The European Agency for the Evaluation of Medicinal Products

Eighth Annual Report
2002

Adopted by the Management Board on 19 December 2002

The annual report for 2002 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 at **http://www.emea.eu.int**

This report covers activities of the EMEA in 2002. 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. Telematics, 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 2001/84/EC.

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The '@emea.eudra.org' e-mail address format was disconnected on 1 October 2002 and messages sent to this address will no longer be delivered.

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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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Contents

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
Keith Jones

Medicines control in both human and veterinary medicine is an important contributor to the high standards of public health enjoyed by citizens of the European Union and this Agency plays a major role in maintaining those high standards. It achieves this through the licensing of innovative new medicines, by examining their safety under normal conditions of use and by ensuring that appropriate action is taken when necessary to maintain those standards. The way in which this public health role has been fully and well executed during 2002 is described in detail in the substance of this report.

The report presents the accomplishments of the agency against last years approved plan and provides good evidence that the standards of service to stakeholders (patients, healthcare professionals, the European Institutions, member states and the pharmaceutical industry) have been maintained at a high level and improved in some important respects. The high quality of work and of decision-making has been achieved through the hard work of all concerned, especially the community's experts working through the scientific committee structure. Appropriate management controls and performance monitoring have been well applied; and efficiency gains have been realised from the organisational changes implemented during last year. The agency has further cemented its excellent relationships with the competent authorities of member states and has also assisted with the coordination of mutual recognition.

The Agency has provided a high level of service for Orphan drugs and supported a number of other important public health initiatives. These have included initiatives on paediatric medicines, support for the regulation of TSE in pharmaceuticals, and the development of a strategy for risk assessment, risk management and risk communication in the post licensing period when medicines are widely marketed in the European Union. Other important and successful initiatives have included those on transparency of the Agency's operations, enlargement of the Community, and review of the licensing process.

An important public health issue first noted this year, has been a substantial reduction in the number of innovative new medicines submitted for licensing. This has occurred globally and could have important implications.

During the year, the management board have re-examined the governance arrangements for the Agency and satisfied themselves regarding its ability to deliver the reasonable expectations of its stakeholders.

The challenges of the future will be numerous, including implementation of the review of the licensing procedures, the implications of enlargement, information management for the community system of medicines control, the clinical trials and pharmacovigilance support systems and further extension of transparency for the operations of the Agency. The board considers that the Agency is in a sound position to take on these challenges.

These accomplishments could not have been achieved without the dedication and hard work of a large number of people both within the Agency, within the competent authorities of member states, the expert committees and the independent experts from around the European Union who have given generously of their time energy and expertise.

Keith Jones.

Introduction by the Executive Director
Thomas Lönngren

The worldwide fall in applications for new medicines made 2002 an unusual year in the history of the Agency, with the lowest number of new applications since the EMEA began its work in 1995. From the public and animal health perspective this represents a clear disappointment and we can only speculate as to the reason or reasons for this apparent downturn in innovation of the global pharmaceutical industry.

As an organisation, the impact of this on the EMEA was particularly felt since the Agency is heavily dependent on revenue of fees paid by the pharmaceutical industry in its budget. Cuts and savings were made towards the end of 2002, all the time ensuring that core business was kept running but postponing many other activities contained in our work programme into 2003.

The Agency did achieve a good number of the goals and objectives set for 2002 and managed to perform well under these difficult circumstances. Cooperation with the major European pharmaceutical trade associations has allowed close monitoring of our performance in 2002 together with EFPIA and FEDESA, although no performance survey was carried out for veterinary medicines in 2002 because of the small number of applications.

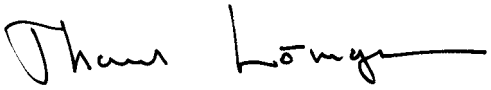
The surveillance of the safe use of medicines – 'pharmacovigilance' – was highlighted as the Agency's major priority for the year. The IT database that is central to the future European pharmacovigilance system and all the EMEA elements of the system are now fully in place. Feedback from industry partners shows positive appreciation for the improvements introduced in the scientific advice procedure, another of the Agency's priorities in 2002. Similarly, the work of the EMEA with regard to orphan medicines continues to go from strength to strength.

Requests for unplanned activities present certain difficulties, but the Agency was pleased to have been able to make a contribution to the European Community's preparations against possible bioterrorism threats. Other important activities in 2002 included preparations for the implementation of the EU directive on the conduct of clinical trials and contributions to the European Commission policy on paediatric medicines.

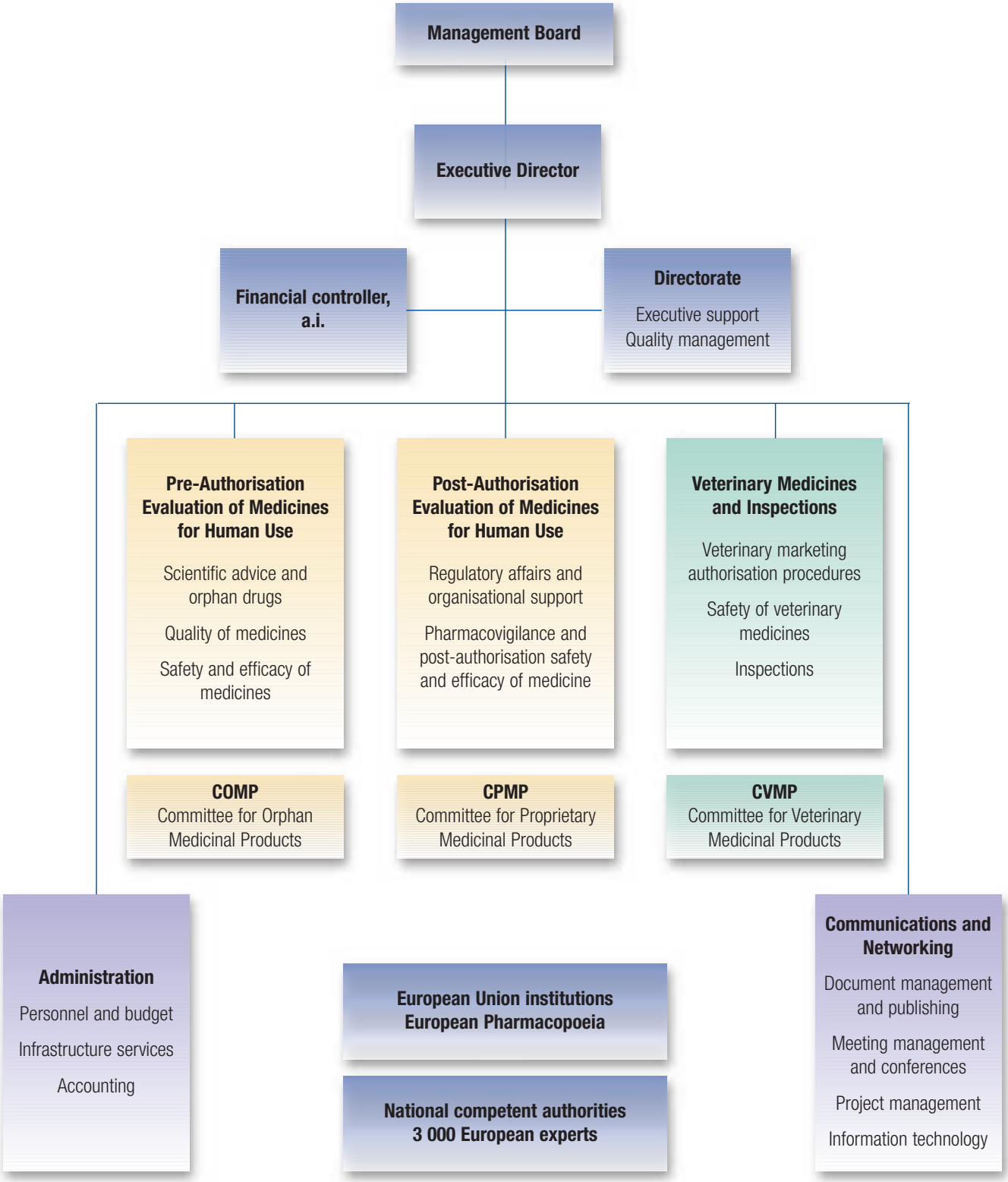
One area of unforeseen increase in the Agency's workload was the dramatic increase in 2002 in referrals coming from Member States. Solving issues relating to nationally approved medicines at Community level is important example of the role of the EMEA at the centre of the European medicines control system.

The future enlargement of the European Union will be a major event and 2002 marked the successful conclusion of the second phase of the PERF programme. Through this continuing programme of training and practical workshops – financed by the European Commission PHARE fund – we aim to ensure that all accession candidate countries are fully able to play a full role within the European regulatory system right from the moment of accession.

We now have 7 years of experience with the European regulatory system. I believe that this system and the Agency have made a positive contribution to public and animal health protection during this time. These are achievements that are only possible with the continuing cooperation and commitment of all parties involved. At the end of a particularly challenging year, I take this opportunity to thank my colleagues at the EMEA, the members of our committees, our network of European experts and our partners in the national competent authorities.



Structure of the EMEA



Chapter 1
EMEA in the European system

1.1 Management Board

Overview of the Management Board

Chairman of the Management Board
Keith JONES

Vice-Chairman of the Management Board
Gerhard Josef KOTHMANN

The Management Board met four times in 2002.

21 February 2002

- Adopted preliminary work programme and budget for 2003 totalling € 94 113 000
- Initial discussion of a three-year programme to implement EU-wide IT strategy for the pharmaceutical regulatory sector

6 June 2002

- Brainstorming discussions on corporate governance and accountability of the EMEA and risk management

3 October 2002

- Reduced EMEA 2002 draft budget from € 70 547 000 to € 61 304 000 to take into account fall in number of applications from pharmaceutical industry
- Agreed in principle to invite accession candidate countries as observers at EMEA starting in 2003

19 December 2002

- Adopted work programme and budget for 2003 totalling € 78 081 000
- Adopted the 2002 annual report
- Gave discharge to the Executive Director for the execution of the 2001 budget

1.2 National competent authorities

Useful web sites:

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

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

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

One of the Agency's main tasks set out in Council Regulation (EEC) No 2309/93 is the coordination of resources of the national competent authorities' resources for the evaluation and supervision of medicinal products. The EMEA participated in all meetings of the heads of national authorities in 2002 to help identification of resource needs for 2002 and 2003.

This was particularly important in light of the planned changes in the working practices of the scientific committees. Changes agreed in 2002 include the introduction of therapeutic advisory groups to assist the CPMP.

EMEA payment to national competent authorities totalled € 15 321 000 in 2002, representing some 25 % of the Agency's total expenditure. These payments are made in return for scientific services provided under contract to the EMEA.

During 2002 the Agency welcomed delegations from the Germany Federal Ministry of Health, the Social Affairs Committee of the Italian Parliament, the Norwegian Medicines Agency, the Swedish Ministry of Social Affairs and the UK Veterinary Medicines Directorate.

1.3 Review of the European marketing authorisation system

Useful web site:

European Commission Unit for Pharmaceuticals: regulatory framework and market authorisations
http://pharmacos.eudra.org

The European Commission proposals for the revision of European pharmaceutical legislation (OJ C 75 E, 26.3.2002, pp. 189, 216 and 234) made good progress in 2002. The Economic and Social Committee adopted its opinion on 18 September 2002 and the European Parliament adopted its first reading on 23 October 2002.

The European Parliament Committee on the environment, public health and consumer protection, led by its chairman Caroline Jackson, visited the EMEA on 25 March 2002. The Committee's two rapporteurs for the review, Rosemary Müller and Françoise Grossetête, also visited the Agency during the year.

The Council working party on pharmaceuticals and medical devices was able to achieve significant consensus on a number of major issues under the Spanish and Danish presidencies.

The Agency also had an opportunity to discuss the progress of the review proposals with David Byrne, European Commissioner with responsibility for public health and consumer protection, during his visit to the EMEA on 28 February 2002 and with Neil Kinnock, Vice-President of the European Commission, during his visit to the Agency on 8 November 2002.

1.4 Revision of EMEA fees

The Agency announced in February 2002 that an increase in the level of fees would be necessary in 2003. The increase is mainly because the level of the general EU contribution has gradually fallen as a proportion of EMEA revenue and an increase in fee levels is needed in order to meet the Agency's work programme.

It was decided to wait for the outcome of the Community review of EU pharmaceutical legislation before making any recommendations to the European Commission on changes to the structure of the fee system.

1.5 Transparency

Initiatives taken by the EMEA in 2002 include:

- Publication of summaries of opinions from the Committee for Orphan Medicinal Products (COMP) on the designation of orphan medicines
- The COMP Working Group with Interested Parties progressed a number of projects relating to communication with sponsors and patients
- Post-authorisation opinions from the Committee for Proprietary Medicinal Products (CPMP) and Committee for Veterinary Medicinal Products (CVMP) were included in press releases and meeting reports for the first time
- Publication of assessment reports for Community referrals

The EU institutions are also looking at other transparency measures as part of the review of the Community pharmaceutical legislation. The initial proposals from the European Commission contained a number of transparency measures, but discussion in the European Parliament and in the Council of Ministers has opened up a number of additional issues.

New EMEA transparency initiatives planned for 2002, including a public consultation exercise announced in October 2002, were postponed pending the outcome of discussions on the review by the EU institutions.

1.6 Interested parties

The COMP held two workshops with interested parties in 2002. The first in early 2002 with learned societies and health professionals and the second in late 2002 with all interested parties including also patient organisations, pharmaceutical industry and research institutions. This second meeting looked at developing a continuity policy for orphan medicines in the European Union and the outcome of the meeting will form part

of a report from the Agency to the European Parliament and European Commission in 2003.

The CPMP organised a workshop in May 2002 with patient organisations, which resulted in the creation of an ad hoc group focusing on ways to improve the quality of information to patients. This group will meet for the first time in 2003. The annual EMEA/EFPIA Info-day was held in October 2002.

Two meetings took place with the CVMP and interested parties, following the focus group approach introduced at the end of 2001. Regular bilateral meetings with the European industry federation were organised on a regular basis, with good outcomes including agreement from FEDESA to the publication of summaries of opinions for marketing applications on the day of adoption. A joint EMEA/FEDESA Info-day was held in September 2002.

1.7 International partners

Useful web sites:

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

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 main focus of the Agency's activities is focused on its work with the EU and EEA-EFTA Member States. The EMEA is aware of the international context in which it operates and is increasingly active with the European Union's international partner organisations and countries.

Activities with accession candidate countries focused on the successful completion of the second Pan-European Regulatory Forum on pharmaceuticals (PERF II). The programme involved the national authorities for medicines for human and veterinary use from EU Member States and candidate countries. A third programme, leading up to the time of accession in 2004, was agreed towards the end of 2003.

The EMEA continued its active participation in the International Conference on Harmonisation processes for human and for veterinary medicines (ICH and VICH). The ICH meetings in 2002 in particular led to the finalisation of the electronic format for the common technical document, first discussions on standards for gene therapy and further guidance on risk management and pharmacovigilance. The second VICH conference was held in Tokyo where significant attention was paid to reaching agreement on pharmacovigilance reporting requirements for veterinary medicines.

The EMEA participated in the WHO 10th International Conference of Drug Regulatory Authorities (ICDRA) held in Hong Kong in June 2002. Work on the development of the joint WHO-EMEA SIAMED application tracking system progressed. Other areas of cooperation between the WHO and EMEA in 2002 included discussion on pharmacovigilance and implementation of the WHO certification scheme for medicinal products.

The EMEA welcomed a number of visitors from non-EU countries in 2002. These include delegations from the national authorities of Canada, China, Cuba, Japan, Singapore, South Africa, Thailand and US.

Distinguished international visitors included Mrs Anne McClellen, Canadian Health Minister, Dr Yuwadee Patanawong, Director of Drug Control of the Thai FDA, Dr Lester Crawford, Deputy Commissioner of the US FDA, Dr Murray Lumpkin, Principal Associate Commissioner of the US FDA, and Dr David Kessler, Dean of the Yale University School of Medicine and former Commissioner of the US FDA.

The Agency hosted two experts from the Japanese Organisation for Science and Pharmaceutical Research under the EMEA visiting experts programme.

1.8 Quality management

A total of 16 internal audits were held in 2002, including a number of concerted audits addressing both the financial and system aspects of the audited processes. There were 6

competence development seminars on integrated quality management for EMEA management.

Following on from the initiative begun in 2001, a third benchmarking meeting was held in May 2002 looking at good regulatory practices and quality management systems. This involved representatives from 31 EU Member States, accession candidate countries and European institutions. The exercise continues to look at issues relating to the implementation of a quality management system and the identification of the processes needed for good regulatory practices and their documentation.

1.9 European Department for the Quality of Medicines

Useful web site:

European Directorate for the Quality of Medicines/ European Pharmacopoeia
http://www.pheur.org

Sampling and testing of centrally authorised medicines is performed in collaboration with the European Directorate for the Quality of Medicines (EDQM). The products are tested on a work-sharing basis by the Official Medicines Control Laboratories of the EU and EEA Member States. Details of the 2002 programme are given in Chapter 4.

The programme has proved useful in highlighting a number of method-related technical issues that were discussed with the relevant rapporteur and co-rapporteur and communicated with the marketing authorisation holders for further action as required. A new 5-year covenant with the EDQM was signed at the end of the year and is expected to facilitate future activities with respect to surveillance of centralised products on the market. A pilot procedure for the follow-up of testing results was also agreed upon in 2002.

The testing programme for 2004 was agreed in 2002.

EDQM representatives participated in several EMEA working party meetings, including meetings of the Quality Working party, Biotechnology Working Party, Herbal Medicinal Products Working Party and ad hoc meetings of GMP inspection services in 2002. EMEA staff also participated at the European Pharmacopoeia Commission sessions and meetings on the sampling and testing programme. Participation in all of these meeting had an important impact on the elaboration and update of guidelines, monographs, position papers, etc, relevant to the quality of medicines in Europe.

1.10 Financial control

EMEA Financial controller, a.i.
Claus CHRISTIANSEN

Preparations for changes to the financial regulations of all EU bodies, including the EMEA, continued in 2002 ahead of the 1 January 2003 entry into force of the new rules. One of the effects will be the abolition of the current financial control function at the EMEA, to be replaced by a system of internal audits to be exercised by the European Commission Internal Audit Service.

Implementation of the new rules within the EMEA was still under discussion at the end of 2002, but include the introduction of an *ex ante* control function at a stage prior to the authorising officer's approval, *ex post* control to operate in cooperation with the Agency's existing internal audit function and the creation of an audit progress committee whose main task will include the supervision of implementation of audit findings and improvement plans. Ahead of any formal decision, a number of concerted financial and process audits were already conducted in 2002.

The financial control function continued in 2002 with the Agency's interim financial controller, together with an assistant. A total of 10 500 transactions were handled in 2002, of which 1.12 % were returned by the financial controller compared to 1.08 % in 2001. Rejection was mainly for reasons of minor irregularities that were all resolved prior to final approval.

- 85 % of submissions to financial control were handled within 2 days
- 99 % of submissions to financial control were handled within 5 days

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

Committee for Proprietary Medicinal Products

Chairman
Daniel BRASSEUR

Vice-chairman
Eric ABADIE

Committee for Orphan Medicinal Products

Chairman
Josep TORRENT i FARNELL

Vice-chairman
Yann LE CAM

Working parties and ad hoc groups

Biotechnology Working Party
Jean-Hugues TROUVIN

Efficacy Working Party
Barbara VAN ZWIETEN-BOOT

Pharmacovigilance Working Party
Anne CASTOT (acting)

Joint CPMP/CVMP Quality Working Party
Jean-Louis ROBERT

Safety Working Party
Beatriz SILVA LIMA

Scientific Advice Review Group
Markku TOIVONEN

ad hoc Working Group on Blood Products
Manfred HAASE

Herbal Medicinal Products Working Party
Konstantin KELLER

Vaccine Expert Group
Roland DOBBELAER

Priorities for medicines for human use in 2002 – progress report

- The number of applications for initial applications for marketing authorisation declined in 2002. There were fewer new active substances and fewer multiple applications than in previous years. The number of applications for authorisation of orphan medicines however rose as a proportion of total applications.
- The provision of scientific advice, improvements to procedures and specific developments for the needs of orphan medicines through protocol assistance increased in 2002.
- Activities relating to orphan medicinal products increased in 2002, including designation procedures, post-designation follow-up of orphan medicines, protocol and regulatory assistance, management of the special orphan medicines fund, policy support to the European Commission and relations with patient organisations.
- Post-authorisation supervision activities increased particularly for manufacturing changes to marketing authorisations and safety-related activities. There was also a high workload associated with the follow-up of commitments by marketing authorisation holders to perform post-authorisation clinical trials to ensure safety of medicines in use.
- Referrals to the EMEA by Member States of nationally authorised medicines to examine safety issues rose substantially in 2002.
- There was a sharp increase in the reporting of adverse reactions from both EU and non-EU sources in 2002. The key EudraVigilance project entered implementation phase following successful testing with national competent authorities and a number of marketing authorisation holders.
- Work on development of an EMEA risk management strategy began. This will include increasing pharmacovigilance expert input as part of the pre-authorisation review of medicines. The aim is to introduce the concept of life-cycle management of a medicine, including pharmacovigilance aspects, right from an early stage.
- Transparency initiatives and collaboration with patient organisations, health care professionals and learned societies was developed in 2002, with the organisation of a number of successful workshops involving both the COMP and the CPMP.

Reorganisation of the Units for the evaluation of medicinal products for human use

The impact of the decision taken in 2000 to restructure the Unit responsible for medicinal products for human use started to be visible in 2002 due to an increase in staff, a better usage of staff competencies and a streamlining of a number of processes in relation with the constant development of the quality management process in the new units.

Examples include the timely publishing of information on Committees opinions, support provided to the development of ad hoc groups for emerging therapies and technologies and for therapeutic drafting groups for guidelines, the efficient manner the Agency has responded to the EC in providing guidelines in the context of biological threats, the success of the implementation of the legislation on orphan drugs or the development of the scientific advice procedure.

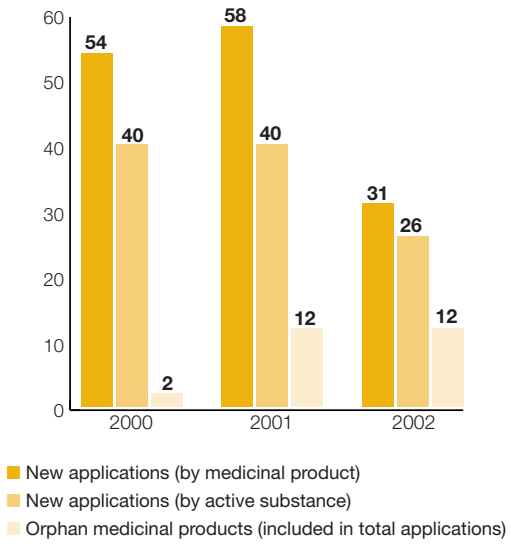
The restructuring has allowed for an improved handling of safety-related issues by the new therapeutic teams. Some EMEA pharmacovigilance staff members began training in 2002 to be able to facilitate the signal identification process undertaken by rapporteurs and to support the Community network in the detection of safety signals for centrally authorised medicines.

2.1 Initial evaluation

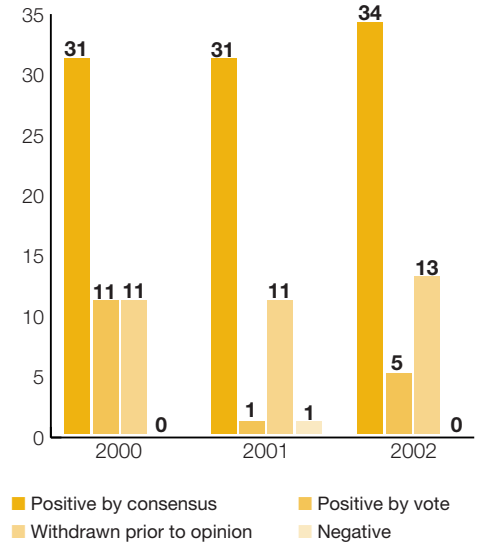
The number of applications for marketing authorisation declined in 2002. There were a total of 31 applications, of which 12 were for authorisation of designated orphan medicines.

This indicates a significant drop in the number of medicinal products reaching the stage of marketing applications compared to previous years. There were fewer new active substances for common diseases and fewer multiple applications, but a higher proportion of products aimed at treating rare diseases.

Initial evaluation applications 2000-2002



Initial evaluation opinions and withdrawals 2000-2002



Nine of the applications were submitted using the new international common technical document (CTD) format, either fully (6) or partially (3). This application format will be a mandatory requirement in the EU from mid-2003.

The CPMP met 11 times in 2002. Membership of the Committee is given in Annex 2.

The CPMP gave 39 positive opinions in 2002 for the authorisation of new medicines. This included four new orphan medicinal products and brings to eight the number of orphan medicinal products available to patients in the EU. Overall these medicinal products will benefit patients affected by diseases such as rare infections, cancer, diabetes, Alzheimer's disease, severe pulmonary conditions or congenital deficiencies. Details of all CPMP opinions are given in Annex 7.

Dialogue with applicants continues to be an important part of the EMEA process. Pre-submission meetings with applicants were organised at the EMEA for 27 products, showing an increase over years. The handling of meetings with rapporteurs and co-rapporteurs, whether held at the EMEA or elsewhere, has also been improved with greater transparency and communication, including use of telephone conferencing to allow participation of all concerned parties.

Quality assurance tools for the preparation of assessment reports were developed to facilitate the work of reviewers, as well as a guidance document for companies appearing before the CPMP during oral explanations.

The EMEA database on product assessment has been further developed and first results were provided to the Committees, and presented during public conferences.

The CPMP procedure has been modified in order to streamline the finalisation of opinions and improve the quality and consistency of related documents.

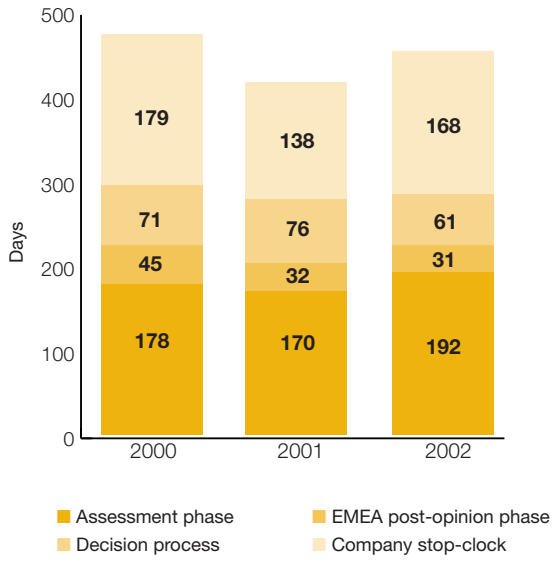
Performance indicators

The average time for the EMEA scientific review has been within the 210-day timeline foreseen in the legislation and has remained relatively stable over the years confirming the predictability of the centralised procedure.

The average assessment time of 192 days results from a mix of opinions adopted at 210 days with an oral explanation at day 180 and those adopted at 180 days without the need for an oral explanation. The average post opinion processing time of translations has remained stable at 31 days with a further shortening of the Commission decision process with an average of 61 days. The average assessment time slowed compared to 2001 due to the fact that there were no accelerated review procedures in 2002.

In 2002 the EMEA introduced a simplified post opinion linguistic checking procedure with a view to reducing the administrative translation burden for both National Authorities and Industry. Progress was also made in the area of improving package leaflet readability through review of readability testing results received from applicants.

Average number of days for centralised procedures 2000-2002



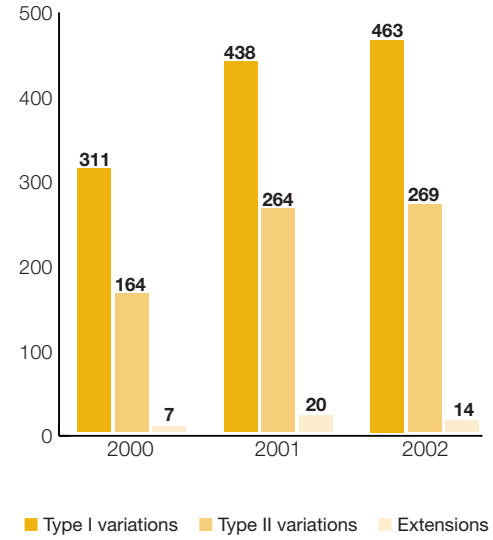
As part of the transparency measures put in place end of 2001, summaries of opinion were published for all CPMP opinions on the day of adoption by the CPMP. European public assessment reports (EPARs) were published shortly after the European Commission granted marketing authorisations for each product.

2.2 Post-authorisation activities

The number of post-authorisation applications and opinions
The number of applications for variations received in 2002 were in line with forecasts and were similar to numbers in 2001.

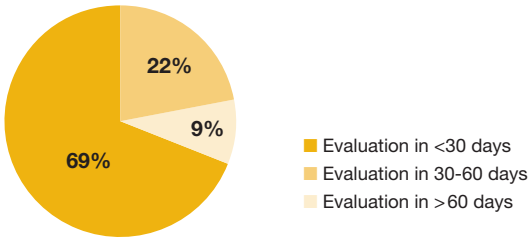
About 40 % of the type I ('minor') variations dealt with changes in manufacture aspects, 12 % with extension of shelf life and 13 % with changes to test methods. Over two-thirds of validated type I variations received were processed within 30 days and a further 22 % within 60 days.

Post-authorisation opinions 2000-2002

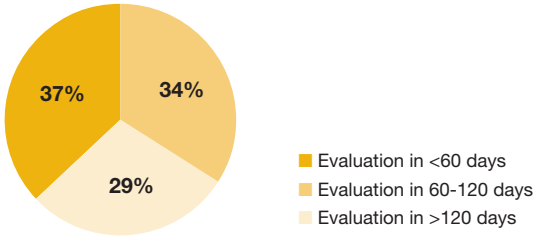


With regard to processing of type II ('major') variations, 37 % were evaluated within 60 days, 34 % within 120 days with the remaining 29 % exceeding 120 days. The latter group included scientifically complicated variation applications distributed between new clinical indications, safety updates and quality changes, particularly for biological products.

Evaluation time for type I variations 2002



Evaluation time for type II variations 2002



The EMEA has presented statistical information on post-authorisation applications as part of the ongoing joint EFPIA/EMEA performance indicators survey since 2001. Following on from this the EMEA has proposed to EFPIA that the exercise should be extended to include performance indicators for post-authorisation activities.

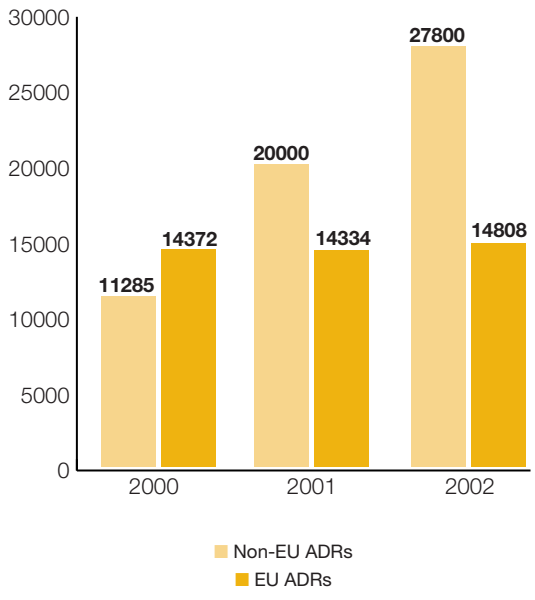
2.3 Pharmacovigilance and maintenance activities

Useful web site:

EudraVigilance
http://www.eudravigilance.org

The Agency received some 43 000 adverse drug reaction reports (ADRs) concerning centrally authorised products during 2002. A system for eliminating duplicate reports was successfully introduced in 2002, resulting in a lower number of total reports received that was nevertheless higher than for 2001.

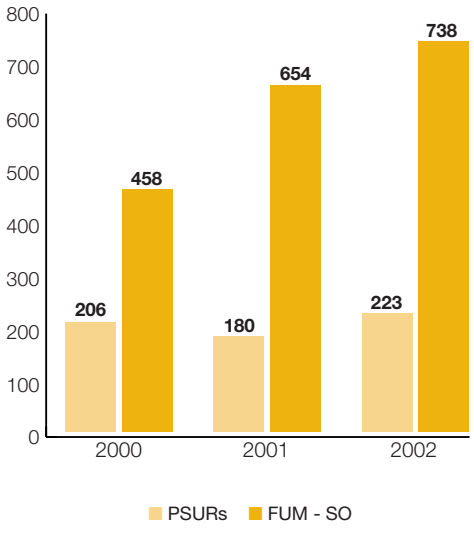
EU and non-EU adverse drug reports 2000-2002



Summary data of ADR listings were regularly transmitted to CPMP members to facilitate EU-wide pharmacovigilance.

The general volume of activity in terms of periodic safety update reports (PSURs) increased only slightly compared to 2001 levels. The number of PSURs is affected by the renewal in 2001 of authorisations granted in 1996 and their subsequent changes to 5-yearly PSUR reporting cycle. The number of follow-up measures and specific obligations processed in 2002 increased significantly and was greater than initial forecasts. This reflects the number of products approved under exceptional circumstances, which typically require close follow-up in the post-authorisation phase.

Periodic safety update reports, follow-up measures and specific obligations 2000-2002



A total of 16 annual reassessments of medicinal products authorised under exceptional circumstances were processed. This was an increase over the previous year, in line with forecasts.

Marketing authorisations were renewed for 18 centrally authorised products, together with 4 transfers of marketing authorisations. This is in line with forecast levels.

There were 4 urgent safety restrictions initiated by marketing authorisation holders for safety concerns, requiring urgent changes to product information and communication to health care professionals and patients.

EudraVigilance

The main EudraVigilance related activity in 2002 was the implementation of the electronic transmission of individual case safety reports (ICSRs) as defined in the policy paper adopted by heads of national competent authorities in November 2001. This included testing with marketing authorisation holders and competent authorities and the preparation of regular electronic reporting to EudraVigilance by these parties.

The EudraVigilance database management system (DBMS) and the EudraVigilance gateway are operational at the EMEA since December 2001. The focus of activity in 2002 was to achieve electronic adverse drug reaction reporting on a large scale using EudraVigilance from end of January 2003. As at the end of 2002, only 2 national competent authorities and 1 pharmaceutical company were systematically using EudraVigilance electronic reporting for adverse drug reaction reports for centrally authorised products.

Seven national competent authorities and 19 pharmaceutical companies began a testing phase with the EMEA. Extended technical support was provided by the EMEA in the implementation of the electronic transmission of individual case safety reports. Thirty-five meetings with individual pharmaceutical companies were organised, over 1 650 requests for information were handled and 2 meetings with European industry associations (EFPIA, AESGP, EGA and EuropaBio) were held.

A dedicated web site – **www.eudravigilance.org** – was developed in 2002 to provide information on the EudraVigilance project.

EMEA risk management strategy

Work began together with the CPMP on the development of an EMEA risk management strategy in 2002. This strategy aims at strengthening the conduct of pharmacovigilance for centrally authorised products. The proposals concentrated on the areas of risk detection, risk assessment, risk minimisation and risk communication and will form the basis of a proactive strategy of product life-cycle management, starting from the pre-authorisation phase. The strategy will lead to a more prospective handling of safety concerns by the Committee in close collaboration with its working parties and experts.

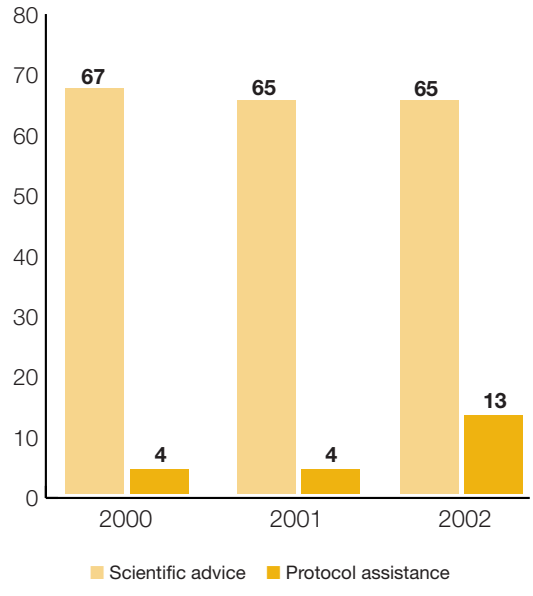
The outcome of these discussions at EMEA will compliment the elaboration of a European Risk Management Strategy initiated by the Heads of Agencies. The overall aim of the collaborative effort of the EMEA and National Competent Authorities is the formulation of a coherent strategy for managing the risks associated with placing medicinal products across the EU market.

2.4 Scientific advice and protocol assistance

The CPMP Scientific Advice Review Group 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. The Group met 11 times in 2002.

The procedure for protocol assistance was fully implemented in 2002 with two members of the Committee for Orphan Medicinal Products participating as members of the Scientific Advice Review Group and directly contributing to this initiative aimed at encouraging the development of medicinal products for rare diseases.

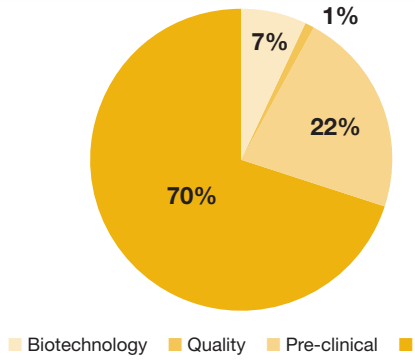
Scientific advice and protocol assistance given (including follow-up advice) 2000-2002



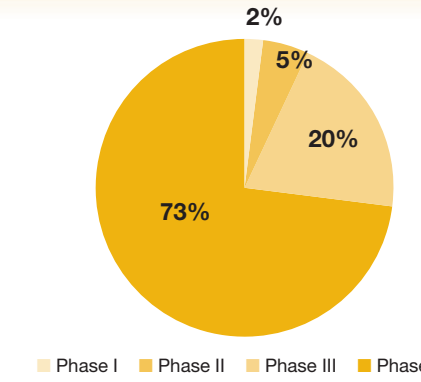
The number of scientific advice given in 2002 remains stable compare to past years 17 % of the workload of the Scientific Advice Review Group in 2002. Oral explanation meetings with sponsor companies were held in almost half of the cases were advice was given in 2002. Pre-submission meetings were held in almost all cases prior to protocol assistance at the request of sponsors but only in 30 % of cases for scientific advice.

Of the requests for scientific advice and protocol assistance finalised in 2002, two-thirds related to the clinical aspects of the development of medicinal products. Of these 70 % related to phase III clinical trials.

Scientific advice requests by topic 2002

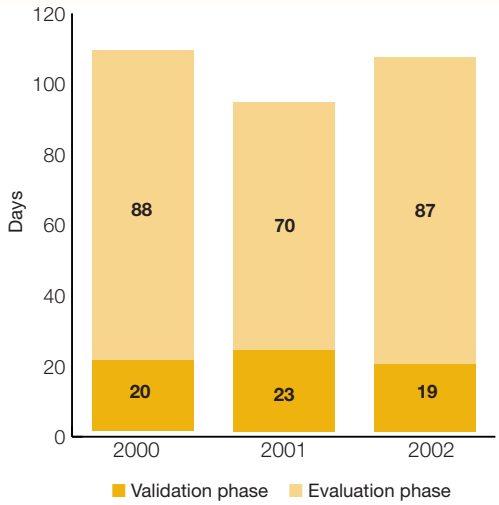


Clinical trial phases of scientific advice requests 2002



Agreed timelines for the scientific advice procedure were respected in 2002 and were below the 120-day timeframe between submission of an application and availability of the advice letter.

Average number of days for scientific advice procedures 2000-2002



The impact of scientific advice on the outcome of the scientific evaluation at the stage of marketing authorisation was assessed in 2002 looking back to January 1999 when the Scientific Advice Review Group started its activities. Some 42 % of the medicinal products that received a positive opinion in 2002 had previously benefited from scientific advice, whereas 90 % of applications that were withdrawn had not requested scientific advice.

2.5 Arbitration and Community referrals

There was a significant and unexpected increase in arbitration and Community referrals in 2002.

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)

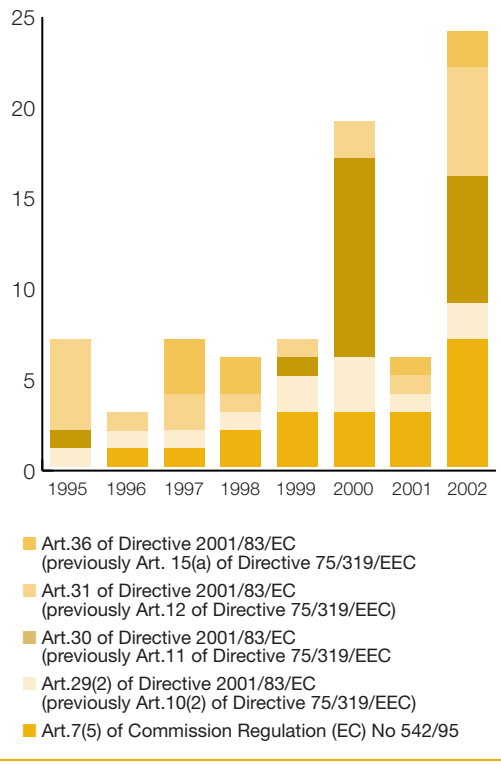
Further to the decision taken by heads of national competent authorities, the Joint CPMP/MFRG working group on harmonisation of summary of product characteristics met 6 times in 2002. The objective of the group was to identify European brand leaders in major therapeutic areas for harmonisation referrals under Article 30 of the Community Code.

The group held discussions with various industry trade associations (including EFPIA and EGA) throughout the year and produced guidance regarding the process. Following recommendations by the working group, the European Commission initiated the first of these referrals for 2 products in November 2002.

Details of all referrals are given in Annex 11.

Referrals to the CPMP now constitute a significant allocation of the Agency's resource both in terms of scientific evaluation and discussion during CPMP plenary meetings. Approximately one-third of CPMP meeting time in 2002 was dedicated to consideration of referrals.

Arbitration and Comunity referrals 1995-2002



Referral workload remained significant throughout 2002 with 15 ongoing referrals under Article 30 and three under Article 29 of Council Directive 2001/83/EC evaluated during the year. The CPMP issued opinions for eight Article 30 procedures and two Article 29 procedures.

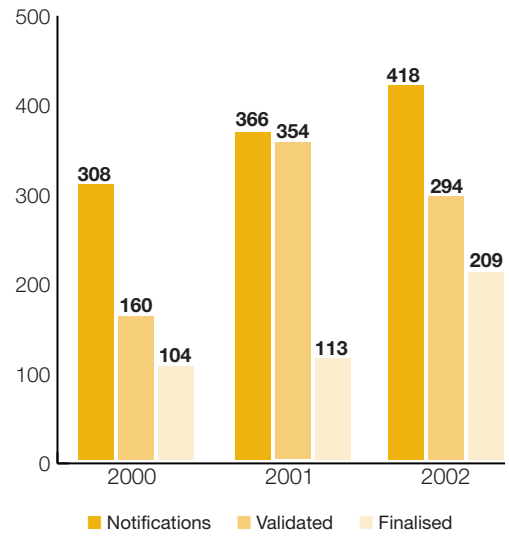
With respect to pharmacovigilance aspects, in particular Community Referrals (under Articles 31 and 36 of the Community Code), there was a continued substantial increase in the work volume with some procedures involving over 150 companies. The complexity of these referrals is also illustrated by the total number of individual marketing authorisations held by these companies in the referrals, which ranged from 44 to 514.

Internal working groups were set up to look at various aspects of referral procedures. The aim of these groups is to look at areas of process improvement and to ensure consistency across procedures. This initiative will also consider ways to increase transparency and strengthen communication.

2.6 Parallel distribution

Initial parallel distribution notifications increased during 2002 with a further increase of notifications of change being processed due to product labelling updates. The average processing time for new notifications exceeded the 30-day

Parallel distribution notifications 2000-2002



target despite additional resources dedicated to this service. This is due to difficulties experienced by distributors gaining access to the most updated medicinal product labelling, requiring multiple exchanges of letters with EMEA to supply the correct mock-ups and specimens.

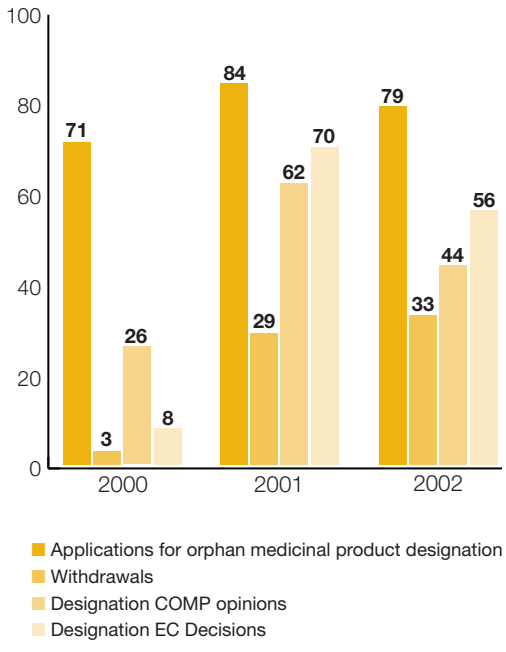
A workshop was held with the European Association of Euro-Pharmaceutical Companies (EAEPC) in October 2002 to explore the reasons for these delays and identify potential improvements to be introduced in the process in 2003.

2.7 Orphan medicinal products

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 2002. Membership of the Committee is given in Annex 4.

Orphan medicinal product procedures 2000-2002



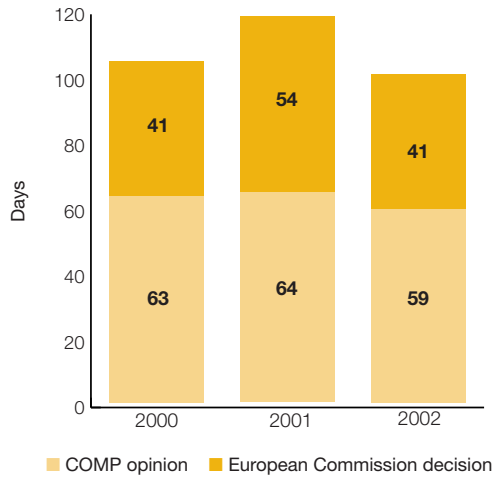
The level of applications for designation of orphan medicines remained at the same high level seen in 2001, with 79 applications made in 2002. This indicates a continuing interest on the part of sponsors to benefit from the incentives of the orphan drug regulation No (EC) 141/2000.

Pre-submission meetings were held for 75 % of applications, leading to a halving of validation time required for these applications.

A total of 33 applications for designation were withdrawn in 2002 since the sponsors were not able to fully justify their requests.

More oral explanations before the COMP were held in 2002. The average time taken by the COMP to adopt recommendations on the designation of orphan medicines in 2002 was 59 days in average, below the target 90 days. The time taken to transform opinions on designation into Commission decision decreased and the overall process for designation remains to a large extend below the 120-day timeframe.

Average number of days for designation of orphan medicinal products 2000-2002

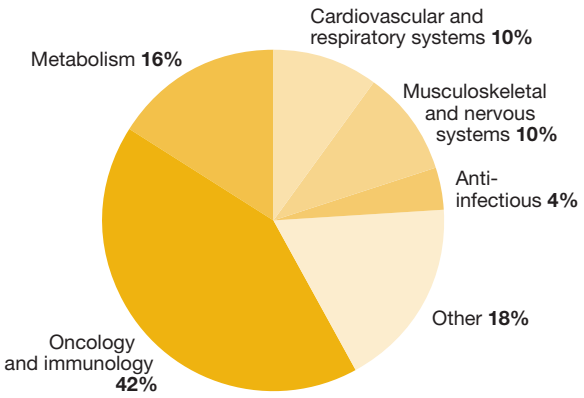


A total of 44 medicinal products received a positive opinion from the COMP in 2002 and the European Commission took 56 decisions on designation.

More than half of the medicinal products that received a COMP opinion in 2002 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 2002 are given in Annex 9.

By end of 2002, less than 3 years after the implementation of the European regulation for orphan medicinal products, a total of 134 products have received orphan medicine status in the European Union.

COMP opinions by therapeutic area 2002



In 2002 a number of new activities in relation with orphan medicines were initiated or developed. The first summaries of COMP opinions were published on the EMEA web site in March 2002. These documents provide brief information on the expected mode of action of the products and a description of the orphan condition. They are published following adoption of the European Commission decision on orphan designation.

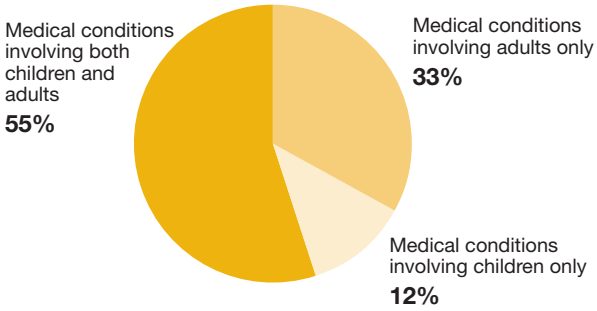
The regular review of annual reports for designated orphan medicinal products provides an update on the development of designated orphan products up to the granting of a marketing authorisation. Fifty-six annual reports were reviewed in 2002.

The COMP created an ad hoc group on significant benefit to consider the practical implications of the need to review the criteria on which a product was given orphan drug status at the time when a subsequent application is made for marketing authorisation.

Of the medicinal products that received an opinion from the COMP in 2002, 12 % are aimed at treating conditions that only affect children and 55 % are aimed at diseases that affect both adults and children.

The COMP finalised a number of guidance documents to facilitate the preparation of applications and annual reports by sponsors. Details of these documents are given in Annex 10.

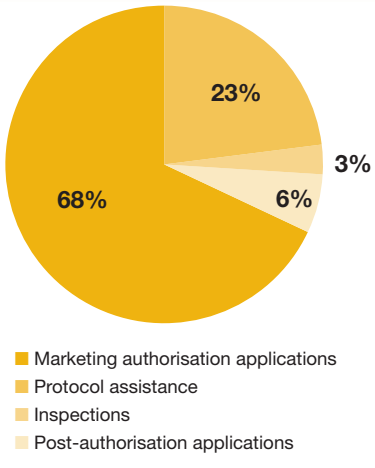
Orphan medicinal products for the treatment of children 2002



An EMEA information brochure on orphan medicinal products was finalised and published in 2002. In follow-up to the two workshops held with patients' organisations and pharmaceutical industry in 2001, a workshop with academia and health professionals was held in January 2002 and a joint meeting with all interested parties was held in December 2002 to address the issues of a continuity policy for orphan medicines in the EU.

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. These reductions are allocated to a special contribution voted each year by the Council and the European Parliament. Fee reductions in 2002 were mainly used for applications for marketing authorisation and protocol assistance.

Use of EU special contribution for orphan medicines 2002



2.8 Working parties and ad hoc groups

The list of guidance documents published in 2002, together with their status, is given in Annex 10.

• Biotechnology Working Party

The Biotechnology Working Party met on 9 occasions in 2002 and was involved in advice on assessment of marketing authorisation applications (pre- and post-authorisation), contributed to the scientific advice procedure and updated a number of guidelines. The group considered 17 guidelines of which 5 were new and 12 were published in 2002.

• Efficacy Working Party

The Efficacy Working Party met 4 times in 2002. Four small groups of specialised experts responsible for drafting guidelines were created in the following therapeutic areas: cardiovascular, anti-infectives, central nervous system and pharmacokinetics. The Working Party was responsible for 28 guidelines of which 12 were new and 7 were published.

• Safety Working Party

The Safety Working Party met 3 times in 2002 and was in charge of 12 guidelines of which 1 were new and 5 were published.

• Vaccine Expert Group

The newly created CPMP Vaccine Expert Group met 5 times in 2002. The Group's priority in 2002 was the preparation of a Note for guidance on the development of vaccinia virus based vaccines against smallpox. This was done at the request of the European Commission as part of the EU response to bioterrorism threats.

• Pharmacovigilance Working Party

The Pharmacovigilance Working Party met 8 times in 2002. Existing data sources, procedures and guidelines were reviewed and proposals for future increasing efficiency and strength of pharmacovigilance in the EU were developed as a contribution to the development of a European risk management strategy. Guidance documents developed by the PhVWP include a concept paper on conduct of pharmacovigilance for medicines used by children. Five videoconference meetings with the US Food and Drug Administration took place in 2002.

• Joint CPMP/CVMP Quality Working Party

The Joint CPMP/CVMP Quality Working Party met 4 times in 2002. The CPMP adopted 4 guidelines and released 4 guidelines for public consultation. The CVMP adopted 2 guidelines, 1 concept paper and released 3 guidelines for public consultation (one of which concerned both human and veterinary medicinal products). The working party contributed to the review of variation regulation and Annex 1 of Directive 2001/83/EC. The work continued on the implementation of the common technical document and collaboration with the European Pharmacopoeia in the framework of the Certification of Suitability scheme.

• Herbal Medicinal Products Working Party

The Herbal Medicinal Products Working Party was established in 2002 as a working party of the CPMP with a new composition, mandate and work programme approved by the EMEA Management Board. Highlights of the year included the finalisation of Points to consider paper on good agricultural and collection practises for starting materials of herbal origin, the publication of core data for 11 herbal drugs/herbal drug preparations and contributions to the proposed Directive on traditional herbal medicinal products. The Working Party was in charge of 13 guidelines of which 8 were new and 12 were published.

CPMP ad hoc working groups

• Organisational Matters Group

This group met 8 times and addressed a variety of organisational topics including discussion on the EMEA risk management strategy, therapeutic assessment groups, reorganisation of the Scientific Advice Review Group, medical device consultation process, well-established use applications and introduction of assessment templates.

• Invented Name Review Group

The group held 9 meetings in 2002 to consider whether applicants' proposed invented name(s) for medicinal products could create public health concerns and more particularly potential safety risks. The Group released a revised guideline on the acceptability of invented names for human medicinal

products processed through the centralised procedure in February 2002. It also developed a working collaboration with the World Health Organization and established an information exchange with the Office for Harmonization in the Internal Market (Trademarks and Designs) in Alicante (OHIM).

- **ad hoc Working Group on Blood Products**

The Group made contributions to the CPMP in relation to efficacy and safety aspects of blood products, and contributed to the scientific advice procedure. The group was in charge of 16 guidelines of which 4 were new and 4 were published.

- **ad hoc Working Group on (Pre-)Clinical Comparability of Biotechnology Products**

This group met 3 times in 2002 and released for consultation an Annex to the Note for Guidance on comparability of medicinal products containing biotechnology-derived proteins as drug substance.

- **Paediatric Expert Group**

The Paediatric Expert Group met three times in 2002 and issued three concept papers on paediatric formulations, pharmacokinetic and pharmacovigilance. The Group contributed to guidelines of the CPMP Efficacy and Safety Working Parties. It also made recommendations on the preparation of extemporaneous formulations of medicines frequently used in children in the EU following a survey of paediatric hospital pharmacies.

- **ad hoc Expert Group on Xenogeneic Cell Therapy**

An expert workshop and one Rapporteur's meeting was held in 2002 which led to the preparation – in consultation with other working parties and the CVMP – to a Points to consider paper on xenogeneic cell therapy medicinal products which was released for 6 months consultation in November 2002.

- **ad hoc Group on Gene Therapy**

During its two meetings in 2002, the Group discussed topics including standardisation, viral shedding studies and new aspects related to lenti-viral vectors in order to prepare for the first worskhop on gene therapy held in September 2002 under the auspices of the ICH process. Three scientific reports of the group as well as the ICH gene therapy workshop communication paper were published by the EMEA.

- **ad hoc group on Pharmacogenetics**

This Group met once in 2002 and finalised a position paper on terminology in pharmacogenetics, which was published in November 2002.

- **ad hoc Groups on Biological and Chemical Threats**

At the request of the European Commission, the EMEA established two CPMP ad hoc groups responsible for drafting guidance documents on medicinal products to be used in the framework of biological and chemical threats (see also Vaccine Expert Group activities).

The first ad hoc group produced a guidance document on the use of medicinal products for treatment and prophylaxis of biological agents that might be used as weapons was published in early 2002 and updated in July 2002. The second ad hoc group working began work on chemical weapons in late 2002.

COMP ad hoc working groups

- **COMP Working Group with Interested Parties**

This group involves COMP members, EMEA, patients and pharmaceutical industry representatives. It met 3 times in 2002 and worked on projects relating to communication to sponsors and patients such as summaries of COMP opinions and the preparation of workshops.

- **COMP Biotechnology Working Group**

The COMP Biotechnology Working Group met twice in 2002 to provide advice to the COMP on aspects relating to significant benefits of orphan medicinal products derived from biotechnology.

Training of Assessors

The initiative began by EMEA in 2001 on the organisation of training for assessors from national authorities within its premises continued in 2002 and the Agency contributed to the coordination of the programme with national competent authorities.

Sessions were organised on IT aspects including preparation for the electronic submission of applications using the new

international common technical dossier format, the methodology of clinical trials following the publication of new CPMP guidance documents and, for junior assessors, jointly with the Unit for the Evaluation of medicines for veterinary use, on all aspects related to networking and processes related to European procedures. Assessors from accession candidate countries were invited to participate to the trainings as a preparation for the enlargement.

2.9 International activities

There was extensive participation in a number of European Commission and Member State meetings in 2002. Key highlights include the ongoing 2001 review process, revision of Annex I of Council Directive 2001/83/EC, revision of the variation regulations and the development of paediatric regulations. The EMEA was also actively involved in providing support to the European Commission's Legal Service in a number of ongoing cases before the European Court of Justice and Court of First Instance. Efforts continued in relation to joint actions with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) based in Lisbon.

Considerable support was provided both to the PERF II programme and the visiting experts programme to facilitate the accession process for Candidate Countries. Evaluations by the EMEA for centrally authorised products may be recognised by the national authorities of central and eastern European countries through a simplified recognition procedure, at the request of the marketing authorisation holder. There has been extensive use of this procedure since its inception in 1999. The EMEA supports this process through provision of information, including safety updates.

Significant support was also provided to the ICH process.

Collaboration with the WHO continued both through interaction with the Collaborating Centre for International Drug Monitoring as well as the WHO International Non-proprietary Name (INN) programme. Contact between the CPMP Invented Name Review Group and the WHO International Non-proprietary Name (INN) programme was established in 2002 and they are now systematically involved in the review process. The EMEA participated in a WHO meeting on the quality of starting materials in July 2002.

2.10 Mutual recognition facilitation group

Web Sites:

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

EMEA/MRFG secretariat (e-mail)
e-mail: mrp@emea.eu.int

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

The Mutual Recognition Facilitation Group (MRFG) reports to the meeting of heads of national competent authorities. The group is made up of delegates from the EU, Iceland and Norway who meet at the EMEA premises to coordinate Member States' positions on topics related to the mutual recognition procedure. Observers from the European Commission and from accession candidate countries also regularly participate in the monthly meetings. The MRFG also provides on request procedural and regulatory advice and develops general guidance papers, which are published on the MRFG website.

The MRFG met eleven times in 2002. Luisa García Vaquero chaired the meetings during the Spanish presidency in the first half of 2002 and Joan Boye during the Danish presidency in the second half of the year. Press releases with statistics and adopted documents are published on the heads of agencies website.

Two informal meetings were held in 2002, which discussed a number of topics including the new EU variations regulation and the common technical document.

The Joint CPMP/MRFG Working Group on Harmonisation of SPCs, created in 2001 under a mandate given by heads of agencies, continued its work in 2002 chaired by Tomas Salmonson. Key issues were the identification of candidate products in the harmonisation process, the initiation of pre-referral discussions with marketing authorisation holders and the preparation of referrals to be initiated by the European Commission.

The Working Group also had a liaison meeting with the generic pharmaceutical industry to discuss how to conform to the Commission Decision for an originator product after a referral procedure.

In accordance with a decision by the heads of agencies, the operation of the EudraTrack procedure tracking system was taken over by the German national authority, BfArM. They will be responsible for the operation and future development of the system. The EudraTrack working group was chaired by Aurelio Fernandez Dominguez and Pia Næsborg Andersen, respectively, under the Spanish and Danish presidencies.

The number of new applications in 2002 has slightly decreased compared to 2001 and there was an increase in the number of arbitrations from variation applications compared to previous years. Statistical information on applications under the mutual recognition procedure is given in the monthly press releases.

Taking into account the ongoing review of Community pharmaceutical legislation, the MRFG proposed procedures for the new types of variations. Other activities included the drafting of rules of procedure for the new Coordination Group and the monitoring of applications in the CTD format.

The MRFG responded to questions from the pharmaceutical industry and developed new guidance papers to assist marketing authorisation holders and national competent authorities. Existing guidance documents were updated at Member States' request and to conform to the new Community Code on human medicines (Council Directive 2001/83/EC).

The MRFG adopted the view of the CPMP Biotechnology Working Party concerning TSE and published a statement on the use of lactose in pharmaceutical products on the web site. Members were involved in joint projects and joint meetings with different CPMP working groups and interested parties.

In 2002 the EMEA supported the chairpersons and the MRFG with their monthly activities, including the organisation of two preparatory meetings for the transition of the presidency.

A new e-mail address – **mrp@emea.eu.int** – was introduced at the EMEA to receive the notifications described in the Notice to Applicants as required under the mutual recognition procedure.

Mutual recognition procedure	Total submitted in 2002*	Under evaluation in 2002*	Ended positively in 2002*	Referrals started in 2002
New applications	587	106	420	2
Type I variations	2 447	224	2 104	N/A
Type II variations	808	223	527	7

**The numbers include multiple procedures as stated at 31 December 2002.*

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
Sheila KENNEDY (acting until 1 July 2002)
Emer COOKE (from 1 July 2002)

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

Committee for Veterinary Medicinal Products

Chairman of the CVMP
Steve DEAN

Vice-chairman of the CVMP
Gérard MOULIN

Working parties and ad hoc groups

Efficacy Working Party
Liisa KAARTINEN

Immunologicals Working Party
David MACKAY

Pharmacovigilance Working Party
Cornelia IBRAHIM

Joint CPMP/CVMP Quality Working Party
Jean-Louis ROBERT

Safety Working Party
Christian FRIIS

ad hoc Group on Antimicrobial Resistance
Margarita ARBOIX

ad hoc Group on Environmental Risk Assessment
Hans HOOGLAND

Priorities for veterinary medicines in 2002 – progress report

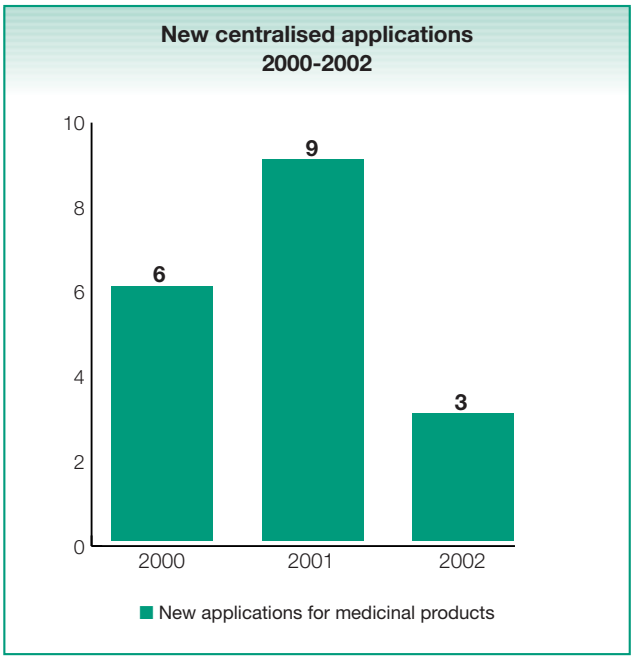
- Significant progress was achieved in the development of guidelines foreseen in the CVMP risk management strategic plan on antimicrobial resistance (EMEA/CVMP/818/99). Two guidelines on pre-authorisation testing for veterinary antimicrobial and on general use of antimicrobial in target animal species were adopted after extensive consultation with interested parties and will come into force in 2003.
- Veterinary regulatory affairs were successfully addressed in the second phase of the Pan-European Regulatory Forum (PERF II), the programme established to prepare the candidate countries from central and eastern Europe for accession to the EU.
- Progress in the implementation of the veterinary aspects of the EudraVigilance project continued to be delayed pending finalisation of VICH guidelines on data elements for transmission of adverse event reports for veterinary medicines. It is anticipated that progress at VICH will only advance during 2003. In the meantime the programme will be progressed by the EU based on its own standards of electronic reporting to be defined by the CVMP and its working party on pharmacovigilance in the early part of 2003.

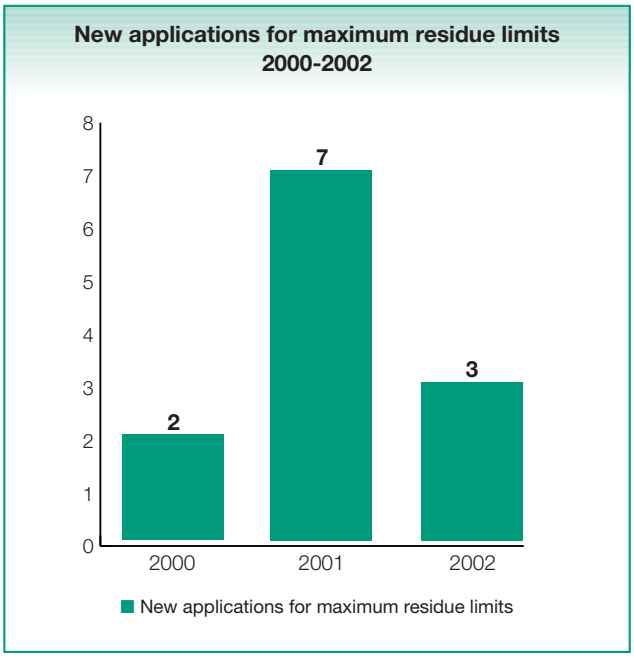
- The EMEA, as part of the EU delegation, continued its active participation in the VICH process in 2002 including at the second VICH conference held in Tokyo in October 2002. Particular attention was focused on the desire to achieve international harmonisation while ensuring that the testing requirements are compatible with the testing standards reflected in EU legislation.
- A pharmacovigilance workshop was jointly organised by the EMEA with interested parties in Madrid in May 2002. Hosted by the Spanish presidency and jointly organised with the Federation of Veterinarians in Europe (FVE) and the European Federation of Animal Health (FEDESA), the workshop looked at options to facilitate the further promotion of pharmacovigilance of veterinary medicines in the European Union. The conclusions of the workshop were considered and agreed to by the CVMP and its working party and a set of recommendations and proposals on initiatives to strengthen pharmacovigilance was discussed and agreed with the heads of veterinary agencies (HEVRA). Proposals will be presented to the EMEA Management Board in early 2003.
- The potential hazards of violative residues in excess of established MRLs remaining at the injection site was highlighted by a referral to the CVMP in 2002 concerning long-acting formulations of benzathine penicillin. The Committee recommended the suspension of authorisations for all such formulations of benzathine penicillin used in food-producing animals in the EU.
- The validation of all applications received in 2002 (centralised procedures and MRL applications) was completed within 10 working days. All evaluation procedures for initial applications (centralised and MRLs) as well as post-authorisation procedures (extensions and variations), as well as referrals, were concluded within the regulatory timeframe in accordance with the Agency's quality management system.

3.1 Initial evaluation

Three applications for marketing authorisation were made under the centralised procedure in 2002. Similarly there were also three applications for maximum residue limits (MRLs) for new substances. Both these figures are below the original forecasts, mainly because some companies experienced delays in their development programme and then postponed applications. This is also an indication of the disappointingly low number of veterinary medicinal products in the development pipeline destined for food-producing animals.

CVMP activities





The CVMP met 11 times under the chairmanship of Steve Dean. Mr Dean resigned as chairman of the CVMP with effect from the end of December 2002 due to his new role as Chief Executive of the UK Veterinary Medicines Directorate. There were no extraordinary meetings of the Committee in the reporting period.

The Strategic Planning Group met on four occasions chaired by the CVMP vice-chairman, Gérard Moulin. The group monitors the organisation and working of the CVMP and also advises the Committee on a range of issues including:

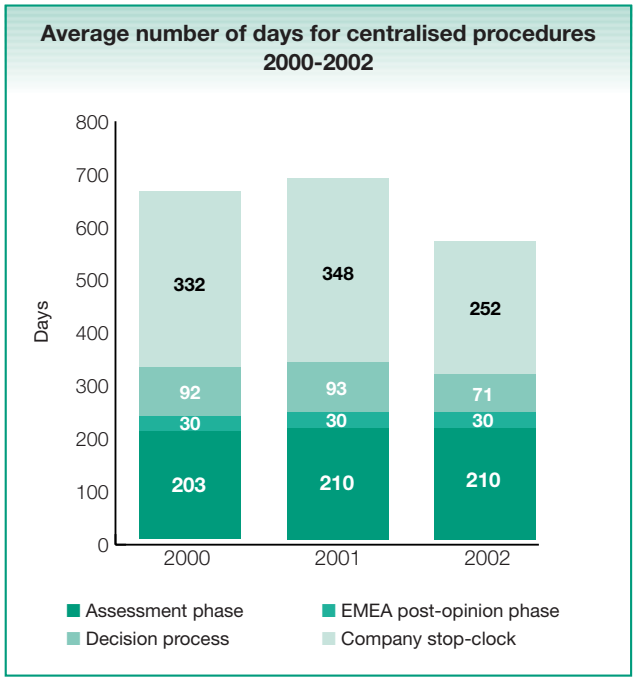
- The appropriate levels of communication between rapporteurs and applicants during the assessment process
- Advice and guidance to the working parties on their working methods and optimising communication between them
- Further transparency issues to improve communication between the CVMP and its interested parties

The Committee has continued to take an active interest in training of assessors in cooperation with the heads of veterinary agencies (HEVRA) and was pleased to support major initiatives with support of the EMEA in 2002 including:

- A joint workshop for the training of junior assessors in cooperation with CPMP
- Development of a training programme for assessors together with Member States

The CVMP and CPMP jointly organised a seminar hosted by Spain for experts of both Committees in the field of antimicrobial resistance. The activities of both Committees and their expert working groups were reviewed and discussed in detail and recommendations for further activities and collaboration were agreed upon.

Performance indicators



3.2 Establishment of maximum residue limits for old substances

Following receipt of data from applicants, the CVMP concluded evaluation of 7 out of the 15 substances remaining in Annex III (provisional MRL) of Council Regulation (EC) No 2377/90 at the beginning of 2002, five of which were recommended for inclusion in Annex I (definitive MRL established). The CVMP concluded that it was not possible to recommend the inclusion of one out of the five substances in any of the annexes of Council Regulation (EC) No 2377/90.

The substances recommended for inclusion in Annex I are:

– Cefalonium (Annex I)
– Colistin (Annex I)
– Josamycin (no recommendation)
– Neomycin (Annex I)
– Oxolinic acid (no recommendation – *opinion under appeal*)
– Oxyclozanide (Annex I)
– Permethrin (Annex I)

The remaining eight substances awaiting responses from applicants to establish final MRLs are:

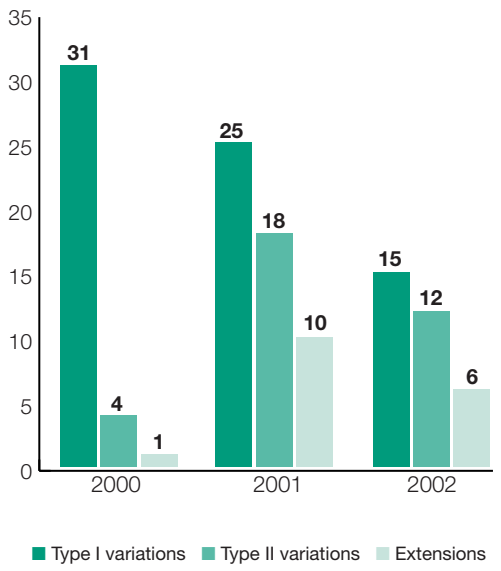
– Alpha-cypermethrin
– Altrenogest
– Cypermethrin
– Deltamethin
– Flugestone acetate
– Kanamycin
– Metamizole
– Morantel

The EMEA continues to respond to a large number of enquiries from the European Commission, interested parties and other sources on the interpretation of Annex entries in Council Regulation (EEC) No 2377/90 for old substances.

3.3 Post-authorisation activities

Post-authorisation activities continue at a reasonable pace in accordance with the increase in number of centrally approved products. The number of type II variations and line extensions was in line with forecasts. The number of type I variations fell a little below initial forecasts.

Post-authorisation applications for centrally authorised medicinal product 2000-2002

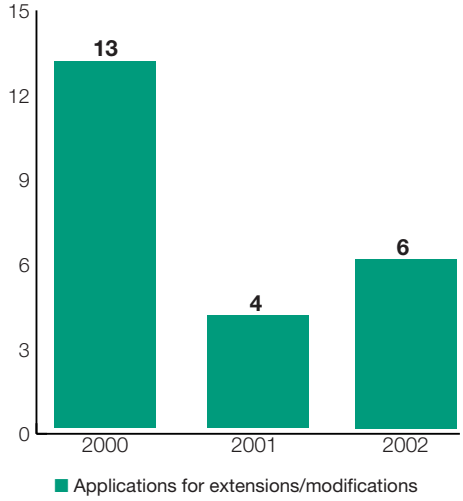


Following on from the adoption in 2001 of the note for guidance on extrapolation of MRLs to further species (EMEA/CVMP/187/00-FINAL), the CVMP adopted opinions on extrapolation of established MRLs to all animal species for 12 substances:

Danofloxacin	Florfenicol	Spectinomycin
Difloxacin	Flumequine	Tilimicosin
Enrofloxacin	Lincomycin	Trimethorpim
Erythromycin	Paromomycin	Tylosin

The number of applications for the extension of existing MRLs, mostly as applications for additional species, was in accordance with the level forecast. This is however disappointingly below the number expected given the possibilities for extrapolation to minor species, which was expected to be an incentive to industry to develop products in such animals. Additional efforts by the CVMP to further extrapolate MRLs without the necessity for applications to be submitted continue to be considered by the Committee.

Applications for extension/modification of maximum residue limits 2000-2002

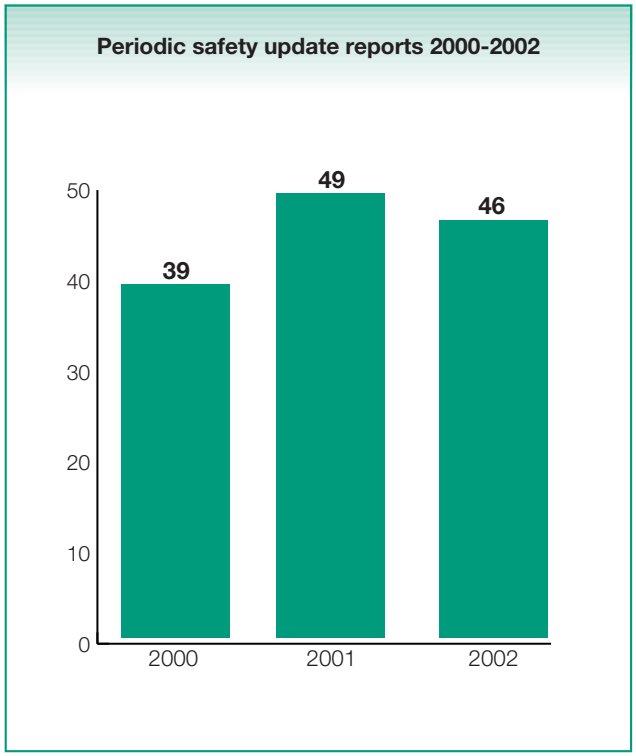


3.4 Pharmacovigilance and maintenance activities

The EMEA is committed to ensuring an efficient, successful pharmacovigilance reporting system for veterinary medicines in the EU and was pleased to co-sponsor a workshop on the subject with CVMP interested parties, hosted by the Spanish presidency in May 2002.

The outcome of this workshop has been a policy paper agreed to by CVMP and discussed by the heads of veterinary agencies (HEVRA). The paper makes a number of recommendations that aim to improve communication and feedback on pharmacovigilance to the veterinary profession in Europe, promote education and training on this important topic and provide further possibilities to promote common systems at all levels in the reporting chain. The paper is available on the EMEA web site and the recommendations will be put into action next year.

The CVMP reviewed 46 periodic safety update reports (PSUR) in 2002, with only one change to the risk/benefit analysis of a centrally approved products requiring changes to the SPC and/or labelling.



EudraVigilance – Veterinary – Countdown during 2002

- First prototype to reflect and test implementation of data elements for transmission of reports is in place in accordance with draft VICH guidelines GL 24, GL 30 and GL 35
- Development of document type definition for the message specification for electronic transmission of reports completed underway
- Veterinary dictionary of clinical terms in place
- Data Processing Network to be established by EMEA in collaboration with Member States and Commission

3.5 Scientific advice

A total of four applications for scientific advice were made in 2002, compared to the initial forecast of just one. The applications related to quality alone in one case, quality and safety in another, safety alone for one application and finally clinical alone.

This increase reflects the efforts made by the EMEA to raise awareness of this service. A questionnaire was conducted by FEDESA in conjunction with the Agency regarding scientific advice and the results were discussed at the EMEA/FEDESA Info-day in September 2002. The CVMP revised its standard operating procedure for scientific advice and a new guidance document on scientific advice was published on the EMEA web site in September 2002.

3.6 Arbitration and Community referrals

Two referrals under Article 33 of Directive 2001/82/EC for two veterinary medicinal products – generic versions of ivermectin – under the mutual recognition procedure were referred to CVMP in February 2002 by Belgium. The referrals both concerned the correlation between the plasma levels of anti-parasitic products and their clinical effectiveness. CVMP did not support the objection of the concerned Member State who made the referral, on the basis that product specific efficacy data for products are required even where bioequivalence has been demonstrated.

In October a referral for arbitration under Article 33 of Directive 2001/82/EC was initiated by both Denmark and Spain concerning a line extension to a product containing orbifloxacin. The area of disagreement concerns the justification of the higher dose in the treatment of skin and associated soft tissue infections. The referral is ongoing and CVMP will reach an opinion early in 2003.

The CVMP considered a safety referral under Article 20 of Council Directive 81/851/EEC (now Article 35 of Directive 2001/82/EC) concerning all long-acting injectable veterinary medicinal products for food producing animals containing benzathine penicillin. This referral had been initiated by Ireland due to concerns of violative residues in excess of established MRLs remaining at the injection site following the use of such products. A lengthy and in-depth procedure following this referral resulted in a CVMP opinion recommending the suspension of all authorisations for this class of compound used in food animals within the EU. The CVMP opinion was the subject of an appeal as at the end of 2002.

Details of referrals are given in Annex 11.

3.7 Working parties and ad hoc groups

• Efficacy Working Party

The Working Party met twice and all planned new guidelines have now been finalised. In support of the CVMP risk management strategic plan for antimicrobial resistance, the revision of the general antimicrobial guideline and a guidance document for standard phrases for product literature for antimicrobial were also completed following consultation. Details of these guidelines are given in Annex 10 to this report. The group supported the VICH EU expert for target animal safety in agreeing contributions to the development of the relevant VICH guideline. Work continues in drafting a document for standardisation of phrases for the SPC.

• Immunologicals Working Party

The Working Party met three times during the course of the year and completed preparation of a position paper and a number of guidelines, which are referenced in Annex 10 of this report. In addition, the Working Party continued to work closely with members of the Biotechnology Working Party of the CPMP resulting in the revision of the Note for guidance on TSE. The Working Party's ad hoc group of experts on foot and mouth disease prepared a position paper on requirements for vaccines on foot and mouth disease, which was adopted for a six-month consultation period in October 2002 by the CVMP.

• Pharmacovigilance Working Party

The Working Party met six times during the course of the year. A Points to consider document on a common EU reporting form for marketing authorisation holders for reporting to competent authorities was released for consultation, for future incorporation in the relevant guideline. The Working Party also completed the revision of VEDDRA, the list of clinical terms to be used for the reporting of suspected adverse reactions to veterinary medicinal products. At the Working Party's initiative more explicit guidance regarding inadvertent self-injection (of humans administering a veterinary product to animals) was included in the revised Guideline on preparation of summary of product characteristics – Immunologicals for veterinary medicinal products, published in volume 6C of *The rules governing medicinal products in the European Union.*

Furthermore the group made good progress in the preparation of new guidance on causality assessment, the triggering of regulatory action through pharmacovigilance, and on the calculation of incidence in PSURs.

• Safety Working Party

The Working Party met four times during 2002 and completed the revision of the guideline on safety evaluation of antimicrobial substances regarding the effects on human gut flora. The group also worked on the revision of the current CVMP injection site guideline as well as a new guideline on user safety. The Working Party continued the evaluation of the answers to the list of questions of old substances having provisional MRLs in Annex III of Council Regulation (EEC) No 2377/90. The group also provided advice to the CVMP on its review of VICH guidelines, as well as on issues concerning the establishment of MRLs at Codex Alimentarius.

• Joint CPMP/CVMP Quality Working Party

The Working Party met four times during the course of the year and completed the preparation and finalisation of a number of veterinary-specific guidelines in addition to a number of guidelines applicable to both medicines for human and veterinary use. These include finalisation of a veterinary-specific position paper, in conjunction with the Immunologicals Working Party, on the maximum in-use shelf life for medicated drinking water. An interested parties meeting was held in June at which veterinary industry representatives were present. The annual meeting between QWP and interested parties was held in April 2002.

• ad hoc group on antimicrobial resistance

The ad hoc group met once during the year and finalised the guideline on pre-authorisation studies in relation to antimicrobial resistance. The group also continued its task to advise the CVMP on all matters relating to antimicrobial resistance subjects. A meeting with experts of the CPMP/CVMP and the ad hoc group took place in Madrid on 3 December 2002.

• ad hoc group on environmental risk assessment

The ad hoc group met twice during the year and worked particularly on providing input into the development of the phase II VICH guideline on environmental impact assessment.

3.8 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 for one day each month (except August) in 2002 at the EMEA, under the chairs of the Spanish and the Danish presidency respectively. 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 2002 – one in Barcelona in June under the Spanish presidency and one in Copenhagen in November under the Danish presidency.

The number of mutual recognition procedures completed increased from 43 in 2001 to 84 in 2002. Ten Member States acted as reference member state in the procedures in 2002, compared to eight in 2001 year.

In 2002 the first mutual recognition procedure involving some of the central and eastern European countries as concerned member states was initiated. Three separate referrals for arbitration under Article 33 of Directive 82/2001/EC were made to CVMP in 2002. The summary reasons for withdrawals in 2001 is published on the HEVRA website.

The VMRF interested parties liaison group met regularly during 2002. The group consists of representatives from VMRFG and from FEDESA and for the first time the new European Generic Association (EGGVP) joined the meeting in July 2002. The joint VMRF-FEDESA survey of the mutual recognition procedure was previously published on the HEVRA website and has been continued in 2002. A report on the activities of the VMRFG was provided at each CVMP meeting in 2002 and the chairperson provided a report to HEVRA at each of that group's meetings.

Chapter 4
Inspections

Overview

Head of Sector
Emer COOKE
Shelia KENNEDY (acting until 1 July 2002)

ad hoc Meeting of GMP inspection services
Katrin NODOP and Shelia KENNEDY

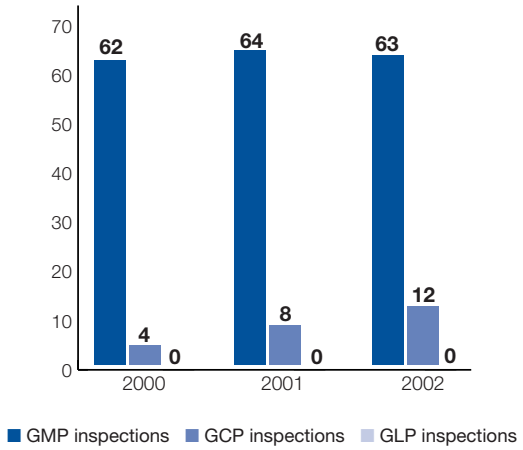
ad hoc Meeting of GCP inspection services
Fergus SWEENEY

Priorities for Inspections in 2002 – progress report

- Good progress was achieved with the mutual recognition agreements (MRA) with Japan and Switzerland. An 18-month confidence-building phase with Japan was initiated on 1 January 2002 with meetings of the sub-committee having taken place both at EMEA and in Tokyo. The MRA with Switzerland entered into force on 1 June 2002. The veterinary part of the MRA with New Zealand also began on 1 June 2002. No progress was made on the MRA with the USA.
- Harmonisation activities continued with ongoing meetings of the ad hoc group of inspectors on Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP). An on-line database for GMP was made available through EudraNet to a number of Member States in April 2002.
- As part of preparations for the implementation of the EU clinical trials directive, the EMEA undertook the rapporteurship for the database of clinical trials and suspected unexpected adverse reactions reporting, the latter being foreseen as a EudraVigilance module.
- In this context, the ad hoc group of GCP inspectors also adopted detailed guidelines on GCP inspection procedures, qualifications of GCP inspectors and trial master file and archiving.
- Three GMP workshops were held as part of the PERF II programme, as well as joint inspections in the accession candidate countries.
- Processing of all inspections proceeded efficiently and within the legal timeframe with those for GCP exceeding the forecasted number and those for GMP falling slightly below. The certificate scheme for centrally approved products continued successfully and efficiently with all documents issued within the five-day timeframe in response to over 13 000 requests for certificates from marketing authorisation holders.

4.1 Coordination of inspections for centralised procedures

Inspections performed 2000-2002



Requests for good manufacturing practice (GMP) inspections continued at a steady level, providing an important contribution to both the pre- and post-approval monitoring of medicinal products in the human and veterinary medicines fields.

There was an increase in the second half of 2002 in the number of quality related defects for centrally authorised products requiring coordination of rapid alerts, highlighting the need for close coordination between supervisory authorities and the EMEA. A total of 20 reports were received and monitored by the EMEA on quality problems concerning centrally authorised products, leading to the recall of six medicinal products.

An on-line database of manufacturing sites for centrally authorised products was made available to seven Member State inspection services in 2002. Once fully operational the database will link all Member State inspection service and offer

a rolling plan of all non-EU country inspections planned by the Member States and provide information on GMP compliance for EU manufacturers of centralised products.

The ad hoc group of GMP inspection services met four times in 2002, and finalised a number of new and revised annexes to the EU GMP Guide. The Inspections sector was also active in initiating GMP harmonisation projects including the handling of quality defects and coordination of surveillance of manufacturing plants in third countries where problems have been identified in the context of a European inspection.

The first visits in the context 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 were initiated in the second half of 2002.

Good clinical practice

The number of good clinical practice (GCP) inspections for human medicinal products requested rose as anticipated in 2002, despite the lower number of centralised applications than forecast. These inspections involved sponsor, investigator and laboratory sites both within and outside the EU. A number of these inspections were conducted post-authorisation and included assessment of compliance with pharmacovigilance obligations as well as in the context of clinical trials.

The ad hoc group of GCP inspection services met four times in 2002, one of these meetings taking place in conjunction with clinical assessors from Member States in a successful attempt to meet the need for greater collaboration between inspectors and assessors. The first referral to the CPMP due to GCP anomalies found during an inspection was also made in 2002.

The Management Board adopted a policy on financial transactions and payments for GCP in February 2002. This policy clarifies the fees due for these inspections.

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

4.2 Implementation of the clinical trials directive

Preparations for the implementation of Directive 2001/20/EC on the conduct of clinical trials progressed well in 2002 ahead of the May 2004 date for entry into force. Both the GMP and GCP inspection groups have been active in drawing up the necessary guidelines for GMP and GCP procedures for investigational medicinal products.

EMEA continued to participate actively in the European Commission Working Party on the preparation of other documents needed under the Directive. In addition EMEA has drafted guidance and begun work on a project to implement the clinical trial database and the clinical trial part of the EudraVigilance database, for which it is rapporteur.

4.3 Mutual recognition agreements

Good progress was achieved with the mutual recognition agreements (MRA) with Japan and Switzerland. An 18-month preparatory confidence-building phase with Japan was initiated on 1 January 2002. Work programmes were agreed involving mutual visits and monitoring of procedures and legislation and evaluation visits in both territories. The MRA with Switzerland entered into force on 1 June 2002 and a conference was hosted at the EMEA to discuss its implications. In parallel to this, the EMEA worked to ensure a smooth implementation at a practical level and expects its implementation to reduce the number of GMP inspections needed to be performed by EU inspectors by about 25 % per annum. The veterinary part of the MRA with New Zealand also began on 1 June 2002. No progress was made on the MRA with the USA. Progress on the MRA with Canada could see the start of the operational phase in early 2003.

Mutual recognition agreement (MRA) implementation status and coverage

EC-Australia

Implementation status:
Human Medicinal products: 1 January 1999
Veterinary medicinal products: 1 June 2001
Coverage:
Human and veterinary medicinal products
Official batch release excluded

EC-Canada

Implementation status:
Operational phase expected to start in early 2003

Coverage:

Human and veterinary medicinal products

Veterinary immunologicals and vaccines excluded

EC-Japan

Implementation status:

1 January 2002, start of 18 months preparatory phase

Operational phase expected to start in second half of 2003

Coverage:

Human medicinal products only

Currently excludes active substances, investigational medicinal products, medicinal gases

Official batch release excluded

EC-New Zealand

Implementation status:

Human Medicinal products: 1 January 1999

Veterinary medicinal products: 1 June 2002

Coverage:

Human and veterinary medicinal products

Official batch release excluded

EC-Switzerland

Implementation status:

1 June 2002

Coverage:

Human and veterinary medicinal products and recognition of official batch control of biologicals

EC-United States

Implementation status:

Not in operation. Transitional period ended. No decision on formal extension of the transitional period has been taken

Coverage:

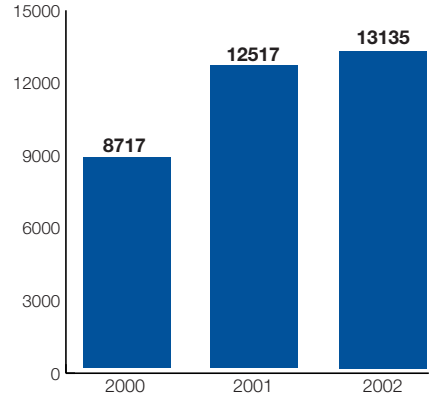
Human and veterinary medicinal products

Official batch release excluded

4.4 Certification of medicinal products

The demand for certificates was uneven during 2002, with slightly lower figures in the first half of the year but significantly higher demand during the second half of the year. The trend now is for an increase in the number of requests submitted but a reduction in the average size of requests. Overall, the number of certificates requested stayed constant 13 135 compared to

Certificates of a medicinal product 2000-2002



12 517 in 2001. These numbers reflect a rise in the number of variations, extensions, renewals and authorisations of centralised products, where certificates are needed for submission of applications in non-EU countries.

Following a meeting with interested parties in February, EMEA launched new forms and interactive guidance for requesting certificates in April 2002. The administrative fee charges for this service were amended by the Management Board at its 19 December 2002 meeting.

4.5 Sampling and testing

The Network of Official Medicines Control Laboratories performs the monitoring of centrally authorised medicinal products. The activities of the network are co-ordinated by the European Department for the Quality of Medicines (EDQM) Council of Europe) and the EMEA. The 2002 testing programme was implemented for 31 centrally authorised products. Limited market availability of samples has led to some delays and a need to reconsider more flexible sampling strategies in practice.

The EMEA developed and introduced a procedure for follow-up actions following testing. As a result of the continued success of the programme, a testing programme for 2004 was agreed including a 50 % increase in the number of products to be tested and a new covenant with the EDQM was signed.

Chapter 5
Communications and networking

Overview

Communications and networking Unit

Head of Unit
Hans-Georg WAGNER

Head of Sector for information technology
Michael ZOURIDAKIS

Deputy Head of Sector for information technology
David DRAKEFORD

Head of Sector for project management
Tim BUXTON

Head of Sector for conference services
Sylvie BÉNÉFICE

Head of Sector for document management and publishing
Beatrice FAYL

The Communications and networking Unit was created in 2001 and is focused on provision of services aimed at the Agency's partners, including the provision of information to the public and extensive logistical and technical support to national competent authorities. It is also responsible for provision of IT services for the EMEA. A Head of Unit was appointed in May 2002.

5.1 Implementation of the EU telematics strategy

Early in 2002, the Project Management and IT Sectors engaged consultants to complete an IT strategy. The general orientation of the IT Sector was changed in line with the direction of this strategy, which encompassed a number of European projects.

EMEA core applications

The IT Sector maintained high levels of IT services throughout 2002, with more than 99.5 % service availability. The EMEA help desk handled 2 344 calls during the year.

The development of core applications continued, including the joint WHO-EMEA SIAMED tracking system, personnel database, SI2 and ActiTrak. Improved storage capacity, together with the replacement of the Agency's local area network, was also implemented. In conjunction with the Meetings management and conference service, the use of videoconferencing facilities was extended within the Agency.

European initiatives and activities

The IT Sector played an active role in the coordination and management of Eudra (European Union drug regulatory authorities' Network) Eudra IT projects in the pharmaceutical sector, with direct participation at the Telematics Management Group and Telematics Implementation Group levels.

The IT Sector was heavily involved in preparation work to provide a range of EudraNet services to Member State Agency and Industry. The Sector took on the responsibility for chairing the EudraNet Telematics Implementation Group, which has defined the future direction of EudraNet in line with the direction of the IT strategy in consultation with Member State national competent authorities.

Preparation to take over EudraNet services from the European Commission Joint Research Centre as of January 2003 began in earnest September 2002, following earlier implementation of an EMEA firewall and new Internet service provider in July 2002.

A new application called EudraLink (EudraSafe II) was successfully implemented to allow secure encrypted message delivery. The application is based on 'open source' products and is intended to replace EudraSafe in 2003. Furthermore, a EudraNet security study was completed in 2002 involving an analysis of requirements and a Public Key Infrastructure pilot with the European Commission (Directorate-General for Enterprise and the IDA programme).

The Sector also provided support throughout 2002 to the EudraVigilance application.

5.2 Project management

The Project Management Sector was set up in order to assume responsibility for cross-Agency and pan-European projects related to communications and networking. The Head of Sector was appointed in May 2002. The Sector was involved in the management of the projects set out below during the year.

PERF

PERF II, which ran from July 2001, was closed in September 2002. The EMEA signed a further contract with European Commission Directorate-General for Enlargement in November 2002 to coordinate a final phase of the initiative, which is scheduled for completion in December 2003.

Concentrating on the areas determined by the PERF Steering Committee in 2000, the programme consisted of a series of meetings, joint inspections and secondments. Achievements during the programme included informal written guidance on specific aspects of the implementation of the *acquis communautaire* (see reflection papers: **http://perf.eudra.org**), and the second PERF conference, which was held in Tallinn in April 2002. In each of these areas, further progress was made in achieving the ultimate aim of the programme, namely to assist competent authorities in the candidate countries in aligning their standards and practices with those obtaining in the European Union.

Electronic submission

The Sector manages two projects in the area of electronic submissions: The implementation of the Electronic Common Technical Document (eCTD) and the Product Information Management (PIM) project. Both projects are run within the remit of the electronic submissions Telematics Implementation Group (TIG), which is chaired by France and met four times during the year. The eCTD is an exchange standard for the submission of information in support of a marketing authorisation application, whose specification was signed off at Step 4 in the ICH process in September 2002. The exchange standard will now be implemented in the three regions, which for the European regulators involves putting in place a system to receive, validate, store and make available submissions in the eCTD format.

PIM is a joint project with EFPIA dealing with the electronic interchange of information that is included in the summary of product characteristics, the patient information leaflet and all the packaging relating to a medicinal product. During 2002, a proof of concept application was successfully tested. The purpose of the testing was to demonstrate that an electronic interchange of information as between applicant and regulator is possible and beneficial, and to increase the robustness of the exchange standard. The results of the testing were reported back to the group involved in the project in December 2002.

EuroPharm database

The EuroPharm database is a proposed database of information on all medicinal products authorised in the EU. Implementation of the database is to be undertaken by the EMEA and the tracking Telematics Implementation Group (TIG) is chaired by Portugal.

Core data elements to be included in the database were defined by the TIG, and the scope of the database re-evaluated in the light of the proposals to amend the Agency's founding regulation. A revised implementation plan was agreed by the TIG. The proposal took into account the fact that funding for the development of this database will become available in 2004. Work to rationalise the use of data elements across all projects currently under way made significant progress, and is expected to bear fruit during 2003.

Clinical trials database

In accordance with Directive 2001/20/EC, a database is being designed for implementation by 1 May 2004. An ad hoc group of experts convened by European Commission Directorate-General for Enterprise drafted six guidelines on the implementation of the directive, two of which deal directly with the database. The guidelines were published for consultation and are being finalised.

The database has been split into two parts: One to deal with the register of clinical trials (provisionally named EUDRACT), and the other to deal with suspected unexpected serious adverse reactions – SUSARs. This second part is expected to be treated as a module of EudraVigilance since the type of data is essentially similar. Work on detailed specification of both these databases has begun.

Electronic document management system

The Agency's implementation of electronic document management met a number of technical problems in aligning the configuration of the product with the Agency's requirements in 2002. The EPAR publishing process, together with the process to manage standard operating procedures (SOPs) were piloted with electronic document management, and a project audit is planned.

SIAMED

SIAMED is an application originally developed by the WHO, and enhanced in the course of a joint WHO-EMEA project. The final enhancements planned for the joint project (adaptation for use in the area of maximum residue limits) are expected to be complete in 2003.

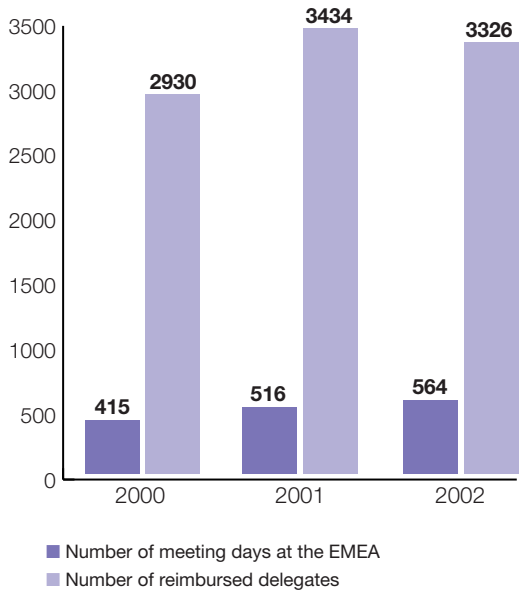
5.3 Meeting management and conferences

Meetings

There was a decrease in meeting activities in 2002 compared to 2001. The cost of interpretation provided at EMEA meetings was reduced by 18 % compared to the initial forecast.

A total of 3 326 delegate visits were reimbursed. Rises in hotel costs in London and a higher daily allowance were compensated by falls in travel costs, resulting in a decrease in expenditure of 4 % compared to 2001.

Meetings and delegates at the EMEA 2000-2002



Improvements to procedures for the organisations of meetings resulted in cost savings of about 20 % compared to 2001. Initiatives included the introduction of the second module of the computerised meetings management system and the development of best meeting practice guidelines. The average time for processing of reimbursement claims was reduced, with payment calculations for all meetings completed within one week.

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 scientific meetings to national authorities to allow better input from experts.

A review was carried out of future technical and logistical requirements resulting from enlargement of the European Union.

5.4 Document management and publishing

Document management

Documentum, the electronic document management system selected for implementation at the Agency, was subject to rigorous testing against EMEA requirements in 2002. Two processes relating to the publication of European public assessment report (EPARs) and management of standard operating procedures were progressed.

Quality and coherence of regulatory documents

A new linguistic review process was implemented at the beginning of 2002, which was put in place at the beginning of the year, whereby at submission and during assessment, only the English language version of the product information is submitted and reviewed, has proven to be successful. Applicants may now present the SPCs and package leaflets/inserts for different strengths of the same pharmaceutical form in one document. Different pack-sizes of the same strength can be presented in one labelling document. Translations of the agreed SPC, labelling and package leaflet/insert text in all EEA languages are provided after adoption of the English language opinion by the scientific committees.

Chapter 6
Administration

Overview

Administration Unit

Head of Unit
Andreas POTT

Head of Sector for personnel and budget
Frances NUTTALL

Head of Sector for infrastructure services
Sara MENDOSA

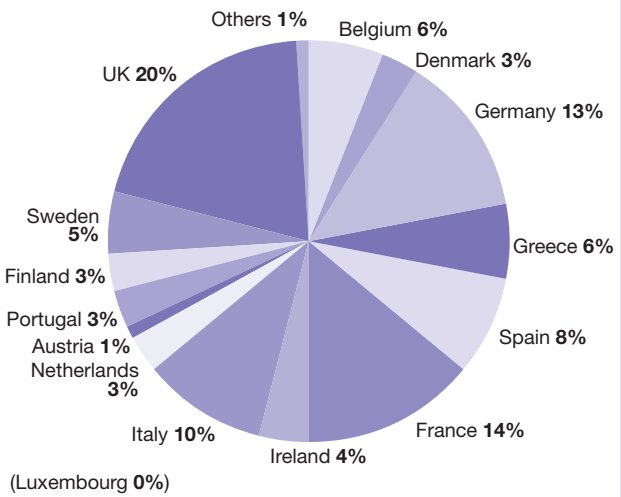
Head of Sector for accounting
Gerard O'MALLEY

The major challenges in 2002 have been the reconstruction and refurbishment of the 6th floor, the accommodation both of staff and the necessary funding for a number of new operational tasks with which the agency has been charged, as well as the continuous adaptation of the budget to growing needs in times of reduced fee revenue.

6.1 Personnel and budget

The number of EMEA staff members grew from 208 to 248 at the end of 2002, an increase of 19 %. A total of 19 internal and external recruitment procedures were organised during the year.

EMEA staff members by nationality in 2002



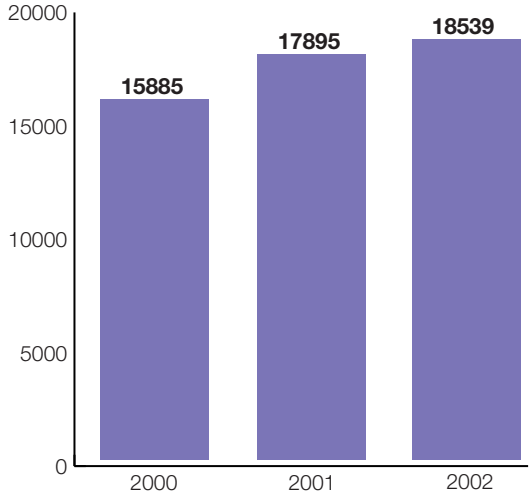
Several new personnel policies were introduced in 2002. These include the possibility of movement between categories to allow better career opportunities for EMEA staff, mutual recognition of experience gained in other Community bodies to facilitate transfer of staff between different community organisation and a scheme for reintegration of former staff if they apply to work again at the Agency. The development of a part-time working policy began following a staff questionnaire.

The Agency's personnel database was further developed, in particular to improve the provision of management information. Staff also benefited with the introduction of on-line administration of holiday and leave entitlements. Budgetary information was also integrated into the system, which will be used to generate budget estimates and reports.

Regular budget management reports were prepared during 2002, with two supplementary and amending budgets submitted and approved by the Management Board. The shortfall in fee revenue in 2002 required savings plans to be put in place to achieve a reduced level of expenditure. Justification for reinforcement of the Community contribution was successfully explained to the European Commission.

6.2 Infrastructure services

Number of visitors to the EMEA 2000-2002



The year 2002 was the first full year of operations for this newly created sector. Its activities cover a wide range of services including security, telecommunications, reception of visitors, switchboard, archiving, mail, reprographics, technical assistance to meeting rooms, confidential waste, health and safety, fire and emergency plans, inventory, office supplies, maintenance and management of the catering facilities.

One of the most important areas of activity in 2002 was the acquisition and refurbishment of the sixth floor at the EMEA headquarters building at 7 Westferry Circus. The works were completed in June and approximately 80 staff moved to their new offices in July. The refurbishment works include a number of small meeting rooms and videoconferencing facilities.

Work began on the development of a business continuity plan for the Agency. Awareness sessions were held for all staff and included an introduction to business continuity planning, risk management, roles and responsibilities in a recovery process, emergency response, strategies for recovery, salvage and communication, exercising and testing of the business continuity plan.

6.3 Accounting

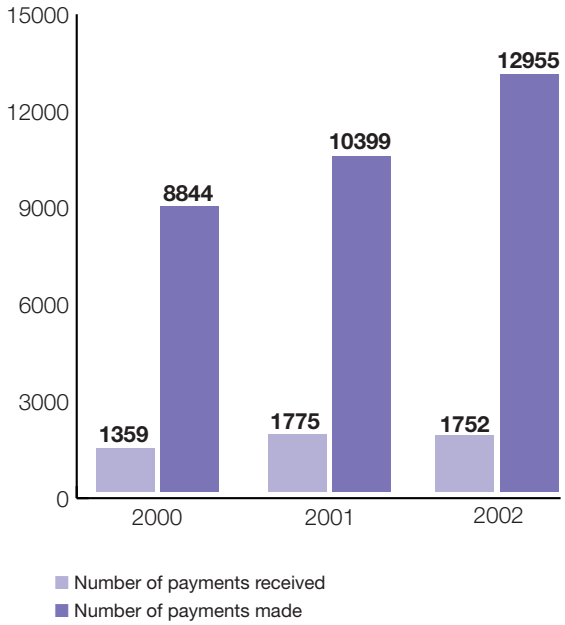
The key objective of the Accounting sector is to maintain the accounts, make payments and collect revenue in accordance with the procedures laid down in the Agency's financial regulation.

A number of internal procedures were improved in 2002 including the procedures for communicating with pharmaceutical companies on payment issues. In addition the customer accounting module in the SAGE software was developed to facilitate the monitoring of overdue invoices. Using the reporting functions in the SI2 accounting system, the actual accounts of the Agency can now be presented monthly within one to two days of the monthly closure.

Work began in 2002 on drafting a new financial regulation for the Agency, based on the framework financial regulation proposed by the European Commission for all EU agencies.

As forecast in the 2002 work programme the workload in accounts increased by 21 % over 2001, coming on top of a 19 % over 2000 activity levels. The effect of the decrease in applications to the centralised evaluation applications had only a minor impact on the Accounts sector as overall the number of revenue related transactions decreased by just 1%.

Payments received and made 2000-2002



Annexes

Annex 1

Members of the Management Board

Chairman	Keith JONES

Members

European Parliament	Gianmartino BENZI, José-Luis VALVERDE LÓPEZ
	Alternates: Dietrich HENSCHLER, Jean-Pierre REYNIER
European Commission	Jean-Paul MINGASSON [1], Bertrand CARSIN
	Alternate: Paul WEISSENBERG [2]
Belgium	André PAUWELS, Frans GOSSELINCKX
Denmark	Ib VALSBORG, Jytte LYNGVIG
Germany	Hans-Peter HOFMANN [3], Gerhard Josef KOTHMANN, *Vice-chairman*
Greece	Michalis MARAGOUDAKIS [4], Elias MOSSIALOS
Spain	Fernando GARCIA ALONSO [5], Carlos LENS CABRERA [6]
France	Philippe DUNETON, Martin HIRSCH
Ireland	Tom MOONEY, Michael GAYNOR [7]
Italy	Nello MARTINI, Romano MARABELLI
Luxembourg	Mariette BACKES-LIES
Netherlands	Huib VAN DE DONK [8], Frits PLUIMERS
Austria	Christian KALCHER [9], Ernst LUSZCZAK
Portugal	Rui dos SANTOS IVO [10], Manuel NEVES DIAS [11]
Finland	Pekka JÄRVINEN, Hannes WAHLROOS
Sweden	Birgitta BRATTHALL, Anders BROSTRÖM
United Kingdom	Roy ALDER, Steve DEAN [12]

Observers

Iceland	Rannveig GUNNARSDÓTTIR, Ingolf J PETERSEN
Liechtenstein	Brigitte BATLINER, Peter MALIN
Norway	Kai FINSNES [13], Gro Ramsten WESENBERG

1 Replaced Paul WEISSENBERG as of October 2002 meeting.

2 Replaced Philippe BRUNET as of October 2002 meeting.

3 Replaced Hermann Josef PABEL as of October 2002 meeting.

4 Replaced Marios MARSELOS as of June 2002 meeting.

5 Replaced María Victoria de la CUESTA GARCÍA as of February 2002 meeting.

6 Replaced Ramón PALOP BAIXAULI as of February 2002 meeting.

7 Resigned at the October 2002 meeting, no replacement nominated.

8 Replaced John LISMAN as of February 2002 meeting.

9 Replaced Alexander JENTZSCH as of June 2002 meeting.

10 Replaced Miguel ANDRADE as of October 2002 meeting.

11 Replaced Rogério GASPAR as of October 2002 meeting.

12 Replaced Michael RUTTER as of the June 2002 meeting.

13 Replaced Andreas DISEN as of June 2002 meeting.

Annex 2

Members of the Committee for Proprietary Medicinal Products

- Daniel BRASSEUR (Belgium), *Chairman*

- Eric ABADIE (France), *Vice-chairman*
- Mark AINSWORTH (Denmark)
- Fernando de ANDRES-TRELLES (Spain)
- Peter ARLETT (United Kingdom)
- Michalis AVGERINOS (Greece)
- Rolf BASS (Germany)
- Gonzalo CALVO ROJAS (Spain) [1]
- Nikolaos DRAKOULIS (Greece) [2]
- Jens ERSBØLL (Denmark)
- Bruno FLAMION (Belgium) [3]
- Silvio GARATTINI (Italy)
- Jacqueline GENOUX-HAMES (Luxembourg)
- Lars GRAMSTAD (Norway)
- Manfred HAASE (Germany)
- Ian HUDSON (United Kingdom) [4]
- Magnús JÓHANNSSON (Iceland)
- Pekka KURKI (Finland)
- Frits LEKKERKERKER (Netherlands)
- David LYONS (Ireland)
- Pieter NEELS (Belgium)
- Per NILSSON (Sweden)
- Heribert PITTNER (Austria)
- Jean-Louis ROBERT (Luxembourg)
- Pasqualino ROSSI (Italy)
- Patrick SALMON (Ireland)
- Tomas SALMONSON (Sweden)
- Cristina SAMPAIO (Portugal)
- Beatriz SILVIA LIMA (Portugal)
- Eva SKOVLUND (Norway) [5]
- Josef SUKO (Austria)
- Sigurdur THORSTEINSSON (Iceland)
- Markku TOIVONEN (Finland)
- Jean-Hugues TROUVIN (France)
- Barbara VAN ZWIETEN-BOOT (Netherlands)

1 Replaced Fernando GARCIA ALONSO as of the March 2002 meeting.

2 Replaced Antonia PANTOUVAKI as of the February 2002 meeting.

3 Replaced Geert DE GREEF as of the September 2002 meeting.

4 Replaced Alex NICHOLSON as of the November 2002 meeting, who replaced Frances ROTBLAT as of the May 2002 meeting

5 Replaced Else HØIBRAATEN as of March 2002 meeting.

Annex 3

Members of the Committee for Veterinary Medicinal Products

- Steve DEAN (United Kingdom), *Chairman*

- Margarita ARBOIX (Spain)
- J. Gabriel BEECHINOR (Ireland)
- Hanne BERGENDAHL (Norway)
- Rory BREATHNACH (Ireland)
- Ricardo de la FUENTE (Spain)
- Johannes DICHTL (Austria)
- Virgilio DONINI (Italy)
- Françoise FALIZE (Belgium)
- Christian FRIIS (Denmark)
- Helle HARTMANN FRIES (Denmark)
- Johannes HOOGLAND (Netherlands)
- Tonje HØY (Norway)
- Eva FABIANSON-JOHNSSON (Sweden)
- Liisa KAARTINEN (Finland)
- Reinhard KROKER (Germany)
- Herman LENSING (Netherlands)
- Jan LUTHMAN (Sweden)
- David MACKAY (United Kingdom)
- Agostino MACRI (Italy)
- Ioannis MALEMIS (Greece)
- Eduardo MARQUES FONTES (Portugal)
- Maria Leonor MEISEL (Portugal)
- Manfred MOOS (Germany)
- Gérard MOULIN (France), *Vice-chairman*
- 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) [1]
- Marc WIRTOR (Luxembourg)

[1] Replaced Paul-Pierre PASTORET as of July 2002 meeting.

Annex 4

Members of the Committee for Orphan Medicinal Products

Members

- Josep TORRENT i FARNELL (Spain), *Chairman*
- Eric ABADIE (EMEA representative)
- Moisés ABASCAL ALONSO (Patient organisation representative)
- Gianmartino BENZI (EMEA representative)
- Heidrun BOSCH-TRABERG (Denmark)
- Brendan BUCKLEY (Ireland)
- Rembert ELBERS (Germany)
- José Manuel GIÃO TOSCANO RICO (Portugal)
- Kalle HOPPU (Finland)
- Bernd JILMA (Austria) [1]
- 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)
- François MEYER (France)
- Harrie SEEVERENS (The Netherlands)
- Rashmi SHAH (United Kingdom)
- George STATHOPOULOS (Greece)
- Domenica TARUSCIO (Italy)
- Kerstin WESTERMARK (Sweden)

Observers

- Randi NORDAL (Norway)
- Sigurdur THORSTEINSSON (Iceland)

[1] Replaced Hans Georg EICHLER as of the July 2002 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*

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Annex 6

EMEA budget summaries 2001-2003

The summarised comparative budget statements for 2001 to 2003 are as follows: (Amounts expressed in euro)

	2001[1] (31.12.2001)		2002[2] (31.12.2002)		2003[3] (19.12.2002)	
Revenue						
Fees	45 771 000	69.49%	39 000 000	63.61%	48 142 000	61.66%
General EU contribution	14 700 000	22.32%	17 135 000	27.95%	15 500 000	19.85%
Special EU contribution for IT telematics strategy	-	-	-	-	7 000 000	8.97%
Special EU contribution for orphan medicinal products	600 000	0.91%	2 750 000	4.49%	3 300 000	4.23%
Contribution from EEA	287 640	0.44%	366 000	0.60%	558 000	0.71%
Contribution from EU programmes (PERF)	2 314 360	3.51%	231 000	0.35%	1 430 000	1.83%
Other	2 193 000	3.33%	1 840 000	3.00%	2 151 000	2.75%
TOTAL REVENUE	**65 866 000**	**100.00%**	**61 304 000**	**100.00%**	**78 081 000**	**100.00%**
Expenditure						
Staff						
Salaries	20 615 000	31.30%	24 337 000	39.70%	29 130 000	37.31%
Interim and other support persons	1 414 000	2.15%	1 760 000	2.87%	1 845 000	2.36%
Other staff-related expenditure	1 683 640	2.55%	1 502 000	2.45%	2 213 000	2.83%
Total title 1	*23 712 640*	*36.00%*	*27 599 000*	*45.02%*	*33 188 000*	*42.50%*
Building/equipment						
Rent/charges	5 149 000	7.82%	5 526 000	9.01%	6 275 000	8.04%
Expenditure on data processing	4 293 000	6.52%	3 083 000	5.03%	6 250 000	8.00%
Other capital expenditure	1 658 000	2.52%	491 000	0.80%	627 000	0.80%
Postage and communications	617 000	0.94%	264 000	0.43%	418 000	0.54%
Other administrative expenditure	1 829 000	2.78%	2 043 000	3.33%	2 083 000	2.67%
Total title 2	*13 546 000*	*20.57%*	*11 407 000*	*18.60%*	*15 653 000*	*20.05%*
Operational expenditure						
Meetings	4 110 000	6.24%	3 535 000	5.77%	4 920 000	6.30%
Evaluations	21 308 000	32.35%	17 855 500	29.13%	21 941 000	28.10%
Translation	428 000	0.65%	477 000	0.78%	451 000	0.58%
Studies and consultants	225 000	0.34%	98 500	0.16%	350 000	0.45%
Publications	190 000	0.29%	119 000	0.19%	148 000	0.19%
EU programmes	2 346 360	3.56%	213 000	0.34%	1 430 000	1.83%
Total title 3	*28 607 360*	*43.43%*	*22 298 000*	*36.38%*	*29 240 000*	*37.45%*
TOTAL EXPENDITURE	**65 866 000**	**100.00%**	**61 304 000**	**100.00%**	**78 081 000**	**100.00%**

Notes

[1] Final appropriations for the 2001 budget. [2] Final appropriations for the 2002 budget. [3] Budget for 2003 as adopted by the Management Board on 19.12.2002.

Annex 7

CPMP opinions in 2002 on medicinal products for human use

Centralised applications

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
• **Invanz** • **ertapenem** • **Part B**	• Merck Sharp & Dohme	• J01DHXX • Parenteral treatment of moderate to severe infections caused by susceptible bacteria	• 26.12.2000 • 17.1.2002 • 212 days • 169 days	• 17.2.2002 • 18.4.2002 • 22.4.2002 • OJ C 129, 31.5.2002, p. 8
• **MicardisPlus** • **telmisartan - hydrochlorothiazide** • **Part B**	• Boehringer Ingelheim	• C09DA • Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on telmisartan alone	• 24.4.2001 • 17.1.2002 • 148 days • 115 days	• 25.2.2002 • 22.4.2002 • 23.4.2002 • OJ C 129, 31.5.2002, p. 8
• **PritorPlus** • **telmisartan - hydrochlorothiazide** • **Part B**	• Glaxo Group	• C09DA • Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on telmisartan alone	• 24.4.2001 • 17.1.2002 • 148 days • 115 days	• 25.2.2002 • 22.4.2002 • 24.4.2002 • OJ C 129, 31.5.2002, p. 8
• **BolusacPlus** • **telmisartan - hydrochlorothiazide** • **Part B**	• Boehringer Ingelheim	• C09DA • Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on telmisartan alone	• 24.4.2001 • 17.1.2002 • 148 days • 115 days	• 25.2.2002 • 19.4.2002 • 23.4.2002 • OJ C 129, 31.5.2002, p. 8
• **Axura** • **memantine** • **Part B**	• Merz Pharmaceuticals	• N06DX01 • Treatment of patients with moderately severe to severe Alzheimer disease	• 26.9.2000 • 21.2.2002 • 210 days • 295 days	• 25.3.2002 • 17.5.2002 • 22.5.2002 • OJ C 157, 2.7.2002, p. 2
• **Tracleer #** • **bosentan** • **Part B**	• Actelion	• C02KX01 • Symptomatic treatment of patients with pulmonary arterial hypertension	• 27.2.2001 • 21. 2.2002 • 187 days • 167 days	• 25.3.2002 • 15.5.2002 • 17.5.2002 • OJ C 129, 31.5.2002, p. 8
• **Opatanol** • **olopatadine** • **Part B**	• Alcon Laboratories	• S01GX09 • Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis	• 27.3.2001 • 21.2.2002 • 223 days • 101 days	• 23.3.2002 • 17.5.2002 • 22.5.2002 • OJ C 157, 2.7.2002, p. 2
• **EVRA** • **norelgestromin - ethinylestradiol** • **Part B**	• Janssen-Cilag	• G03AA • Female Contraception	• 27.3.2001 • 21.2.2002 • 177 days • 147 days	• 1.7.2002 • 22.8.2002 • 26.8.2002 • OJ C 237, 2.10.2002, p. 5
• **Ebixa** • **memantine** • **Part B**	• H. Lundbeck	• N06DX01 • Treatment of patients with moderately severe to severe Alzheimer disease	• 22.10.2001 • 21.2.2002 • 55 days • 64 days	• 25.3.2002 • 15.5.2002 • 17.5.2002 • OJ C 129, 31.5.2002, p. 8
• **Tamiflu** • **oseltamivir** • **Part B**	• Roche	• J05AH02 • Treatment of influenza and post-exposure prophylaxis of influenza	• 27.2.2001 • 21.3.2002 • 204 days • 180 days	• 23.4.2002 • 20.6.2002 • 24.6.2002 • OJ C 178, 26.7.2002, p. 4

# 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
• **Pegasys** • **peginterferon alfa-2a** • **Part A**	• Roche	• L03AB11 • Treatment of chronic hepatitis C in adults	• 30.1.2001 • 21.3.2002 • 205 days • 216 days	• 19.4.2002 • 20.6.2002 • 24.6.2002 • OJ C 178, 26.7.2002, p. 4
• **Velosulin** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AB01 • Treatment of diabetes mellitus	• 22.5.2001 • 25.4.2002 • 200 days • 133 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Monotard** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AC01 • Treatment of diabetes mellitus	• 17.7.2001 • 25.4.2002 • 200 days • 78 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Ultratard** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AE01 • Treatment of diabetes mellitus	• 17.7.2001 • 25.4.2002 • 200 days • 78 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Protaphane** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AC01 • Treatment of diabetes mellitus	• 17.7.2001 • 25.4.2002 • 200 days • 78 days	• 1.8.2002 • 7.10.2002 • 10.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Actraphane** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AD01 • Treatment of diabetes mellitus	• 19.6.2001 • 25.4.2002 • 201 days • 105 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Mixtard** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AD01 • Treatment of diabetes mellitus	• 19.6.2001 • 25.4.2002 • 201 days • 105 days	• 1.8.2002 • 7.10.2002 • 11.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Insulatard** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AC01 • Treatment of Diabetes mellitus	• 17.7.2001 • 25.4.2002 • 200 days • 78 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Actrapid** • **insulin human, rDNA** • **Part A**	• Novo Nordisk	• A10AB01 • Treatment of diabetes mellitus	• 22.5.2001 • 25.4.2002 • 200 days • 133 days	• 1.8.2002 • 7.10.2002 • 9.10.2002 • OJ C 258, 25.10.2002, p. 2
• **Neupopeg** • **pegfilgrastim** • **Part A**	• Amgen Europe	• L03AA13 • Reduction in the duration of neutropenia in patients treated with cytotoxic chemotherapy	• 22.5.2001 • 30.5.2002 • 177 days • 191 days	• 5.7.2002 • 22.8.2002 • 26.8.2002 • OJ C 237, 02.10.2002, p. 5
• **Xigris** • **drotrecogin alfa (activated)** • **Part A**	• Eli Lilly Nederland	• B01AD10 • Treatment of adult patients with severe sepsis with multiple organ failure, when added to best standard care	• 30.1.2001 • 30.5.2002 • 211 days • 270 days	• 2.7.2002 • 22.8.2002 • 26.8.2002 • OJ C 237, 02.10.2002, p. 5
• **Neulasta** • **pegfilgrastim** • **Part A**	• Amgen Europe	• L03AA13 • Reduction in the duration of neutropenia in patients treated with cytotoxic chemotherapy	• 22.5.2001 • 30.5.2002 • 177 days • 191 days	• 5.7.2002 • 22.8.2002 • 26.8.2002 • OJ C 237, 02.10.2002, p. 5

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
• **InductOs** • **dibotermin alfa** • **Part A**	• Genetics Institute of Europe	• M05BC01 • Adjunct treatment of tibia fractures in adults	• 27.3.2001 • 30.5.2002 • 210 days • 224 days	• 2.7.2002 • 9.10.2002 • 11.9.2002 • OJ C 237, 02.10.2002, p. 5
• **Ambirix** • **inactivated hepatitis A virus hepatitis B surface antigen, rDNA** • **Part A**	• GlaxoSmithKline Biologicals	• J07BC • Immunisation against hepatitis A and B infections	• 19.6.2001 • 30.5.2002 • 178 days • 163 days	• 27.6.2002 • 30.8.2002 • 5.9.2002 • OJ C 237, 02.10.2002, p. 5
• **Cialis** • **tadalafil** • **Part B**	• Lilly ICOS	• G04BE • Treatment of erectile dysfunction	• 17.7.2001 • 25.7.2002 • 202 days • 166 days	• 26.8.2002 • 12.11.2002 • 14.11.2002 •
• **Bextra** • **valdecoxib** • **Part B**	• Pharmacia-Pfizer EEIG	• M01AH • Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea	• 17.7.2001 • 25.7.2002 • 203 days • 165 days	• 29.8.2002 • • •
• **Valdyn** • **valdecoxib** • **Part B**	• Pharmacia Europe	• M01AH • Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea	• 17.7.2001 • 25.7.2002 • 203 days • 165 days	• 29.8.2002 • • •
• **Valdecoxib Pharmacia Europe EEIG** • **valdecoxib** • **Part B**	• Pharmacia Europe	• M01AH • Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea	• 17.7.2001 • 25.7.2002 • 203 days • 165 days	• 29.8.2002 • • •
• **Kudeq** • **valdecoxib** • **Part B**	• Pfizer	• M01AH • Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea	• 17.7.2001 • 25.7.2002 • 203 days • 165 days	• 29.8.2002 • • •
• **Valdecoxib-Pfizer Europe EEIG** • **valdecoxib** • **Part B**	• Pfizer	• M01AH • Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea	• 17.7.2001 • 25.7.2002 • 203 days • 165 days	• 29.8.2002 • • •
• **Zavesca #** • **miglustat** • **Part B**	• Oxford GlycoScience	• A16AX06 • Treatment of mild to moderate type 1 Gaucher disease when enzyme replacement therapy is unsuitable	• 17.7.2001 • 25.7.2002 • 200 days • 168 days	• 26.8.2002 • 20.11.2002 • •
• **Somavert #** • **pegvisomant** • **Part A**	• Pharmacia Enterprise	• H01AX (proposed) • Treatment of patients with acromegaly who had an inadequte response to surgery and/or radiation therapy and who did not respond to treatment with somatostatin analogues	• 29.3.2001 • 25.7.2002 • 177 days • 299 days	• 26.8.2002 • 13.11.2002 • 15.11.2002 •
• **Theryttrex** • **yttrium(Y-90) chloride** • **Part B**	• MDS Nordion	• Pending • Radiolabelling of carrier molecules, specifically developed and authorised for radiolabelling with this radionuclide	• 17.9.2001 • 19.9.2002 • 212 days • 150 days	• • • •
• **Carbaglu #** • **carglumic acid** • **Part B**	• Orphan Europe	• A16AA05 • Treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency	• 22.10.2001 • 17.10.2002 • 191 days • 164 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
• **Vivanza** • **vardenafil** • **Part B**	• Bayer	• G04B E09 • Treatment of erectile dysfunction	• 22.4.2002 • 21.11.2002 • 96 days • 115 days	• • • •
• **Levitra** • **vardenafil** • **Part B**	• Bayer	• G04B E09 • Treatment of erectile dysfunction	• 28.1.2002 • 21.11.2002 • 180 days • 115 days	• • • •
• **Ytracis** • **yttrium(Y-90)** • **Part B**	• CIS bio International	• V10X • Radiolabelling of carrier molecules, specifically developed and authorised for radiolabelling with this radionuclide	• 22.10.2001 • 21.11.2002 • 176 days • 209 days	• • • •
• **Hepsera** • **adefovir dipivoxil** • **Part B**	• Gilead Science	• J05 (pending) • Treatment of chronic hepatitis B in adults	• 22.4.2002 • 21.11.2002 • 152 days • 59 days	• • • •
• **Forsteo** • **teriparatide** •	• Eli Lilly	• • Treatment of established osteoporosis in postmenopausal women	• 19.6.2001 • 18.12.2002 • 207 days • 339 days	• • • •

Annex 8

CVMP opinions in 2002 on medicinal products for veterinary use

Centralised applications

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
• **Eurifel RCP-FelV** • **Vaccine** • **Part A**	• Mérial	• Cats • Vaccine against feline rhinotracheitis, calcivirus, panleucopenia and leukaemiac	• 19.12.2000 • 5.12.2001 • 210 days • 141 days	• 4.1.2002 • 8.3.2002 • 12.3.2002 • OJ C 77, 28.3.2002, p. 36
• **Porcilis Porcoli Diluvac Forte** • **Vaccine** • **Part A extension**	• Mérial	• Pigs (sows & gilts) • Vaccine against neonatal diarrhoea	• 16.1.2001 • 13.2.2002 • 210 days • 183 days	• 15.3.2002 • 22.5.2002 • 24.5.2002 • OJ C 157, 2.7.2002, p. 5
• **Quadrisol** • **Vedaprofen** • **Part B extension**	• Intervet International	• Dogs • Control of inflammation and relief of pain	• 13.2.2001 • 13.3.2002 • 210 days • 183 days	• 12.4.2002 • 10.7.2002 • 15.7.2002 • OJ C 178, 26.7.2002, p. 7
• **Metacam** • **Meloxicam** • **Part B extension**	• Boehringer Ingelheim	• Cats • Alleviation of pain and inflammation	• 13.6.2001 • 17.4.2002 • 210 days • 99 days	• 17.5.2002 • 9.8.2002 • 13.8.2002 • OJ C 206, 30.8.2002, p. 5
• **Gallivac HVT IBD** • **Live vaccine** • **Part A**	• Mérial	• Chickens • Infectious Bursal disease/ Marek's disease	• 12.7.2000 • 17.4.2002 • 210 days • 436 days	• 17.5.2002 • 9.8.2002 • 13.8.2002 • OJ C 206, 30.8.2002, p. 5
• **Dexdomitor** • **Dexmedetonidine** • **Part B**	• Orion Pharma	• Dogs and cats • Restraint, sedation and analgesia	• 15.5.2001 • 15.5.2002 • 210 days • 155 days	• 14.6.2002 • 30.8.2002 • 5.9.2002 • OJ C 237, 2.10.2002, p. 9
• **Nobivac Bb** • **Vaccine** • **Part B**	• Intervet International	• Cats • Vaccine against Bordetella bronchiseptica	• 13.2.2001 • 12.6.2002 • 210 days • 274 days	• 12.7.2002 • 10.9.2002 • 12.9.2002 • OJ C 237, 2.10.2002 p. 9
• **Sevoflo** • **Sevoflurane** • **Part B**	• Cyton Biosciences	• Dogs • Inhalation anaesthetic	• 11.7.2001 • 4.9.2002 • 210 days • 211 days	• 5.10.2002 • 11.12.2002 • 13.12.2002 • OJ C 2, 7.1.2003, p. 15
• **Nobilis OR inac** • **Vaccine** • **Part B**	• Intervet International	• Chickens • Immunisation against ornithobacterium rhinotracheale	• 18.1.2000 • 2.10.2002 • 206 days • 783 days	• 1.11.2002 • • •
• **Proteqflu** • **Vaccine** • **Part A**	• Merial	• Horses • Vaccine against equine influenza	• 13.11.2001 • 13.11.2002 • •	• 13.12.2002 • • •

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
• **Proteqflu-Te** • **Vaccine** • **Part A**	• Merial	• Horses • Vaccine against equine influenza and tetanus	• 13.11.2001 • 13.11.2002 • •	• 13.12.2002 • • •
• **Advocate** • **Imidacloprid/ Moxidectin** • **Part B**	• Bayer	• Dogs and cats • Antiparasitic	• 18.12.2001 • 11.12.2002 • 210 days • 149 days	• • • •
• **Ibaflin** • **Ibafloxacin** • **Part B extension**	• Intervet International	• Dogs • Antibacterial	• 7.8.2001 • 11.12.2002 • 210 days • 267 days	• • • •

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
• **Methylprednisolone**	• Bovine	• 13.7.1999 • 11.7.2001 • 177 days • 535 days	• 2.8.2001 • 17.1.2002 • OJ L 16, 18.1.2002
• **Acetyllisovaleryltylosin (extension)**	• Porcine	• 12.4.2001 • 11.7.2001 • 84 days • 0	• 3.8.2001 • 17.1.2002 • OJ L 16, 18.1.2002
• **Abamectin (extension)**	• Ovine	• 23.4.1999 • 5.12.2001 • 283 days • 674 days	• 3.1.2002 • 24.5.2002 • OJ L 137, 25.5.2002
• **Allantoin**	• All food producing species	• 12.7.2001 • 10.10.2001 • 90 days • 0	• 8.11.2001 • 24.5.2002 • OJ L 137, 25.5.2002
• **Benzocaine (extension)**	• Salmonidae	• 12.10.2000 • 7.11.2001 • 120 days • 271 days	• 29.11.2001 • 24.5.2002 • OJ L 137, 25.5.2002
• **Meloxicam (extension)**	• Equidae	• 13.12.2001 • 13.3.2002 • 90 days • 0	• 8.4.2002 • 27.8.2002 • OJ L 230, 28.8.2002
• **Azagly-nafarelin**	• Salmonidae	• 21.2.2001 • 13.2.2002 • 120 days • 237 days	• 11.3.2002 • 27.8.2002 • OJ L 230, 28.8.2002

Substance INN	Therapeutic area • Target species	EMEA/CVMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of regulation • Official Journal
• **Deslorelin acetate**	• Equidae	• 15.11.2001 • 13.2.2002 • 90 days • 0	• 11.3.2002 • 27.8.2002 • OJ L 230, 28.8.2002
• **Ceftiofur (modification)**	• To permit intramammary administration	• 17.1.2002 • 17.4.2002 • 90 days • 0	• 13.5.2002 • 1.10.2002 • OJ L 264, 2.10.2002
• **Hydroxyethylsalicylate (extension)**	• Extension of evaluation for salicylate	• 6.9.2001 • 17.4.2002 • 114 days • 109 days	• 13.5.2002 • 1.10.2002 • OJ L 264, 2.10.2002
• **Xylazine (extension)**	• Dairy cows	• 17.1.2002 • 17.4.2002 • 90 days • 0	• 13.5.2002 • 1.10.2002 • OJ L 264, 2.10.2002
• **Fenvalerate**	• Bovine	• 13.7.2001 • 15.5.2002 • 87 days • 219 days	• 13.6.2002 • 30.10.2002 • OJ L 297, 31.10.2002
• **Omeprazole**	• Equidae	• 12.4.2001 • 12.6.2002 • 120 days • 306 days	• 12.7.2002 • 30.10.2002 • OJ L 297, 31.10.2002
• **Tulathromycin**	• Bovine and swine	• 9.8.2001 • 12.6.2002 • 120 days • 187 days	• 12.7.2002 • 30.10.2002 • OJ L 297, 31.10.2002
• **Trichlormethiazide (extension)**	• Bovine milk	• 11.4.2002 • 10.7.2002 • 90 days • 0	• 1.8.2002 • •
• **Bacitracin (extension)**	• Rabbits	• 16.8.2002 • 13.11.2002 • 86 days • 0	• • •

Annex 9

COMP opinions in 2002 on designation of orphan medicinal products

Positive COMP designation opinions

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **4-(3,5-Bis(hdroxy-phenyl) -1,2,4) triazol-1-yl) benzoic acid (ICL670)**	• Novartis Europharm Limited	• Treatment of chronic iron overload requiring chelation therapy	• 10.10.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 13.3.2002
• **Beclomethasone 17, 21-dipropionate**	• Voisin Consulting SARL	• Treatment of intestinal Graft-versus-Host Disease	• 11.7.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 13.3.2002
• **Nitisinone**	• Swedish Orphan International AB	• Treatment of alkaptonuria	• 14.11.2001 • 30.11.2001 • 23.1.2002 • 54 days	• 31.1.2002 • 13.3.2002
• **GM-CSF receptor antagonist**	• British Biotech Pharmaceuticals Ltd	• Treatment of juvenile myelomonocytic leukaemia	• 15.11.2001 • 30.11.2001 • 23.1.2002 • 54 days	• 31.1.2002 • 18.3.2002
• **Human transferrin conjugated to mutant diptheria toxin**	• KS Biomedix Holdings PLC	• Treatment of gliomas	• 15.11.2001 • 30.11.2001 • 23.1.2002 • 54 days	• 31.1.2002 • 19.3.2002
• **Chimeric IgG monoclonal antibody cG250 for use with 131Iodine**	• Wilex AG	• Treatment of renal cell carcinoma	• 3.9.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 19.3.2002
• **Chimeric IgG monoclonal antibody cG250**	• Wilex AG	• Treatment of renal cell carcinoma	• 3.9.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 19.3.2002
• **TGF-ß2-specific phosphorothioate antisense oligodeoxynucleotide (Oncomun)**	• Antisense Pharma GmbH	• Treatment of high-grade glioma	• 14.11.2001 • 30.11.2001 • 23.1.2002 • 54 days	• 31.1.2002 • 22.3.2002
• **Humanized anti-KSA monoclonal antibody - human interleukin-2-fusion protein (EMD 273066)**	• Merck KGaA	• Treatment of renal cell carcinoma	• 11.10.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 22.3.2002
• **Epothilone B (EPO 906 A)**	• Novartis Europharm Limited	• Treatment of ovarian cancer	• 11.10.2001 • 26.10.2001 • 23.1.2002 • 89 days	• 31.1.2002 • 22.3.2002

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **Pseudomonas exotoxin (domains II/III)-Interleukin 13 chimeric protein**	• PPD Global Ltd	• Treatment of glioma	• 16.1.2002 • 31.1.2002 • 26.3.2002 • 54 days	• 28.3.2002 • 30.4.2002
• **Bryostatin-1**	• GPC Biotech AG	• Treatment of oesophageal cancer	• 11.1.2002 • 31.1.2002 • 26.3.2002 • 54 days	• 28.3.2002 • 30.4.2002
• **Recombinant human alpha-1 antitrypsin**	• Baxter AG	• Treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency	• 10.8.2001 • 31.1.2002 • 26.3.2002 • 54 days	• 28.3.2002 • 30.4.2002
• **Recombinant human porphobilinogen deaminase**	• HemeBiotech A/S	• Treatment of acute intermittent porphyria	• 12.12.2001 • 31.1.2002 • 30.4.2002 • 89 days	• 6.5.2002 • 12.6.2002
• **Miltefosine**	• Zentaris AG	• Treatment of visceral leishmaniasis	• 15.11.2001 • 31.1.2002 • 30.4.2002 • 89 days	• 6.5.2002 • 12.6.2002
• **Mitotane (Lysodren)**	• Laboratoire HRA Pharma	• Treatment of adrenal cortical carcinoma	• 14.1.2002 • 31.2.2002 • 30.4.2002 • 89 days	• 6.5.2002 • 12.6.2002
• **Carbamic acid, [[4-[[3-[[4-[1-(4-hydroxyphenyl)-1-methyl-ethyl]phenoxy] methyl]phenyl]methoxy]-phenyl]iminomethyl]-,ethyl ester (Amelubant)**	• Boehringer Ingelheim International GmbH	• Treatment of cystic fibrosis	• 7.2.2002 • 25.2.2002 • 22.5.2002 • 86 days	• 30.5.2002 • 26.6.2002
• **Thymalfasin (Zadaxin)**	• SciClone Pharmaceuticals Italy S.r.l.	• Treatment of hepatocellular carcinoma	• 4.4.2002 • 22.4.2002 • 27.6.2002 • 66 days	• 3.7.2002 • 30.7.2002
• **Antisense NF-κBp65 Oligonucletide (Kappaproct)**	• InDex Pharmaceuticals AB	• Treatment of active ulcerative colitis	• 12.3.2002 • 25.3.2002 • 27.6.2002 • 94 days	• 3.7.2002 • 30.7.2002
• **Oregovomab (OvaRex)**	• Dorian Regulatory Affairs	• Treatment of ovarian cancer	• 5.4.2002 • 22.4.2002 • 27.6.2002 • 66 days	• 3.7.2002 • 30.7.2002
• **Myristolated-peptidyl-recombinant SCR1-3 of human complement receptor type I**	• Adprotech Ltd	• Prevention of post transplantation graft dysfunction	• 8.3.2002 • 25.3.2002 • 27.6.2002 • 94 days	• 3.7.2002 • 30.7.2002
• **Purified bromelain (Debrase Gel Dressing)**	• Prof. Keith Judkins	• Treatment of partial deep dermal and full thickness burns	• 6.3.2002 • 25.3.2002 • 27.6.2002 • 94 days	• 3.7.2002 • 30.7.2002

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **Benzoic acid, sodium salt (Benzoate)**	• Ethicare GmbH	• Treatment of non-ketotic hyperglycinaemia	• 5.4.2002 • 17.6.2002 • 17.7.2002 • 30 days	• 24.7.2002 • 11.9.2002
• **Doxorubicin iron/carbon magnetically targeted microparticles (MTC-DOX for Injection)**	• Interface International Consultancy Ltd	• Treatment of hepatocellular carcinoma	• 27.5.2002 • 17.6.2002 • 17.7.2002 • 30 days	• 24.7.2002 • 11.9.2002
• **Myristolated-peptidyl-recombinant Human CD59**	• Adprotech Ltd	• Treatment of paroxysmal nocturnal haemoglobinuria	• 5.4.2002 • 22.4.2002 • 17.7.2002 • 86 days	• 24.7.2002 • 11.9.2002
• **Mitotane (Lysodren 500 mg Tablets)**	• AGEPS-EPHP Agence Générale des Équipements et Produits de Santé	• Treatment of adrenal cortical carcinoma	• 5.4.2002 • 17.6.2002 • 17.7.2002 • 30 days	• 24.7.2002 • 11.9.2002
• **(-)-17(cyclopropylmethyl)-1,14 ß-dihydroxy-4,5 alpha-epoxy-6ß-[N-methyl-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (Nalfurafine)**	• Toray Europe Limited	• Treatment of uremic pruritus	• 5.4.2002 • 17.6.2002 • 1.8.2002 • 45 days	• 5.8.2002 • 11.9.2002
• **Autologous Renal Cell Tumor Vaccine**	• Liponova GmbH	• Treatment of renal cell carcinoma	• 31.5.2002 • 17.6.2002 • 12.9.2002 • 87 days	• 23.9.2002 • 21.10.2002
• **Boswellia serrata resin dry extract (Boswelan)**	• Pharmasan GmbH	• Treatment of peritumoral edema derived form brain tumour	• 6.2.2002 • 17.6.2002 • 12.9.2002 • 87 days	• 23.9.2002 • 21.10.2002
• **Recombinant glycoprotein gp350 of Epstein-Barr Virus (Henogen 350)**	• Henogen SA	• Prevention of post-transplantation lympho-proliferative disorders	• 9.8.2001 • 17.6.2002 • 12.9.2002 • 88 days	• 23.9.2002 • 22.10.2002
• **Anti-CD 147 murine monoclonal IgM**	• SangStat UK Limited	• Treatment of Graft versus Host Disease	• 2.8.2002 • 19.8.2002 • 9.10.2002 • 52 days	• 16.10.2002 • 14.11.2002
• **Etilefrine**	• SERB	• Treatment of low flow priapism	• 29.7.2002 • 19.8.2002 • 9.10.2002 • 52 days	• 16.10.2002 • 13.11.2002
• **Duramycin**	• Gerd Döring	• Treatment of cystic fibrosis	• 29.7.2002 • 19.8.2002 • 9.10.2002 • 52 days	• 16.10.2002 • 13.11.2002
• **Iodine 131 radiolabeled anti-nucleohistone H1 chimeric biotinylated monoclonal antibody (Cotara)**	• Interface International Consultancy Ltd	• Treatment of glioma	• 26.7.2002 • 19.8.2002 • 9.10.2002 • 52 days	• 16.10.2002 • 13.11.2002

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **5-Aminolevulinic acid hydrochloride**	• Medac Gesellschaft fuer klinische Spezialpräparate mbH	• Intra-operative photodynamic diagnosis of residual glioma	• 26.7.2002 • 19.8.2002 • 9.10.2002 • 52 days	• 16.10.2002 • 13.11.2002
• **Monoclonal antibody to human interleukin-6**	• OPi Orphan Pharma International	• Treatment of post-transplantation lymphoproliferative disorders	• 5.9.2002 • 16.9.2002 • 15.11.2002 • 61 days	• 20.11.2002 • 18.12.2002
• **Recombinant inhibitor of human plasma kallikrein (DX-88)**	• Dyax s.a.	• Treatment of angioedema	• 1.8.2002 • 19.8.2002 • 15.11.2002 • 89 days	• 20.11.2002 • 18.12.2002
• **Cholic Acid**	• AGEPS-EPHP Agence Générale des Équipements et Produits de Santé	• Treatment of inborn errors of primary bile acid synthesis	• 27.6.2002 • 19.8.2002 • 15.11.2002 • 89 days	• 20.11.2002 • 18.12.2002
• **3,4 diaminopyridine phosphate**	• AGEPS-EPHP Agence Générale des Équipements et Produits de Santé	• Treatment of Lambert-Eaton myasthenic syndrome	• 29.8.2002 • 16.9.2002 • 15.11.2002 • 67 days	• 20.11.2002 • 18.12.2002
• **Sodium oxybate (Xyrem)**	• IDIS Ltd	• Treatment of narcolepsy	• 28.8.2002 • 16.9.2002 • 13.12.2002 • 89 days	• •
• **G17(9) gastrin-Diphtheria Toxoid Conjugate**	• Orion Clinical Service Limited	• Treatment of gastric cancer	• 27.9.2002 • 14.10.2002 • 13.12.2002 • 61 days	• •
• **G17(9) gastrin-Diphtheria Toxoid Conjugate**	• Orion Clinical Service Limited	• Treatment of pancreatic cancer	• 27.9.2002 • 14.10.2002 • 13.12.2002 • 61 days	• •
• **Carboxypeptidase G2**	• Enact Pharma plc	• Adjunctive treatment in patients at risk of methotrexate toxicity	• 30.8.2002 • 16.9.2002 • 13.12.2002 • 89 days	• •

Negative COMP designation opinions

Product INN	Sponsor	Summary of indication	EMEA/COMP • Submission • Start Date • Opinion • Active Time	European Commission • Opinion received • Date of decision
• **Chlorproguanil hydrochloride and dapsone (LAPDAP)**	• SmithKline Beecham plc	• Treatment of acute uncomplicated Plasmodium falciparum malaria	• 5.9.2001 • 20.9.2001 • 22.5.2002 • 244 days (including appeal)	• 30.5.2002 • 26.7.2002
• **Mycobacterial cell wall complex (MCC)**	• Bioniche Teoranta	• Treatment of carcinoma in situ of the urinary bladder	• 24.5.2002 • 17.6.2002 • 12.9.2002 • 88 days	• 16.10.2002 • 18.12.2002

Annex 10

Guidelines and working documents in 2002

CPMP Biotechnology Working Party

Reference number	*Document title*	*Status*
CPMP/BWP/2490/00	Note for guidance on Cell Culture Inactivated Influenza Vaccines Annex to NfG on Harmonisation of requirements for Influenza Vaccines (CPMP/BWP/214/96)	Adopted January 2002
EMEA/CPMP/571/02	Public Statement on Lactose prepared using Calf Rennet: Risk Assessment in relation to Bovine Spongiform Encephalopathies (BSE)	Adopted February 2002
CPMP/BWP/6622/02	Concept Paper on the Development of a CPMP Note for Guidance on requirements for the Evaluation of New Adjuvants in Vaccines	Adopted April 2002
CPMP/BWP/1412/02	Testing for SV40 in Polio Virus Vaccines	Adopted April 2002
CPMP/BWP/1571/02	CPMP Position Statement on the Quality of Water used in the production of Vaccines for parenteral use	Adopted April 2002
CPMP/BWP/852/02	Committee for Proprietary Medicinal Products (CPMP), Final EU recommendations for the influenza vaccine composition for the season 2002/2003	Adopted May 2002
CPMP/BWP/337/02	Public Report on Risk and Regulatory Assessment of Lactose and other products prepared using CalfRennet	Adopted May 2002
CPMP/BWP/1818/02	CPMP Position Statement on Non-Remunerated and Remunerated Donors: Safety and Supply of Plasma-derived Medicinal Products	Adopted May 2002
EMEA/22314/02 rev. 1	Position Paper on Re-establishment of Working Seeds and Working Cell Banks using TSE compliant materials	Adopted October 2002
CPMP/BWP/1793/01	Note for Guidance on the Use of Bovine Serum in the manufacture of Human Biological Medicinal Products	Released for consultation April 2002
CPMP/BWP/764/02	Points to Consider on Quality Aspects of Medicinal Products containing Active Substances Produced by Stable Transgene Experession in Higher Plants	Released for consultation May 2002
CPMP/BWP/2758/02	Note for Guidance on Pharmaceutical Aspects of the Product Literature for Human Vaccines	Adopted for release for consultation July 2002

CPMP ad hoc Working Group on Blood Products

Reference number	*Document title*	*Status*
CPMP/BPWG/2220/99	Note for Guidance on the Clinical Investigation of Plasma derived Antithrombin Products	Adopted January 2002
CPMP/BPWG/3226/99	Core SPC for Human Plasma derived Antithrombin	Adopted January 2002
CPMP/BPWG/283/00	Note for Guidance on the Clinical Investigation of Human Normal Immunoglobulin for Subcutaneous and Intramuscular use	Adopted July 2002
CPMP/BPWG/282/00	Core SPC for Human Normal Immunoglobulin for Subcutaneous and Intramuscular use	Adopted July 2002

CPMP Efficacy Working Party

Reference number	*Document title*	*Status*
CPMP/EWP/1412/01	Concept paper for the development of the revision of the CPMP Note for Guidance on evaluation of new anti-bacterial medicinal products (CPMP/EWP/558/95) and the CPMP Note for Guidance on the pharmacodynamic section of the SPC for anti-bacterial medicinal products (CPMP/EWP/520/96)	Adopted January 2002
CPMP/EWP/226/02	Concept paper on the development of a CPMP Note for Guidance on the clinical pharmacokinetic investigation of the pharmacokinetics of peptides and proteins	Adopted March 2002
CPMP/EWP/225/02	Concept paper on the development of a CPMP Note for Guidance on the evaluation of the pharmacokinetics of medicinal products in patients with impaired renal failure	Adopted March 2002
CPMP/EWP/518/97 rev. 1	Note for Guidance on clinical investigation of medicinal products in the treatment of depression	Adopted April 2002
CPMP/EWP/714/98 rev. 1	Note for Guidance on clinical investigation of medicinal products for the treatment of peripheral arterial occlusive disease	Adopted April 2002
CPMP/EWP/1080/00	Note for Guidance on Clinical investigation of medicinal products in the treatment of diabetes mellitus	Adopted May 2002
CPMP/EWP/968/02	Concept paper on the development of a CPMP Points to consider on the evaluation of the pharmacokinetics of medicinal products in the paediatric population	Adopted May 2002

Reference number	*Document title*	*Status*
CPMP/EWP/2455/02	Concept paper on the development of a CPMP Points to consider on allergic rhino-conjuctivitis.	Adopted July 2002
CPMP/EWP/282/02	Position paper on the regulatory requirements for the authorisation of low-dose modified release ASA formulations in the secondary prevention of cardiovascular events.	Adopted July 2002
CPMP/EWP/2454/02	Concept paper on the development of a CPMP Note for Guidance on clinical investigation of medicinal products for the treatment of psoriasis.	Adopted July 2002
CPMP/EWP/2339/02	Concept paper on the development of a CPMP Note for Guidance on the evaluation of the pharmacokinetics of medicinal products in patients with hepatic impairment.	Adopted July 2002
CPMP/EWP/2459/02	Concept Paper on the development of a CPMP Points to Consider on methodological issues in confirmatory clinical trials with flexible design and analysis plan.	Adopted July 2002
CPMP/EWP/908/99	Points to consider on multiplicity issues in clinical trials.	Adopted September 2002
CPMP/EWP/4279/02	Concept paper on the development of a CPMP Note for Guidance on clinical investigation of medicinal products for the treatment of obsessive compulsive disorder.	Adopted November 2002
CPMP/EWP/4280/02	Concept paper on the development of a CPMP Note for Guidance on clinical investigation on medicinal products for the treatment of panic disorder.	Adopted November 2002
CPMP/EWP/2922/01	Note for Guidance on the clinical investigation of medicinal products in the treatment of asthma	Adopted November 2002
CPMP/EWP/612/00 rev. 1	Note for Guidance on clinical investigation of medicinal products for treatment of nociceptive pain	Adopted November 2002
CPMP/EWP/4914/02	Concept Paper on the Development of a CPMP Note for Guidance on Clinical investigation of medicinal products for the treatment of Generalised Anxiety Disorder	Adopted November 2002
CPMP/EWP/18/01	Note for Guidance on the clinical investigation of medicinal products for the treatment of urinary incontinence	Adopted December 2002
CPMP/EWP/4151/00	Points to consider on the requirements for clinical documentation for metered dose inhalers (MDI)	Release for consultation January 2002

Reference number	*Document title*	*Status*
CPMP/EWP/49/01	Appendix to the NfG 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	Released for consultation February 2002
CPMP/EWP/785/97	Points to consider on the evaluation of medicinal products for the treatment of irritable bowel syndrome	Released for consultation April 2002
CPMP/EWP/556/95 rev. 1	Points to consider on clinical investigation of medicinal products for treatment of rheumatoid arthritis	Released for consultation July 2002
CPMP/EWP/1343/01 rev. 1	Points to consider on the evaluation of new anti-fungal agents for invasive fungal infections	Release for consultation July 2002
CPMP/EWP/633/02	Note for Guidance on the clinical development of medicinal products for the treatment of HIV infection	Released for consultation July 2002
CPMP/EWP/788/01	Note for Guidance on clinical investigation of medicinal products for the treatment of migraine	Released for consultation September 2002
CPMP/EWP/596/02	Note for Guidance on evaluation of anticancer medicinal products in man (CPMP/EWP/205/95 rev. 2) – Addendum on paediatric oncology	Released for consultation September 2002
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 infarction (STEMI)	Released for consultation November 2002

CPMP Pharmacovigilance Working Party

Reference number	*Document title*	*Status*
CPMP/PhVWP/4838/02	Concept Paper on Conduct of Pharmacovigilance For Medicines Used by Children	Adopted October 2002
CPMP/1199/02	Points to consider on Xenogeneic Cell Therapy for Medicinal Products	Released for consultation November 2002
CPMP/ICH/4679/02	Addendum to ICH E2C – Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs	Transmission by CPMP to Interested Parties at ICH step 3 in September 2002

CPMP Safety Working Party

Reference number	*Document title*	*Status*
CPMP/SWP/2600/01	Points to consider on the need for assessment of reproductive toxicity of human insulin analogues	Adopted March 2002
CPMP/SWP/668/02	Concept paper on the development of a CPMP position paper on the non-clinical safety studies to support low dose clinical screening studies in humans	Adopted March 2002
CPMP/SWP/398/01	Note for Guidance on photosafety testing	Adopted June 2002
CPMP/SWP/2592/02	SWP Conclusions and recommendations with regard to the use of genetically modified animal models for carcinogenicity assessment	Adopted June 2002
CPMP/SWP/2877/00 rev. 1	Note for Guidance on carcinogenic potential	Adopted July 2002
CPMP/SWP/2599/02	Position Paper on the Non-clinical safety studies to support clinical trials with a single low dose of a compound	Released for consultation June 2002
CPMP/SWP/4446/00	Note for Guidance on specification limits for residues of metal catalysts	Re-released for consultation June 2002
CPMP/3097/02	Note for Guidance on Comparability of Medicinal Products Containing Biotechnology-derived Proteins as Drug Substance: Annex on Non-Clinical and Clinical Considerations	Released for consultation July 2002
CPMP/SWP/799/95	Note for Guidance on the Non-Clinical Documentation of Medicinal Products with Well-Established Use	Released for consultation November 2002
CPMP/SWP/5199/02	Position Paper on the limits of genotoxic impurities	Released for consultation December 2002

EMEA Herbal Medicinal Products Working Party

Reference number	*Document title*	*Status*
EMEA/HMPWP/41/01	SOP: Recording of core data for herbal drugs/herbal drug preparations (*)	Published May 2002
EMEA/HMPWP/18123/00	Compilation of general quality questions answered by the HMPWP (*)	Published May 2002
EMEA/HMPWP/31/99 rev. 3	Points to consider on good agricultural and collection practice for starting materials of herbal origin (*)	Published May 2002
EMEA/HMPWP/13/00	Proposal for a core-data for *Plantaginis psyllium* (Psyllium seed) (*)	Released for consultation July 2002

Reference number	*Document title*	*Status*
EMEA/HMPWP/14/00	Proposal for a core-data for *Plantaginis ovatae semen* (Ispaghula seed) (*)	Released for consultation July 2002
EMEA/HMPWP/15/00	Final draft Proposal for a core-data for *Plantaginis ovatae testa* (Ispaghula husk) (*)	Released for consultation July 2002
EMEA/HMPWP/17/00	Proposal for a core-data for *Calendula flos* (Calendulae flower) (*)	Released for consultation July 2002
EMEA/HMPWP/18/00	Proposal for a core-data for *Passiflora herba* (Passion flower) (*)	Released for consultation July 2002
EMEA/HMPWP/19/00	Proposal for a core-data for *Melissae folium* (Melissa leaf) (*)	Released for consultation July 2002
EMEA/HMPWP/20/00	Proposal for a core-data for *Lupuli flos* (Hop strobile) (*)	Released for consultation July 2002
EMEA/HMPWP/21/00	Proposal for a core-data for *Harpagophyti radix* (Devil's Claw root) (*)	Released for consultation July 2002
EMEA/HMPWP/1417/02	Proposal for a core-data for *Menthae piperitae aetheroleum* (Peppermint oil) (*)	Released for consultation December 2002
EMEA/HMPWP/1418/02	Proposal for a core-data for *Menthae piperitae folium* (Peppermint leaf) (*)	Released for consultation December 2002
EMEA/HMPWP/1416/02	Proposal for a core-data for *Urticae folium* (Nettle leaf) (*)	Released for consultation December 2002

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

Scientific Advice Review Group

Reference number	*Document title*	*Status*
EMEA/H/238/02	EMEA guidance for companies requesting protocol assistance regarding scientific issues	Published February 2002

Invented Name Review Group

Reference number	*Document title*	*Status*
CPMP/328/98 rev. 3	Guideline on the acceptability of Invented Names For Human Medicinal Products Processed Through The Centralised Procedure	Adopted January 2002

CVMP Efficacy Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/411/01	Specific efficacy requirements for ectoparasiticides in sheep	Adopted July 2002
EMEA/CVMP/612/01	SPC for antimicrobial products	Adopted December 2002
EMEA/CVMP/627/01	Demonstration of efficacy for veterinary medicinal products containing antimicrobial subsatnces	Adopted December 2002
EMEA/CVMP/1166/02	Standard statements for the SPC of certain classes/ types of veterinary medicinal products	Released for consultation December 2002

CVMP Immunologicals Working Party

Reference number	*Document title*	*Status*
CVMP/VICH/095/01	Biologicals: Testing of residual formaldehyde	Adopted May 2002
CVMP/VICH/096/01	Biologicals: Testing of residual moisture	Adopted May 2002
CVMP/VICH/463/02	Testing for the detection of mycoplasma contamination	Released for consultation May 2002
EMEA/CVMP/552/02	EU requirements for batches with maximum and minimum titre or batch potency for developmental safety and efficacy studies	Released for consultation June 2002
EMEA/CVMP/550/02	Requirements for compatibility statements for veterinary vaccines	Released for consultation June 2002

CVMP General

Reference number	*Document title*	*Status*
EMEA/CVMP/695/01	Processing of renewals in the centralised procedure	Adopted February 2002
EMEA/CVMP/328/98 – Revision 2	Acceptability of invented names for veterinary medicinal products processed through the centralised procedure	Adopted March 2002

CVMP Safety Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/234/01	Safety evaluation of antimicrobial substances regarding the effects on human gut flora	Adopted January 2002
EMEA/CVMP/244/01	Pre-authorisation studies to assess the potential for resistance resulting from the use of antimicrobial veterinary medicinal products	Adopted July 2002
CVMP/VICH/645/01	Studies to evaluate the safety of residues of veterinary drugs in human food: Carcinogenicity testing	Adopted November 2002

Reference number	*Document title*	*Status*
CVMP/VICH/484/02	Safety studies for veterinary drug residues in human food: Repeat-dose (90 days) toxicity testing	Adopted November 2002
CVMP/VICH/485/02	Safety studies for veterinary drug residues in human food: Developmental toxicity testing	Adopted November 2002
CVMP/VICH/486/02	Safety studies for veterinary drug residues in human food: General approach to teting	Adopted November 2002
CVMP/VICH/486/02	Safety studies for veterinary drug residues in human food: General approach to testing	Released for consultation May 2002
CVMP/VICH/485/02	Safety studies for veterinary drug residues in human food: Developmental toxicity testing	Released for consultation May 2002
CVMP/VICH/484/02	Safety studies for veterinary drug residues in human foods: Repeat-dose (90 days) toxicity testing	Released for consultation May 2002

Joint CPMP/CVMP Quality Working Party

Reference number	*Document title*	*Status*
CPMP/QWP/1719/00	Medicinal gases – pharmaceutical documentation	Adopted January 2002
CPMP/ICH/2737/99 CPMP/ICH/142/95	ICH Q3A – Impurities testing: Impurities in new drug substances	Adopted February 2002
CPMP/ICH/4104/00	ICH Q1D – Bracketing and matrixing designs of drug substances and drug products	Adopted February 2002
CVMP/424/02	In-use stability testing of veterinary medicinal products (excluding immunological veterinary medicinal products)	Adopted February 2002
EMEA/CVMP/424/01	In-use stability testing of veterinary medicinal products	Adopted February 2002
CPMP/QWP/2845/00	Requirements for pharmaceutical documentation for pressurised metered dose inhalation products	Adopted March 2002
CPMP/ICH/1507/02	ICH Q3C (M) Maintenance document for guidance on impurities	Adopted April 2002
CPMP/QWP/158/01	Quality of water for pharmaceutical use	Adopted May 2002
CVMP/115/01	Quality of water for pharmaceutical use – Revision	Adopted May 2002
EMEA/CVMP/115/01 – Revision	Quality of water for pharmaceutical use	Adopted May 2002
CPMP/ICH/1940/00	ICH Q3C (M) Maintenance document for guidance on impurities : Residual solvents THF and NMP	Adopted September 2002
EMEA/CVMP/1055/02	Concept paper for the development of guideline on quality aspects of pharmaceutical veterinary medicines administered via drinking water	Adopted November 2002

Reference number	*Document title*	*Status*
CPMP/QWP/122/02 CPMP/QWP/556/96	Stability testing: stability testing of existing active substances and related finished products	Adopted December 2002
CPMP/QWP/122/02 CPMP/QWP/556/96	Stability testing: stability testing of existing active substances and related finished products – Revision	Released for consultation February 2002
CPMP/QWP/227/02 CVMP/134/02	European Drug Master File – Revision	Released for consultation February 2002
CPMP/ICH/420/02	ICH Q1E Evaluation of stability data	Released for consultation February 2002
CPMP/ICH/421/02	ICH Q1F Stability data package for registration in climatic zones III and IV	Released for consultation February 2002
EMEA/CVMP/134/02	European drug master file procedure	Released for consultation February 2002
EMEA/CVMP/422/99	Declaration of storage conditions for veterinary medicinal products and active substances – Revision	Released for consultation March 2002
EMEA/CVMP/422/99 – Revision	Declaration of storage conditions for pharmaceutical veterinary medicinal products in the product particulars and active substances. Annex to note for guidance on stability testing of new active substances and medicinal products. Annex to note for guidance on stability testing of existing active substances and related finished products.	Released for consultation March 2002
EMEA/CVMP/680/02	Quality of modified release dosage forms for veterinary use	Released for consultation July 2002
CPMP/ICH/4680/02	ICH M4Q Questions and Answers / Location issues for common technical documents for the registration of pharmaceuticals for human use	Released for consultation September 2002

Committee for Orphan Medicinal Products

Reference number	*Document title*	*Status*
COMP/436/01	Points to consider on the calculation and reporting of the prevalence of a condition for orphan designation	Adopted March 2002
COMP/189/01	Note for guidance on the format and content of the annual report on the state of development of an orphan medicinal products	Adopted April 2002
EMEA/14222/00	Procedures for orphan medicinal product designation – General principles	Revision 2, October 2002
ENTR/6283/00	Guideline on the format and content of applications for designation as orphan medicinal products	Revision 1, October 2002
EMEA/4795/00	General information for sponsors of orphan medicinal products	Revision 1, October 2002

Annex 11

Arbitration and Community referrals overview 2002

Referrals made to the CPMP

Type of referral	*Date of CPMP opinion*	*International non-proprietary name (INN)*
Article 29 (2) Referrals	April 2002	Dacarbazine
	June 2002	Alteplase
	Ongoing	Isotretinoin
	Ongoing	Clostridium botulinum type A neutoxin
Article 7 (5) Referrals	Ongoing	Norditropin
	Ongoing	Genotropin
	Ongoing	Salmeterol/fluticasone proprionate
	Withdrawn by the company	Fenofibrate
	Ongoing	Lisinopril Biochemie
	Ongoing	Lisinopril Cardiostat
	Ongoing	Somatropin
	Ongoing	Laurina
	Ongoing	Mononine
Article 30 Referrals	September 2002	Fluoxetine
	January 2002	Fluvoxamine
	May 2002	Captopril
	April 2002	Captopril/hydrochlorothiazide
	February 2002	Midazolam
	September 2002 (company appealed)	Enalapril
	June 2002	Domperidone
	July 2002	Clozapine
	Ongoing	Calcium folinate
	Ongoing	Ranitidine
	Ongoing	Isotretinoin
	Ongoing	Lisinopril
	Ongoing	Calcium 500/1000
	Ongoing	Calcium 500 + Vitamin D 400 IU
	Ongoing	Calcium 500 + Vitamin D 200 IU
	Ongoing	Pravastatin
	Ongoing	Simvastatin
Article 31 Referrals	November 2002	Calcitonins
	October 2002 (company appealed)	Human coagulation factor VIII
	Ongoing	Loratadine
	June 2002	Sibutramine
	Ongoing	Gatifloxacin
	Ongoing	Nimesulide
	Ongoing	COX-2-Inhibitors: Celecoxib, Parecoxib, Valdecoxib, Rofecoxib, Etoricoxib
Article 36 Referrals	March 2002	Cerivastatin
	July 2002	Bupropion
	October 2002	Felodipine

Referrals made to the CVMP

Community harmonisation and pharmacovigilance referrals

Type of referral	*Date of CVMP opinion*	*International non-proprietary name (INN)*
Article 33 Directive 2001/82/EC	June 2002	Ivermectin
	June 2002	Ivermectin
	Ongoing	Orbifloxacin
Article 20 Council Regulation 81/851 (EEC) now Article 35 Directive 2001/82/EC	December 2002 (under appeal)	Benzathine penicillin

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:
Jonna SUNELL-HUET
Direct telephone (44-20) 74 18 84 65
E-mail: certificate@emea.eu.int

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 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 lists

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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