0.00 %
Other	1 840 000	3.00 %	2 949 000	3.50 %	2 746 000	2.84 %
TOTAL REVENUE	**61 304 000**	**100.00 %**	**84 179 000**	**100.00 %**	**96 619 000**	**100.00 %**
Expenditure						
Staff						
Salaries	24 337 000	39.70 %	27 352 500	32.49 %	32 596 000	33.74 %
Interim and other support persons	1 760 000	2.87 %	1 845 000	2.19 %	2 046 000	2.12 %
Other staff-related expenditure	1 502 000	2.45 %	2 355 500	2.80 %	2 493 000	2.58 %
Total title 1	*27 599 000*	*45.02 %*	*31 553 000*	*37.48 %*	*37 135 000*	*38.44 %*
Building/equipment						
Rent/charges	5 526 000	9.01 %	5 686 000	6.76 %	5 670 000	5.87 %
Expenditure on data processing	3 083 000	5.03 %	9 517 000	11.31 %	8 209 000	8.50 %
Other capital expenditure	491 000	0.80 %	1 959 000	2.33 %	1 737 000	1.80 %
Postage and communications	264 000	0.43 %	418 000	0.50 %	505 000	0.52 %
Other administrative expenditure	2 043 000	3.33 %	2 075 000	2.46 %	2 780 000	2.88 %
Total title 2	*11 407 000*	*18.60 %*	*19 655 000*	*23.35 %*	*18 901 000*	*19.56 %*
Operational expenditure						
Meetings	3 535 000	5.77 %	3 946 800	4.70 %	8 835 000	9.14 %
Evaluations	17 855 500	29.14 %	26 810 800	31.85 %	30 075 000	31.13 %
Translation	477 000	0.78 %	701 000	0.83 %	1 375 000	1.42 %
Studies and consultants	98 500	0.16 %	27 000	0.03 %	50 000	0.05 %
Publications	119 000	0.19 %	78 000	0.09 %	248 000	0.26 %
EU programmes	213 000	0.34 %	1 407 400	1.67 %	p.m.	0.00 %
Total title 3	*22 298 000*	*36.38 %*	*32 971 000*	*39.17 %*	*40 583 000*	*42.00 %*
TOTAL EXPENDITURE	**61 304 000**	**100.00 %**	**84 179 000**	**100.00 %**	**96 619 000**	**100.00 %**

Notes

1 Final appropriations for the 2002 budget. 2 Final appropriations for the 2003 budget.
3 Budget for 2004 as adopted by the Management Board on 18.12.2003.

Annex 7

CPMP opinions in 2003 on medicinal products for human use

Positive CPMP opinions

Product • Brand name • INN • Part A or B	Marketing authorisation holder	Therapeutic area • ATC code • Summary of indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Aldurazyme#** • **laronidase** • **Part A**	Genzyme BV	• A16AB05 • Enzyme replacement therapy in patients with Mucopolysaccharidosis I (MPS I; a-L-iduronidase deficiency)	• 26.3.2002 • 20.2.2003 • 205 days • 119 days	• 8.4.2003 • 10.6.2003 • 12.6.2003 • OJ C 153, 1.7.2003, p. 2
• **Fuzeon** • **enfuvirtide** • **Part B**	Roche Registration Ltd	• J05A X (pending) • Treatment of HIV-1 infection in combination with other antiretroviral agents.	• 21.10.2002 • 19.3.2003 • 139 days • 9 days	• 15.4.2003 • 27.5.2003 • 29.5.2003 • OJ C 153, 1.7.2003, p. 2
• **Busilvex#** • **busulfan** • **Part B**	Pierre Fabre Medicament	• L01AB01 • Treatment prior to conventional haematopoietic progenitor cell transplantation (HPCT)	• 26.3.2002 • 19.3.2003 • 173 days • 180 days	• 7.5.2003 • 9.7.2003 • 11.7.2003 • OJ C 176, 25.7.2003, p. 2
• **Humira** • **adalimumab** • **Part A**	Abbott Laboratories	• L04AA • Treatment of moderate to severe, active rheumatoid arthritis in adult after inadequate response to disease-modifying anti-rheumatic drugs including methotrexate	• 22.4.2002 • 22.5.2003 • 181 days • 209 days	• 10.7.2003 • 1.9.2003 • 3.9.2003 • OJ C 230, 26.9.2003, p. 5
• **Trudexa** • **adalimumab** • **Part A**	Abbott Laboratories	• L04AA • Treatment of moderate to severe, active rheumatoid arthritis in adult after inadequate response to disease-modifying anti-rheumatic drugs including methotrexate	• 22.4.2002 • 22.5.2003 • 181 days • 209 days	• 10.7.2003 • 1.9.2003 • 3.9.2003 • OJ C 230, 26.9.2003, p. 5
• **Ventavis#** • **iloprost** • **Part B**	Schering AG	• B01AC • Treatment of patients with primary pulmonary hypertension, classified as NYHA functional class III	• 28.1.2002 • 22.5.2003 • 209 days • 265 days	• 9.7.2003 • 16.9.2003 • 18.9.2003 • OJ C 262, 31.10.2003, p. 2
• **Onsenal#** • **celecoxib** • **Part B**	Pharmacia-Pfizer EEIG	• L01XX • Indicated for the reduction of adenomatous intestinal polyps in familial adenomatous polyposis (FAP), as an adjunct to surgery	• 20.11.2001 • 26.6.2003 • 208 days • 369 days	• 12.8.2003 • 17.10.2003 • 22.10.2003 • OJ C 285, 28.11.2003, p. 5
• **Omnitrop** • **somatropin** • **Part A**	Sandoz GmbH	• H01AC01 • Treatment of growth hormon deficiency	• 22.5.2001 • 26.6.2003 • 210 days • 544 days	

# Denotes an orphan medicinal product designated under Regulation (EC) No 121/2000

Product • Brand name • INN • Part A or B	Marketing authorisation holder	Therapeutic area • ATC code • Summary of indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Avandamet** • **rosiglitazone / metformin** • **Part B**	SmithKline Beecham plc	• A10BH01 • Treatment of type 2 diabetes mellitus, particularly overweight patients unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone	• 21.10.2002 • 26.6.2003 • 178 days • 67 days	• 14.08.2003 • 20.10.2003 • 22.10.2003 • OJ C 285, 28.11.2003, p. 5
• **Stalevo** • **levodopa, carbidopa, entacapone** • **Part B**	Orion Corporation	• N04BA03 • Treatment of patients with Parkinson's disease and end-of-dose motor fluctuations not stabilised on levodopa.dopa decarboxylase (DDC) inhibitor treatment	• 23.9.2002 • 26.6.2003 • 194 days • 79 days	• 12.8.2003 • 17.10.2003 • 22.10.2003 • OJ C 285, 28.11.2003, p. 5
• **Dukoral** • **vibrio cholerae and recombinant cholera toxin B-submit** • **Part A**	SBL Vaccin AB	• J07AE01 • Immunisation against Vibrio cholerae serogroup O1 in adults and children from 2 years of age visiting endemic epidemic areas	• 23.3.2002 • 24.7.2003 • 201 days • 277 days	• 10.9.2003
• **Xagrid#** • **anagrelide** • **Part B**	Shire Pharmaceutical Contracts Ltd	• L01X • Reduction of elevated platelet in at risk essential thrombocythaemia	• 22.4.2002 • 24.7.2003 • 181 days • 271 days	
• **Emtriva** • **emtricitabine** • **Part B**	Triangle Pharma Ltd	• JO5AF09 • Treatment of HIV-1 infection in combination with other antiretroviral agents	• 6.1.2003 • 24.7.2003 • 170 days • 28 days	• 10.9.2003 • 24.10.2003 • 28.10.2003 • OJ C 285, 28.11.2003, p. 5
• **Emend** • **aprepitant** • **Part B**	Merck Sharp & Dohme	• A04A • Prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy	• 18.11.2002 • 24.7.2003 • 182 days • 64 days	• 10.9.2003 • 11.11.2003 • 13.11.2003 • OJ C 285, 28.11.2003, p. 5
• **Zevalin** • **ibritumomab tiuxetan** • **Part A**	Schering AG	• L01XC • Treatment of adult patients with rituximab relapsed or refractory CD20+ follicular B-cell non-Hodgkin's lymphoma (NHL)	• 24.3.2003 • 25.9.2003 • 153 days • 28 days	• 12.11.2003 • 16.1.2004 • 21.1.2004 • OJ C 52, 27.2.2004, p. 2
• **Ibandronic acid Roche 2.5 mg film-coated tablet** • **ibandronic acid** • **Part B**	Roche Registration Ltd	• M05BA06 • Treatment of osteoporosis in postmenopausal women to reduce the risk of vertebral fractures	• 22.7.2002 • 22.10.2003 • 207 days • 244 days	• 16.12.2003
• **Bonviva** • **ibandronic acid** • **Part B**	Roche Registration Ltd	• M05BA06 • Treatment of osteoporosis in postmenopausal women in order to reduce the risk of vertebral fractures	• 22.7.2002 • 22.10.2003 • 207 days • 244 days	• 16.12.2003
• **Litak#** • **cladribine** • **Part B**	Lipomed GmbH	• L01BB04 • Symtomatic treatment of advanced adrenal cortical carcnoma	• 22.7.2002 • 22.10.2003 • 206 days • 244 days	

# Denotes an orphan medicinal product designated under Regulation (EC) No 121/2000

Product • Brand name • INN • Part A or B	Marketing authorisation holder	Therapeutic area • ATC code • Summary of indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Advate** • **octocog alfa** • **Part A**	Baxter AG	• B02BD02 • Treatment and prophylaxis of bleeding in haemophilia A (congenital factor VIII deficiency)	• 21.10.2002 • 22.10.2003 • 200 days • 156 days	• 8.1.2004
• **Oxybutynin Nicobrand** • **oxybutynin** • **Part B**	Nicobrand Ltd	• G04BD04 • Treatment of urge incontinece in unstable bladdder	• 24.2.2003 • 20.11.2003 • 180 days • 87 days	
• **Faslodex** • **fulvestrant** • **Part B**	AstraZeneca	• L02BA03 • Treatment of locally advanced or metastatic breast cancer	• 24.2.2003 • 20.11.2003 • 176 days • 54 days	• 19.1.2004
• **Cholestagel** • **colesevelam hydrocholrise** • **Part B**	Genzyme BV	• C10AC04 • Adjunctive therapy to diet for the reduction of LDL cholesterol	• 23.9.2002 • 20.11.2003 • 201 days • 204 days	• 12.1.2004
• **Reyataz** • **atazanavir sulphate** • **Part B**	Bristol Myers Squibb Pharma EEIG	• J05AE • Combination treatment of HIV-1 infection	• 20.5.2002 • 20.11.2003 • 200 days • 326 days	• 12.1.2004
• **Photobarr#** • **porfimer sodium** • **Part B**	Axcan International Pharma BV	• L01CD01 • Ablation of high-grade dysplasia (HGD) in patients with Barrett's Esophagus (BE)	• 20.5.2002 • 18.12.2003 • 197 days • 321 days	

Negative CPMP opinions

Product • Brand name • INN • Part A or B	Marketing authorisation holder	Therapeutic area • ATC code • Summary of indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Yondelis#** • **ecteinascidin** • **Part B**	PharmaMar S.A.	• pending • Treatment of patients with advanced soft tissue sarcoma after failure of conventional chemotherapy	• 20.11.2001 • 24.7.2003 • 207 days • 390 days	• 6.1.2004
• **Serostim#** • **somatropin** • **Part A**	Ares Serono (Europe) Ltd	• H01A • Treatment of AIDS wasting	• 17.7.2001 • 25.4.2003 • 177 Days • 460 Days	• 3.10.2003 • 1.12.2003 • 3.12.2003 • OJ C 6, 10.1.2004, p. 2

# Denotes an orphan medicinal product designated under Regulation (EC) No 121/2000

Annex 8

CVMP opinions in 2003 on medicinal products for veterinary use

Positive CVMP 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
• **Metacam** • **meloxicam** • **Part B extension**	Merial	• Pigs • Diarrhoea/respiratory infections/MMA	• 18.12.2001 • 15.1.2003 • 204 days • 148 days	• 27.2.2003 • 12.5.2003 • 14.5.2003 • OJ C 129, 3.6.2003, p. 18
• **Metacam** • **meloxicam** • **Part B extension**	Merial	• Cattle • Mastitis	• 10.3.2002 • 15.1.2003 • 150 days • 120 days	• 27.2.2003 • 12.5.2003 • 14.5.2003 • OJ C 129, 3.6.2003, p. 18
• **Gonazon** • **azagly-nafarelin** • **Part B**	Intervet International	• Female Salmonid fish • Ovulation induction and synchronization	• 18.12.2001 • 9.4.2003 • 204 days • 274 days	• 28.5.2003 • 22.7.2003 • 24.7.2003 • OJ C 204, 29.8.2003, p. 6
• **Metacam** • **meloxicam** • **Part B extension**	Merial	• Horses • Muscle – skeltal disorders	• 12.11.2002 • 18.6.2003 • 210 days • 8 days	• 1.8.2003 • 8.10.2003 • 10.10.2003 • OJ C 262, 31.10.2003, p. 6
• **Draxxin** • **tulathroycin** • **Part B**	Pfizer	• Cattle and pigs • Treatment of respiratory disease	• 15.10.2002 • 23.7.2003 • 182 days • 99 days	• 6.9.2003 • 11.11.2003 • 13.11.2003 • OJ C 285, 28.11.2003, p. 5
• **Ibaflin** • **ibafloxacin** • **Part B extension**	Intervet	• Dogs	• 13.8.2002 • 17.9.2003 • 210 days • 189 days	• 30.10.2003
• **Gallivac HTV IBD** • **live vaccine** • **Part A extension**	Merial	• Chickens	• 15.10.2002 • 15.10.2003 • 204 days • 162 days	• 1.12.2003
• **Metacam 5mg/ml** • **moloxicam** • **Part B extension**	Merial	• Cattle and pigs	• 14.10.2003 • 10.12.2003 • 57 days • 0 days	• 22.1.2004
• **Novem 5mg/ml** • **meloxicam** • **Part B abridged**	Merial	• Cattle • Muscle – skeltal disorders	• 15.10.2003 • 10.12.2003 • 57 days • 0 days	• 5.1.2004
• **Novem 20mg/ml** • **meloxicam** • **Part B abridged**	Merial	• Cattle • Muscle – skeltal disorders	• 15.10.2003 • 10.12.2003 • 57 days • 0 days	• 5.1.2004

There were no negative opinions in 2003.

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
• **cypermetrin (extension)**	Salmonidae	• 29.7.1996 • 15.1.2003 • 335[1] days • 483 days	• 14.2.2003 • 17.6.2003 • OJ L 149, 17.6.2003, p. 15
• **phoxim (extension)**	Chicken	• 17.10.2002 • 18.6.2003 • 120 days • 124 days	• 17.7.2003 • 15.11.2003 • OJ L 297, 15.11.2003, p. 15
• **cefquinome (extension)**	Horses	• 24.4.2003 • 23.7.2003 • 90 days • 0	• 18.8.2003 • 9.12.2003 • OJ L 322, 9.12.2003, p. 5
• **imidocarb (extension)**	Sheep	• 24.4.2003 • 23.7.2003 • 90 days • 0	• 18.8.2003 • 9.12.2003 • OJ L 322, 9.12.2003, p. 5
• **diclofenac**	Cattle and pigs	• 4.2.2002 • 17.9.2003 • 119 days • 471 days	
• **nafcillin (extension)**	All ruminants	• 7.6.2002 • 12.11.2003 • 115 days • 390 days	
• **oxalic**	Honey bees	• 11.9.2003 • 10.12.2003 • 90 days • 0	• 6.1.2004
• **oxolinic acid (extension)**	Cattle	• 11.12.2003 • 10.12.2003 • 90 days • 0	• 6.1.2004

1 Active time for the evaluation of the initial application and submission or responses to outstanding issues following the establishment of provisional MRLs and extension of the provisional MRLs.

Annex 9

COMP opinions in 2003 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
• **tositumomab**	Amersham plc	• Treatment of follicular lymphoma	• 23.10.2002 • 11.11.2002 • 10.1.2003 • 61 days	• 20.1.2003 • 14.2.2003
• **decitabine**	EuroGen Pharmaceuticals Ltd	• Treatment of myelodysplastic syndromes	• 22.10.2002 • 11.11.2002 • 10.1.2003 • 61 days	• 20.1.2003 • 14.2.2003
• **iodine (131I) tositumomab**	Amersham plc	Treatment of follicular lymphoma	• 23.10.2002 • 11.11.2002 • 10.1.2003 • 61 days	• 20.1.2003 • 14.2.2003
• **serum Amyloid P radiolabelled with iodine 123 (Amysap)**	Mediam	• Diagnosis of extent and severity of histologically proven amyloidosis	• 27.9.2002 • 14.10.2002 • 10.1.2003 • 89 days	• 20.1.2003 • 14.2.2003
• **caffeine citrate**	Combino Pharm SL	• Treatment of primary apnoea of premature newborns	• 19.8.2002 • 14.10.2002 • 10.1.2003 • 89 days	• 20.1.2003 • 17.2.2003
• **icatibant acetate**	Jerini AG	• Treatment of angioedema	• 27.9.2002 • 14.10.2002 • 10.1.2003 • 89 days	• 21.1.2003 • 17.2.2003
• **bosentan (Tracleer)**	Actelion Registration Ltd	• Treatment of systemic sclerosis (scleroderma)	• 5.12.2002 • 20.12.2002 • 7.2.2003 • 50 days	• 17.2.2003 • 17.3.2003
• **tobramycin (inhalation powder)**	Chiron Corporation Ltd	• Treatment of pulmonary infection due to Pseudomonas aeruginosa in cystic fibrosis	• 5.12.2002 • 20.12.2002 • 7.2.2003 • 50 days	• 17.2.2003 • 17.3.2003
• **Alpha-1-acid glycoprotein**	Bio Products Laboratory	• Treatment of tricyclic anti-depressants poisoning	• 17.10.2002 • 11.11.2002 • 7.2.2003 • 89 days	• 17.2.2003 • 20.3.2003
• **2-chloro-9-[2-deoxy-2-fluoro-ß-D-arabinofuranosyl] adenine (Clofarex)**	Bioenvision Ltd	• Treatment of acute myeloid leukaemia	• 5.11.2002 • 20.12.2002 • 19.3.2003 • 90 days	• 26.3.2003 • 8.5.2003

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
•Anti-CEA sheep-human chimeric monoclonal antibody labeled with iodine-131	KS Biomedix Holdings plc	• Treatment of pancreatic cancer	• 5.12.2002 • 20.12.2002 • 19.3.2003 • 90 days	• 26.3.2003 • 8.5.2003
• rubitecan	EuroGen Pharmaceuticals Ltd	• Treatment of pancreatic cancer	• 4.12.2002 • 10.2.2003 • 15.4.2003 • 65 days	• 28.4.2003 • 10.6.2003
• liarozole	Barrier Therapeutics NV	• Treatment of congenital ichtyoses	• 13.12.2002 • 16.1.2003 • 15.4.2003 • 90 days	• 28.4.2003 • 10.6.2003
• 5-10-methylene-tetrahydrofolate	Biofol AB	• Treatment pancreatic cancer in combination with 5-fluorouracil	• 20.12.2002 • 16.1.2003 • 15.4.2003 • 90 days	• 28.4.2003 • 11.6.2003
• aldesleukin (inhalation use)	Chiron BV	• Treatment of renal cell carcinoma	• 24.1.2003 • 10.2.2003 • 8.5.2003 • 88 days	• 16.5.2003 • 30.6.2003
• cytochrome P450 isoform 2B1 gene transfected human embryonic kidney 293 cells encapsulated in polymeric cellulose sulphate	FSG Biotechnologie Austrianova GmbH	• Treatment of pancreatic cancer in combination with ifosfamide	• 24.1.2003 • 10.2.2003 • 8.5.2003 • 88 days	• 16.5.2003 • 30.6.2003
• chimeric anti-interleukin-6 monoclonal antibody	Centocor BV	Treatment of renal cell carcinoma	• 22.1.2003 • 10.2.2003 • 8.5.2003 • 88 days	• 16.5.2003 • 30.6.2003
• amiloride hydrochloride dihydrate	Pulmo Tec GmbH	• Treatment of cystic fibrosis	• 27.12.2002 • 17.3.2003 • 8.5.2003 • 53 days	• 16.5.2003 • 30.6.2003
• aplidine	Pharma Mar SA Sociedad Unipersonal	• Treatment of acute lymphoblastic leukaemia	• 11.4.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• Recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor bindin protein-3 (Somatokine)	Insmed Incorporated	• Treatment of primary growth hormone insensitivity syndrome (Laron syndrome)	• 24.10.2002 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• Recombinant human arylsulfatase A	HemeBiotech A/S	• Treatment of metachromatic leukodystrophy	• 10.4.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• murine anti-idiotypic antibody against OC125 antibody against CA125 antigen	Cell Control Biomedical Laboratories AG	• Treatment of ovarian cancer	• 9.4.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **Recombinant dog gastric lipase (Merispase)**	Meristem Therapeutics SA	• Treatment of cystic fibrosis	• 6.3.2003 • 17.3.2003 • 13.6.2003 • 89 days	• 23.6.2003 • 9.7.2003
• **hydroxyurea**	OTL Pharma	• Treatment of sickle cell syndrome	• 28.3.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• **Engineered protein inhibitor of human neutrophil elastase**	Debioclinic SA	• Treatment of cystic fibrosis	• 10.4.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• **adenovirus-Interferon gamma-coding DNA sequence**	Transgene SA	• Treatment of Cutaneous T cell lymphoma	• 25.2.2003 • 17.3.2003 • 13.6.2003 • 89 days	• 23.6.2003 • 9.7.2003
• **Herpes simplex virus lacking infected cell protein 34.5**	Crusade Laboratories Ltd	• Treatment of glioma	• 10.4.2003 • 2.5.2003 • 13.6.2003 • 43 days	• 23.6.2003 • 9.7.2003
• **prasterone (Fidelin)**	Medicom Healthcare BV	• Treatment of adrenal insufficiency	• 27.2.2003 • 17.3.2003 • 13.6.2003 • 89days	• 23.6.2003 • 28.7.2003
• **Antisense oligonucleotide (TATCCGGAGGGCTCG CCATGCTGCT) (NorVess)**	Gene Signal SAS	• Treatment of neovascular glaucoma	• 7.3.2003 • 2.5.2003 • 30.7.2003 • 90 days	• 7.8.2003 • 2.10.2003
• **Alpha-1-acid glycoprotein**	Bio Products Laboratory	• Treatment of cocaine poisoning	• 13.5.2003 • 13.6.2003 • 30.7.2003 • 48 days	• 7.8.2003 • 2.10.2003
• **5,6,7,8-tetrahydrobiopterin**	Prof Dr Adelbert A. Roscher	• Treatment of hyperphenylalaninemia	• 27.5.2003 • 13.6.2003 • 30.7.2003 • 48 days	• 7.8.2003 • 2.10.2003
• **Antisense oligonucleotide (TATCCGGAGGGCTCG CCATGCTGCT) (NorVess)**	Gene Signal SAS	• Treatment of Retinopathy of Prematurity	• 7.4.2003 • 2.5.2003 • 30.7.2003 • 90 days	• 7.8.2003 • 2.10.2003
• **nolatrexed (Thymitaq)**	SCIREX Ltd	• Treatment of hepatocellular carcinoma	• 27.5.2003 • 13.6.2003 • 30.7.2003 • 48 days	• 11.8.2003 • 2.10.2003
• **yttrium (90Y) antiferritin polyclonal antibodies (Ferritarg P)**	Monoclonal Antibody Therapeutics	• Treatment of Hodgkin lymphoma	• 10.4.2003 • 13.6.2003 • 30.7.2003 • 48 days	• 7.8.2003 • 2.10.2003

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **trabectedin (Yondelis)**	Pharma Mar SA Sociedad Unipersonal	• Treatment of ovarian cancer	• 26.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 17.10.2003
• **eculizumab**	QuadraMed	• Treatment of paroxysmal nocturnal haemoglobinemia	• 26.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 17.10.2003
• **H-tyrosine-glycine-phenylalanine-glycine-glycine-OH**	Abiogen Pharma SpA	• Treatment of chronic idiopathic myelofibrosis	• 27.5.2003 • 13.6.2003 • 10.9.2003 • 90 days	• 17.9.2003 • 20.10.2003
• **Herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes**	MolMed SpA	• Adjunctive treatment in hematopoietic cell transplantation	• 25.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 20.10.2003
• **Human immunoglobulin**	Orfagen	• Treatment of Dermatomyositis	• 25.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 20.10.2003
• **Human immunoglobulin**	Orfagen	• Treatment of Polymyositis	• 25.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 24.10.2003
• **trientine dihydrochloride**	Univar Ltd	• Treatment of Wilson's disease	• 26.6.2003 • 14.7.2003 • 10.9.2003 • 59 days	• 17.9.2003 • 24.10.2003
• **gimatecan**	Sigma Tau Industrie Farmaceutiche Riunite SpA	• Treatment of glioma	• 22.7.2003 • 11.8.2003 • 10.10.2003 • 61 days	• 21.10.2003 • 1.12.2003
• **Recombinant antibody derivative against human CD19 and CD3**	Micromet AG	• Treatment of chronic lymphocytic leukemia	• 23.7.2003 • 11.8.2003 • 10.10.2003 • 61 days	• 21.10.2003 • 1.12.2003
• **vasoactive intestinal peptide**	Mondobiotech Laboratories Anstalt	• Treatment of Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	• 27.3.2003 • 14.7.2003 • 10.10.2003 • 89 days	• 24.11.2003 • 22.12.2003
• **Recombinant antibody derivative against human CD19 and CD3**	Micromet AG	• Treatment of Mantle cell lymphoma	• 23.7.2003 • 11.8.2003 • 10.10.2003 • 61 days	• 21.10.2003 • 1.12.2003
• **5-methyl-pyridine-2-sulfonic acid {6-(2-hydroxy-ethoxy)-5-(2-methoxy-phenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl} -amide sodium salt**	Axovan Europe Ltd	• Treatment of aneurysmal subarachnoid hemorrhage	• 25.7.2003 • 11.8.2003 • 6.11.2003 • 88 days	• 17.11.2003 • 12.12.2003

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **N-acetylarcosyl-glycyl-L-valyl-D-alloisoleucyl-L-threonyl-L-norvalyl-L-isoleucyl-L-arginyl-L-prolyl-N-ethylamide**	Abbott International European Office	• Treatment of soft tissue sarcoma	• 21.8.2003 • 8.9.2003 • 6.11.2003 • 60 days	• 17.11.2003 • 12.12.2003
• **3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione**	Gregory Fryer Associates Ltd	• Treatment of multiple myeloma	• 20.8.2003 • 8.9.2003 • 6.11.2003 • 60 days	• 17.11.2003 • 12.12.2003
• **4,5-dihydro-2-(2,4-dihydroxyphenyl)-4-methylthiazole-4(S)-carboxylic acid**	Genzyme Europe BV	• Treatment of chronic iron overload requiring iron requiring chelation therapy	• 21.8.2003 • 8.9.2003 • 6.11.2003 • 60 days	• 17.11.2003 • 12.12.2003
• **Recombinant human factor XIII (composed of two A subunits)**	Chiltern International Ltd	• Treatment of hereditary factor XIII deficiency	• 23.7.2003 • 8.9.2003 • 6.11.2003 • 60 days	• 17.11.2003 • 12.12.2003
• **sildenafil citrate**	Pfizer Ltd	• Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	• 24.7.2003 • 11.8.2003 • 6.11.2003 • 89 days	• 17.11.2003 • 12.12.2003
• **cilengitide**	Merck KGaA	• Treatment of glioma	• 1.10.2003 • 17.10.2003 • 5.12.2003 • 50 days	
• **tacrolimus hydrate**	Sucampo Pharma Ophthalmics Ltd	• Treatment of vernal keratoconjunctivitis	• 2.10.2003 • 17.10.2003 • 5.12.2003 • 50 days	
• **temocillin sodium**	Belpharma NV	• Treatment of *Burkholderia Cepacia* lung infection in cystic fibrosis	• 21.5.2003 • 8.9.2003 • 5.12.2003 • 89 days	

There were no negative opinions in 2003.

Annex 10

Guidelines and working documents in 2003

CPMP Biotechnology Working Party

Reference number	*Document title*	*Status*
CPMP/BWP/2879/02	CPMP position statement on CJD and plasma-derived and urine-derived medicinal products	Adopted February 2003
CPMP/BWP/2289/02	CPMP points to consider on the development of live attenuated influenza vaccines	Adopted February 2003
EMEA/6011/03	Final EU recommendations for the influenza vaccine composition for the season 2003/2004	Adopted March 2003
CPMP/BWP/3068/03	Guidance on the description of composition of pegylated (conjugated) proteins in the SPC	Adopted July 2003
CPMP/BWP/1793/02	Note for guidance on the use of bovine serum in the manufacture of human biological medicinal products	Adopted July 2003
CPMP/BWP/3752/03	CPMP position statement on West Nile Virus and plasma-derived medicinal products	Adopted July 2003
EMEA/410/01 rev. 2	TSE revision of joint CPMP/CVMP note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products	Published in OJ C 24, 28.1.2004, p. 6
CPMP/BWP/5136/03	Discussion paper on the investigation of manufacturing processes for plasma-derived medicinal products with regard to vCJD risk	Adopted November 2003
CPMP/BWP/5092/03	CPMP biotechnology working party work programme for 2004-2005	Adopted December 2003
CPMP/BWP/1571/02	Position statement on the quality of water used in the production of vaccines for parenteral use	Adopted December 2003
CPMP/BWP/2758/02	Note for guidance on pharmaceutical aspects of the product information for human vaccines	Adopted December 2003
CPMP/BWP/3207/00 rev. 1	Guideline on comparability of medicinal products containing biotechnology-derived proteins as active substances: quality issues	Adopted December 2003
CPMP/BWP/3715/03	Procedural guidance on plasma master file (PMF) and vaccine antigen master file (VAMF)	Released for consultation October 2003
CPMP/BWP/3734/03	Note for guidance on scientific data requirements for a vaccine antigen master file (VAMF)	Released for consultation October 2003
CPMP/BWP/3794/03	Note for guidance on scientific data requirements for plasma master file (PMF)	Released for consultation October 2003

Reference number	*Document title*	*Status*
CPMP/BWP/5180/03	Note for guidance on assessing the risk for virus transmission – new chapter 6 of the note for guidance on plasma-derived medicinal products (CPMP/BWP/269/95)	Released for consultation October 2003
CPMP/BPWG/BWP/561/03	Note for guidance on the warning on transmissible agents in summary of product characteristics (SPCs) and package leaflets for plasma-derived medicinal products	Released for consultation October 2003

CPMP Ad Hoc Working Group on Blood Products

Reference number	*Document title*	*Status*
CPMP/BPWG/BWP/561/03	Note for guidance on the warning on transmissible agents in summary of product characteristics (SPCs) and package leaflets for plasma-derived medicinal products	Adopted October 2003
CPMP/BPWG/1089/00	Note for guidance on the clinical investigation of plasma derived fibrin sealant products	Released for consultation March 2003
CPMP/BPWG/153/00	Core SPC for plasma derived fibrin sealant products	Released for consultation March 2003
CPMP/BPWG/3726/02	Core SPC for human Varicella immunoglobulin for intramuscular use	Released for consultation March 2003
CPMP/BPWG/3728/02	Core SPC for human rabies immunoglobulin for intramuscular use	Released for consultation March 2003
CPMP/BPWG/3730/02	Core SPC for human tetanus immunoglobulin for intramuscular use	Released for consultation March 2003
CPMP/BPWG/3732/02	Core SPC for human tick-borne encephalitis immunoglobulin for intramuscular use	Released for consultation March 2003
CPMP/BPWG/2048/01	Core SPC for human plasma coagulation factor VII products	Released for consultation March 2003
CPMP/BPWG/2231/99 rev. 1	Core SPC for human albumin	Released for consultation March 2003
CPMP/BPWG/278/02	Core SPC for human plasma derived von Willebrand factor	Released for consultation July 2003
CPMP/BPWG/220/02	Note for guidance on the clinical investigation of human plasma derived von Willebrand factor products	Released for consultation July 2003

Reference number	*Document title*	*Status*
CPMP/BPWG/4027/02	Core SPC for human plasma derived hepatitis-B immunoglobulin for intravenous use	Released for consultation July 2003
CPMP/BPWG/4222/02	Core SPC for human plasma derived hepatitis-B immunoglobulin for intramuscular use	Released for consultation July 2003
CPMP/BPWG/3735/02	Core SPC for human plasma prothrombin complex concentrate	Released for consultation July 2003

CPMP Ad Hoc Vaccine Expert Group

Reference number	*Document title*	*Status*
CPMP/3390/02	Workplan for 2003-2004	Adopted January 2003
CPMP/VEG/5246/03	Work programme for 2004-2005	Adopted December 2003
CPMP/VEG/4717/03	Note for guidance on dossier structure and content for pandemic influenza vaccine marketing authorisation application	Released for consultation November 2003
CPMP/VEG/4986/03	Guideline on submission of marketing authorisation applications for pandemic influenza vaccines through the centralised procedure	Released for consultation November 2003

CPMP Efficacy Working Party

Reference number	*Document title*	*Status*
CPMP/EWP/252/03	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products in neuropathic pain management	Adopted February 2003
CPMP/EWP/49/01	Appendix to the note for guidance on the clinical investigation of medicinal products in the treatment of schizophrenia (CPMP/EWP/559/95) – methodology of clinical trials concerning the development of depot preparations of approved medicinal products in schizophrenia	Adopted February 2003
CPMP/EWP/633/02	Note for guidance on the clinical development of medicinal products for treatment of HIV infection	Adopted March 2003
CPMP/EWP/785/97	Points to consider on the evaluation of medicinal products for the treatment of irritable bowel syndrome	Adopted March 2003

Reference number	*Document title*	*Status*
CPMP/EWP/2863/99	Points to consider on adjustment for baseline covariates	Adopted May 2003
CPMP/EWP/1343/01	Points to consider on the clinical evaluation of new agents for invasive fungal infections	Adopted May 2003
CPMP/EWP/967/01	Points to consider on the clinical development of fibrinolytic medicinal products in the treatment of patients with ST segment elevation acute myocardial infarcation (STEMI)	Adopted June 2003
CPMP/EWP/205/95 rev. 2	Note for guidance on evaluation of anticancer medicinal products in man	Adopted July 2003
CPMP/EWP/569/02	Note for guidance on evaluation of anticancer medicinal products in man (CPMP/EWP/205/95 rev. 2) – addendum on paediatric oncology	Adopted July 2003
CPMP/EWP/3635/03	Concept paper on clinical investigation of medicinal products for the treatment of social anxiety disorder (social phobia)	Adopted September 2003
CPMP/EWP/4891/03	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the treatment of Ankylosing Spondylitis	Adopted October 2003
CPMP/EWP/4713/03	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the treatment of sepsis	Adopted November 2003
CPMP/EWP/556/95 rev. 1	Points to consider on clinical investigation of medicinal products other than NSAIDS for treatment of rheumatoid arthritis	Adopted December 2003
CPMP/EWP/788/01	Note for guidance on clinical investigation of medicinal products for the treatment of migraine	Adopted December 2003
CPMP/EWP/1875/03	Points to consider on the clinical requirements of modified release products released as a line extension of an existing marketing authorisation	Adopted December 2003
CPMP/EWP/225/02	Note for guidance on the evaluation of the pharmacokinetics of medicinal products in patients with impaired renal function	Released for consultation March 2003
CPMP/EWP/558/95 rev. 1	Note for guidance on evaluation of medicinal products indicated for treatment of bacterial infections	Released for consultation May 2003
CPMP/EWP/1875/03	Points to consider on the clinical requirements of modified release products released as a line extension of an existing marketing authorisation	Released for consultation June 2003

Reference number	*Document title*	*Status*
CPMP/EWP/3020/03	Note for guidance on clinical investigation of medicinal products in the treatment of lipid disorders	Released for consultation June 2003
CPMP/EWP/2986/03	Note for guidance on clinical investigation of medicinal products for the treatment of cardiac failure (CPMP/EWP/235/95) – addendum on acute cardiac failure	Released for consultation July 2003
CPMP/EWP/2998/03	Note for guidance on the inclusion of appendices to clinical study reports in marketing authorisation applications	Released for consultation July 2003
CPMP/EWP/2455/02	Note for guidance on the clinical development of medicinal products for the treatment of allergic rhino-conjunctivitis	Released for consultation September 2003
CPMP/EWP/4284/02	Note for guidance on clinical investigation of medicinal products for treatment of generalised anxiety disorder	Released for consultation September 2003
CPMP/EWP/4280/02	Note for guidance on clinical investigation of medicinal products for the treatment of panic disorder	Released for consultation September 2003
CPMP/EWP/4279/02	Note for guidance on clinical investigation of medicinal products for the treatment of obsessive compulsive disorder	Released for consultation September 2003
CPMP/EWP/2454/02	Note for guidance on clinical investigation of medicinal products indicated for the treatment of psoriasis	Released for consultation November 2003

CPMP Pharmacovigilance Working Party

Reference number	*Document title*	*Status*
CPMP/ICH/3945/03	ICH-E2D: Post-approval safety management: definitions and standards for expedited reporting and good case management practices	Adopted November 2003
CPMP/ICH/5716/03	ICH-E2E: Pharmacovigilance planning	Released for consultation November 2003

CPMP Safety Working Party

Reference number	*Document title*	*Status*
CPMP/SWP/2599/02	Position paper on the non-clinical safety studies to support clinical trials with a single low dose of a compound	Adopted January 2003
CPMP/SWP/2965/03	Concept paper on the development of CPMP position paper on the contamination of control samples in toxicology studies	Adopted June 2003
CPMP/SWP/5958/03	Concept paper on the development of a CPMP. Note for guidance on the non-clinical investigation of the dependence potential of medicinal products	Adopted December 2003
CPMP/SWP/4447/00	Note for guidance on environmental risk assessment on medicinal products for human use	Released for consultation July 2003

CPMP Herbal Medicinal Products Working Party

Reference number	*Document title*	*Status*
HMPWP/1416/02 rev. 1	Final proposal for a core-data* on *Urticae folium* (Nettle leaf)	Adopted July 2003
HMPWP/244/03	Final proposal for a core-data* on *Lini semen* (Linseed)	Adopted November 2003
HMPWP/1418/02	Final proposal for a core-data* on *Menthae piperitae folium* (Peppermint leaf)	Adopted November 2003
HMPWP/41/03	Final Position paper* on the use of herbal medicinal products containing asarone	Adopted November 2003
HMPWP/340/03	Final Position paper* on Capsicum/capsaicin containing herbal medicinal products	Adopted November 2003
HMPWP/243/03	Proposal for a core-data* on *Primulae radix* (Primula root)	Released for consultation March 2003
HMPWP/341/03	Proposal for a core-data* on *Salicis cortex* (Willow bark)	Released for consultation July 2003
HMPWP/342/03	Proposal for a core-data* on *Urticae radix* (Nettle root)	Released for consultation July 2003
HMPWP/343/03	Proposal for a core-data* on *Thymi herba* (Thyme herb)	Released for consultation July 2003
HMPWP/337/03	Draft position paper* on the use of herbal medicinal products containing methyleugenol	Released for consultation July 2003
HMPWP/338/03	Draft position paper* on the use of herbal medicinal products containing estragole	Released for consultation July 2003
HMPWP/345/03	Draft position statement* on Chamomilla containing herbal medicinal products	Released for consultation July 2003
HMPWP/344/03	Draft position paper* on the biopharmaceutical characterisation of herbal medicinal products	Released for consultation July 2003

* The views presented in this document are those of the HMPWP, which has been created as a forum for exchange of experience in the field of herbal medicinal products. This document is released for the purpose of transparency and has no legal force with respect to Directive 2001/83/EC.

Ad-Hoc meeting on preclinical and clinical comparability of biotechnology medicinal products

Reference number	*Document title*	*Status*
CPMP/3097/02	Guideline on comparability of Medicinal Products containing Biotechnology derived Proteins as active substance: non-clinical and clinical issues	Adopted in December 2003

ORGAM –Regulatory and Procedural guidelines

Reference number	*Document title*	*Status*
H/19984/03 rev. 1	Post-authorisation guidance document	Adopted in June 2003

CVMP Efficacy Working Party

Reference number	*Document title*	*Status*
CVMP/625/03	Specific efficacy requirements for ectoparasiticides in cattle	Released for consultation July 2003

CVMP Immunologicals Working Party

Reference number	*Document title*	*Status*
CVMP/205/03	CVMP advisory notice to veterinary surgeons regarding the development of fibrosarcaomas at sites of injection of veterinary medicinal products in cats	Adopted March 2003
CVMP/042/97 rev. 1	Revised position paper on indications and specific claims for veterinary vaccines under the centralised procedure	Adopted June 2003
CVMP/550/02	Requirements for concurrent administration of immunological veterinary medicinal products	Adopted October 2003
CVMP/865/03	Position paper on the data requirements for removing the target animal batch safety test for immunological veterinary medicinal products in the EU	Released for consultation October 2003

CVMP Pharmacovigilance Working Party (PhVWP-V)

Reference number	*Document title*	*Status*
CVMP/601/02	Points to consider regarding reporting of suspected serious adverse reaction to veterinary medicinal products: Common EU reporting form for marketing authorisation holders	Adopted February 2003
CVMP/065/03	Guideline on data elements for electronic submission of adverse reaction reports related to veterinary medicinal products	Adopted July 2003
CVMP/552/03	Causality assessment for adverse drug reaction to veterinary medicinal products	Released for consultation July 2003
CVMP/553/03	Points to consider list of species and breeds for electronic reporting of adverse reactions in veterinary pharmacovigilance	Released for consultation in July 2003

CVMP General

Reference number	*Document title*	*Status*
CVMP/558/03	Future strategy on antimicrobial resistance	Adopted June 2003

CVMP Safety Working Party

Reference number	*Document title*	*Status*
CVMP/457/03	Position paper regarding availability of veterinary medicinal products – extrapolation of MRLs	Adopted December 2003
CVMP/VICH/468/03	Repeat-dose (chronic) toxicity testing	Released for consultation May 2003
CVMP/VICH/467/03	General approach to establish a microbiological ADI	Released for consultation May 2003
CVMP/477/03	Position paper regarding availability of products for minor uses and minor species (MUMS)	Released for consultation June 2003

CVMP Ad-hoc Group on Environmental Risk Assessment

Reference number	*Document title*	*Status*
CVMP/VICH/790/03	Environmental impact assessments (EIAs) for veterinary medicinal products (VMPs) phase II	Released for consultation October 2003

Joint CPMP/CVMP Quality Working Party

Reference number	*Document title*	*Status*
CPMP/QWP/130/96	Note for guidance on the chemistry of new active substance	Adopted January 2003
CPMP/QWP/3309/01 CVMP/961/01	Note for guidance on the use of near infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations	Adopted February 2003
CPMP/ICH/2738/99	ICH Topic Q3B: Note for guidance on impurities in new drug products	Adopted February 2003
CPMP/ICH/420/02	ICH Topic Q1E: Note for guidance on evaluation of stability data	Adopted February 2003
CPMP/ICH/421/02	ICH Topic Q1F: Note for guidance on stability data package for registration in climatic zones III and IV	Adopted February 2003
CPMP/QWP/415/03	Concept Paper on the development of guidance on formulations of choice for paediatric population	Adopted February 2003
CPMP/QWP/609/96 rev. 1	Note for guidance on declaration of storage conditions for medicinal products particulars and active substances Annex to: Note for guidance on stability testing of new active substances and medicinal products Note for guidance on stability of existing active substances and related finished products	Adopted April 2003
CPMP/QWP/450/03	Position paper on specifications for class 1 and class 2 residual solvents	Adopted April 2003
CVMP/422/99 rev. 2	Note for guidance on the declaration of storage conditions: a) in the product information of pharmaceutical veterinary medicinal products, and b) for active substances Annex to: Guideline on the stability testing of new veterinary drug substances and medicinal products Note for guidance on stability testing of existing active substance and related finished products	Adopted July 2003
CVMP/680/02	Note for guidance on the quality of modified release dosage forms for veterinary use	Adopted July 2003
CPMP/QWP/4818/03	Concept paper on the development of note for guidance on stability of active substances and medicinal products manufactured in climatic zones III and IV and to be marketed in the EU	Adopted October 2003
CPMP/QWP/4812/03	Concept paper on the revision note for guidance on stability testing for variations	Adopted October 2003

Reference number	*Document title*	*Status*
CPMP/QWP/4815/03	Concept paper on the revision of a CPMP and CVMP note for guidance on plastic primary packing materials (3AQ10A)	Adopted October 2003
CVMP/1028/03	Concept paper on the revision of the CVMP and CPMP note for guidance on plastic primary packing materials	Adopted November 2003
CPMP/QWP/130/96 rev. 1	Guideline on the chemistry of new active substance	Adopted December 2003
CPMP/QWP/122/02 rev. 1	Guideline on stability testing of existing active substances and related finished products	Adopted December 2003
CPMP/QWP/6203/03 CVMP/059/04	Guideline on control of impurities of pharmacopoeial substances: Compliance with the European Pharmacopoeia general monograph "Substances for pharmaceutical use" and general chapter "Control of impurities in substances for pharmaceutical use"	Adopted by CPMP December 2003, awaiting adoption by CVMP
CPMP/QWP/297/97 rev. 1 CVMP/1069/02	Note for guidance on summary of requirements for active substances in the quality part of the dossier	Released for consultation in January 2003
CPMP/QWP/419/03	Note for Guidance on excipients, antioxidants and antimicrobial preservatives in the dossier for application for marketing authorisation of a medicinal product	Released for consultation February 2003
CPMP/QWP/2054/03 CVMP/395/03	Annex II to note for guidance on process validation: Non-standard processes	Released for consultation April 2003
CVMP/540/03	Note for guidance on quality aspects of pharmaceutical veterinary medicines for administration via drinking water	Released for consultation July 2003
CVMP/541/03	Note for guidance on the chemistry of new active substances	Released for consultation July 2003
CPMP/QWP/576/96 rev. 1	Guideline on stability testing for applications for variations to a marketing authorisation	Released for Consultation December 2003
CVMP/1027/03	Concept paper on the development of a note for guidance on the stability test data to be submitted for variation applications to a marketing authorisation	Released for Consultation December 2003

Committee for Orphan Medicinal Products

Reference number	*Document title*	*Status*
EMEA/4795/00 rev. 2	General information for sponsors of orphan medicinal products	Adopted December 2003

Annex 11

Arbitration and Community referrals overview 2003

Referrals made to the CPMP under Council Directive 2001/83/EC

Type of referral	*Date of CPMP opinion*	*International non-proprietary name (INN)*
Article 29	February 2003	clostridium botulinum type A neurotoxin
	April 2003	isotretinoin
	July 2003	fluconazole
	Ongoing	amlodipine maleate
Article 7(5)	January 2003	salmeterol + fluticasone
	March 2003	somatropin
	May 2003	mononine
	May 2003	factor VIII
	July 2003	lisinopril
	September 2003	desogestrel + ethinylestradiol
	Ongoing	donepezil
Article 6(12) previously 7(5)	Ongoing	alendronate sodium
Article 30	March 2003	calcium folinate
	April 2003	isotretinoin
	June 2003	calcium carbonate
	June 2003	calcium carbonate 500 + calciferol 10
	June 2003	calcium carbonate 500 + calciferol 5
	Ongoing	gemfibrozil
	July 2003	perindopril
	September 2003	lisinopril
	November 2003	pravastatin
	Ongoing	simvastatin
Article 31	September 2003	gatifloxacin
	November 2003	celecoxib
	November 2003	etoricoxib
	November 2003	parecoxib
	November 2003	rofecoxib
	November 2003	valdecoxib
	November 2003	loratadine
	December 2003	nimesulide
	Ongoing	paroxetine

Referrals made to the CVMP under Council Directive 2001/82/EC

Type of referral	*Date of CVMP opinion*	*International non-proprietary name (INN)*
Article 34	Ongoing	Eprinex Pour-on (eprinomectin)

Annex 12

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 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.eu.int**

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.eu.int**

For product defect and other quality-related matters:

E-mail: qualitydefects@emea.eu.int
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 Organisation. 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.eu.int**
Fax: **(44-20) 74 18 85 95**

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 either on the Internet at *http://www.emea.eu.int* or by writing to:

EMEA Documentation service
European Agency for the Evaluation of Medicinal Products
7 Westferry Circus
Canary Wharf
UK – London E14 4HB

Further information (including general information packs) can be obtained from the above address or from:

E-mail: **emearequests@emea.eu.int**
Fax: **(44-20) 74 18 86 70**

Requests for general information packs should be sent to:

Amanda BOSWORTH
Direct telephone: **(44-20) 74 18 84 08**
E-mail: **amanda.bosworth@emea.eu.int**

European experts list

Approximately 3 000 are used by the EMEA in its scientific evaluation work. The list of these European experts is available for examination on request at the EMEA offices.

Requests should be sent in writing to the EMEA or to:

E-mail: **europeanexperts@emea.eu.int**

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