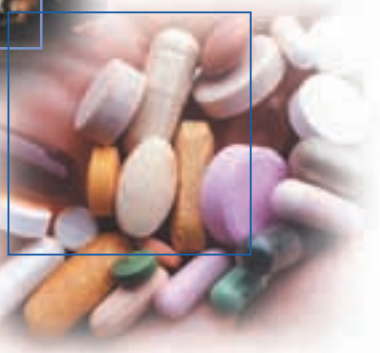
The European Agency for the Evaluation of Medicinal Products

Seventh Annual Report
2001

Adopted by the Management Board on 18 December 2001



The annual report for 2001 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 on request in all the 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 2001. Chapter 1 sets out the activities of the Management Board. It also covers the Agency's partnership with national competent authorities and European institutions, and other general aspects of the EMEA, including transparency and international activities.

The operational and technical work of the EMEA in 2001 is reported in Chapter 2 on human medicines, Chapter 3 on veterinary medicines and Chapter 4 on inspection activities. Administration and other support activities are described in Chapter 5.

The Report, in accordance with Article 15c(1) of Council Directive 75/319/EEC and Article 23c(1) of Council Directive 81/851/EEC, also summarises the operation of the decentralised (mutual recognition) procedure during 2001.

New e-mail addresses for the EMEA staff members were introduced with effect from 1 November 2001 with the introduction of the 'emea.eu.int' domain for e-mail:

firstname.familyname@emea.eudra.org becomes:
firstname.familyname@emea.eu.int

The general e-mail address for the EMEA becomes **mail@emea.eu.int** and other functional e-mail addresses will change in the same way, e.g. **certificate@emea.eu.int**

The 'emea.eudra.org' e-mail address format will continue to be recognised until 1 October 2002.

This change of domain follows on from the change of the Agency's web site to **www.emea.eu.int** at the beginning of 2001 and is part of the alignment of the EMEA with other European Union institutions and bodies.

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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

The year 2001 was a year of continuing success for the EMEA, achieved against a background of considerable change. We welcomed Thomas Lönngren at the start of the year as the new Executive Director. The Management Board elected a new chairman and several organisational changes were adopted within the Agency with a view to improving both efficiency and effectiveness. The environment within which the EMEA operated also saw significant change, the nature and extent of which is likely to increase even further in the future. The Agency, its management, its staff and its advisors, took all of these changes in their stride, and achieved all that was expected of them, as is described in this report.

The Agency already has a unique operational role in implementing the Community policy for high standards of public health and completion of the single market in pharmaceuticals, without prejudicing the development of an important internationally competitive industry. It must now look forward and prepare for an interesting, exciting and challenging future with the prospect of increasing demands in new areas of therapeutics and regulation. The Agency's many stakeholders, including the European institutions, the competent authorities of Member States, citizens of the European Community, patients, patient representatives and the pharmaceutical industry, will continue to have high expectations of this Agency, and the Agency is in my opinion, in a position to deliver against those expectations.

The important challenges of the future, against which the EMEA is determined to deliver, include enlargement of the Community, implementation of the 2001 Review, increasing clinical trials, pharmacovigilance and inspection functions, responsibility for Community pharmaceutical information management systems, extending the process of transparency to every aspect of its function, improving its ability to enforce regulation, and fulfilling its international role. To achieve all of this it will need to ensure a sound and stable basis of good corporate governance, and maintain the highest standards of management practice, including performance management. The Management Board will have an important role to ensure that the Agency's management is fully prepared and adequately supported to meet all of these challenges.

None of this will be achieved in isolation and the Agency will work hard to harness the good will, experience, knowledge and expertise of all existing regulators in this venture. A closer association of heads of the national authorities to the Agency's resource planning will be important in achieving better joint management of the resources available across the entire Community.

I, together with my colleagues on the Management Board, would like to thank everyone who has contributed to the success of the EMEA, especially the staff for their hard work and dedication throughout the year. Without that dedication it would not have been possible to achieve the many accomplishments described in this report. The Management Board also wishes to thank all of the members of the Agency's expert committees and the 3 000 independent European experts for their important contribution to these accomplishments.

Introduction by the Executive Director
Thomas Lönngren

This is my first annual report as Executive Director of the European Agency for the Evaluation of Medicinal Products. As you will see from reading the report, it has been an exciting and challenging year for the Agency.

One of my first tasks was to draw up a work programme and I am pleased to see that most of the priorities and targets we set have been achieved. Overall we have been able to handle incoming applications within the required timelines, despite an increase in the level of overall activities. Significant resource has been directed to implementation of a new computerised system to improve the way the safety of medicines is monitored in the European Community. Similarly the EMEA has had to deal with a number of referrals made to it concerning medicines authorised through national procedures. The number of applications for designation of orphan medicines also exceeded original forecasts.

The provision of scientific advice to companies as they conduct their research and development of new medicines is one of the Agency's priorities. A survey of companies who have used the procedure shows that we have improved the service and I hope to build on this progress. Important progress has also been made in the field of antimicrobial resistance, particularly in the field of veterinary medicines.

An event that will have an important effect on the EMEA was the announcement by the European Commission of its proposals to reform the European system for the authorisation and supervision of medicines. The proposals contain a number of new responsibilities for the Agency and an analysis of the resource and organisational consequences is already underway.

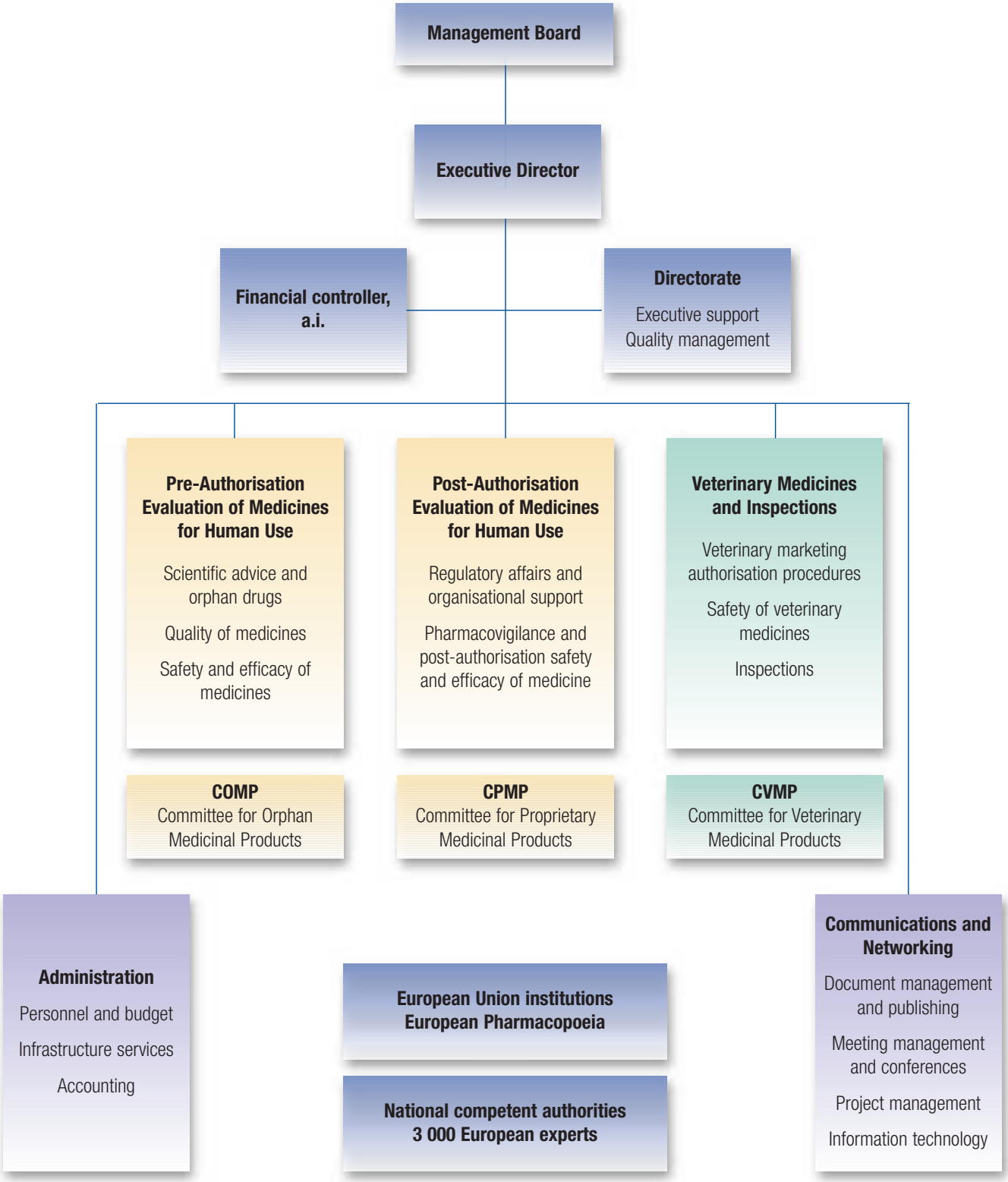
The EMEA became involved in a number of new activities during the year that had not been foreseen in the work programme. The European Commission and Member States asked the EMEA to take over responsibility for the pharmaceutical regulatory IT network from 2003 and we began preparation for this. Towards the end of the year we became actively involved together with the European Commission in preparing the Community response to the threats of bio-terrorism.

Looking outwards from the European Union, we have continued our programme of cooperation with colleagues in the accession candidate countries through the PERF and I am happy to say that good progress has been achieved during the year. We have also worked closely with partners elsewhere in the world, both through the ICH and VICH initiatives and bilaterally.

With the launch of a new web site at the beginning of 2001, we have begun also to look at ways of providing more information to people outside of the regulatory and pharmaceutical industry circles. One important step forward that has been especially welcomed is the publication of summaries of opinions at the time they are adopted by our scientific committees.

Amidst all this the Agency's staff has been involved in a process of internal reorganisation throughout the year, including the creation of two units dealing with medicines for human use and of a new unit responsible for communications and networking with the Agency's external partners. They, together with the experts from national competent authorities, have made tremendous efforts in successfully managing the European system. I take this opportunity to thank them all for their hard work.

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 2001. One of the first tasks of the Board was to elect Dr Keith Jones as its new chairman. The Board also welcomed Mr Thomas Lönngren as he began as the new Executive Director of the EMEA, with effect from 3 January 2001.

Details of membership of the Management Board are given in Annex 1.

The key outcomes of each meeting:

21-22 February 2001

- Elected Dr Keith Jones as chairman for a three-year term of office
- Adopted the EMEA work programme for 2001-2002
- Adopted the preliminary draft budget for 2002 totalling € 70 332 000
- Mandated Executive Director to implement transparency recommendations

6 June 2001

- Agreed, with the support from the European Commission and national competent authorities, that the EMEA should act as the future focus from 2003 of the Community-wide IT strategy for pharmaceuticals
- Began reflection on the impact of enlargement with heads of regulatory agencies from Member States and central and eastern European countries
- Introduced a regular report of EMEA highlights for the Board's information

4 October 2001

- Endorsed a report on the EMEA experience with the current fee system paid by applicants and marketing authorisation holders to the Agency
- Agreed new initiatives to improve transparency in the EMEA process
- Introduced a regular half-yearly report by the Executive Director
- Agreed an important position on the way forward for the Herbal Medicinal Product Working Party

18 December 2001

- Adopted budget and work programme for 2002
- Adopted annual report for 2001
- Granted discharge to the Executive Director for execution of 2000 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

With a view to reinforcing the links with national competent authorities, the Executive Director invited them to become more closely associated with the EMEA in planning of resources. The future transfer of responsibility for implementation of the Community pharmaceutical IT strategy will in particular require greater cooperation and planning between the EMEA and national authorities.

A new Unit was created in October 2001 with responsibility for facilitating communications and networking between the Agency's partners. The Unit will focus on the communication tools and IT systems needed in particular to optimise the

relationship bring the Agency, the 27 different national competent authorities and the European Commission.

1.3 Transparency and regulatory dialogue

The Executive Director received a mandate from the Management Board at its February 2001 meeting for a phased implementation of the recommendations stemming from the transparency workshop held on 23 November 2000. Recommendations implemented in 2001 include publication of summaries of opinions adopted by the Committee for Proprietary Medicinal Products (CPMP) and Committee for Veterinary Medicinal Products (CVMP).

The new EMEA web site was launched at the beginning of 2001. This is the third re-design of the web site since its inauguration in September 1995. The new site offers improved access to an ever-increasing number and range of documents.

Recognising the increased media interest in the work of the EMEA and its scientific committees, a press officer for the Agency was appointed in September 2001.

1.4 Revision of EMEA fees

The Management Board working group on fees and costing met three times in 2001. The group examined data submitted by rapporteurs, co-rapporteurs and national inspection services on the costs associated with the operation of the centralised procedure. The expected revision of the level and structure of fees payable to the EMEA was postponed in 2001 due to insufficient data being available on which to base any changes. The group also reviewed data generated by the EMEA activity tracking system – ActiTrak.

On the basis of the group's findings, the Management Board endorsed a report on the EMEA experience with the current fee system at its meeting in October 2001. The report considered that it was premature to make definitive recommendations, particularly in light of the impact of future enlargement of the European Union and the proposed revision of EMEA tasks and responsibilities.

The report was forwarded to the European Commission as part of the planned report to the European Parliament and Council on the implementation of the fee system.

1.5 Review of the European marketing authorisation system

Useful web sites:

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

The EMEA followed closely the preparation by the European Commission of proposals for the revision of the European marketing authorisation system and offered support as appropriate. The Management Board was regularly informed of developments.

Mr Erkki Liikanen, Member of the European Commission with responsibility for pharmaceutical policy, visited the EMEA on 25 June 2001.

The European Commission adopted its proposals on 18 July 2001 and they were transmitted to the European Parliament and Council on 23 and 26 November 2001, following completion of the codification of existing Community pharmaceutical legislation (COM(2001) 404 final, 26.11.2001.

1.6 Quality management

A total of 15 internal audits were conducted in 2001 looking at cross-functional activities across the EMEA. The audits in particular looked at interfaces between the EMEA and stakeholders and interested parties. ISO 9001:2000 auditor training was provided for 12 staff members to prepare them for auditing of integrated management systems.

Two benchmarking meetings looking at good regulatory practices and quality management systems were held on 5 March and 18 October 2001. The meetings brought together representatives from EU Member States, accession candidate

countries and European institutions. Areas of best practices looked at by the meetings included practical implementation of a quality management system, with particular focus on staff motivation and commitment of management, and identification of the processes needed for good regulatory practices and their documentation.

Good regulatory practices:

A quality system to ensure that users of medicinal products, applicants and regulators are satisfied with the scientific advice, opinions, the establishment of maximum residue levels, inspection and assessment reports and related documents, taking into consideration legal requirements and guidance in order to protect and promote human and animal health.

1.7 International partners

Useful web sites:

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

International Conference on Harmonisation
http://www.ifpma.org/ich1.html

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

The second Pan-European Regulatory Forum (PERF II) began in June 2001. PERF is funded from the European Commission PHARE programme and is part of the pre-accession strategy for central and eastern European countries. The forum involves considerable resource contribution from both the EMEA and EU national competent authorities and will continue in 2002.

The EMEA continued to support the activities within both the International Conferences for Harmonisation for registration of medicines for human and for veterinary use – the ICH and VICH. Of particular importance was the implementation in 2001 of the common technical document (CTD) format for submission of applications for marketing authorisations agreed within the ICH process. The first CTD application was made simultaneously to the EMEA and the US Food and Drug Administration in 2001. Progress was also made in the VICH process, with a number of guidelines released for consultation in 2001.

The EMEA participated in a range of activities with the World Health Organisation (WHO) in 2001 relating to medicines for both human and veterinary use. Work also proceeded with the joint development of an application tracking system. The Agency also continued to issue certificates of medicinal products in accordance with the WHO certification scheme.

Meetings and workshops in 2001

Priority action area

• Implementation of Community legislation for human and veterinary medicines	2
• Good manufacturing practice *(Other activities in 2001: 1 observed inspection together with an evaluation for PECA*)*	1
• Pharmacovigilance	3
• Veterinary topics	6
• Inter-agency training	
- Quality systems and benchmarking	2
- Telematics	1
- Dossier assessment	4

Other meetings

• Steering Committee	1
• Programme Committee	3
Total meetings and workshops	**23**

** Protocol to the Europe Agreement on conformity assessment and acceptance of industrial products*

In addition to colleagues from central and eastern European countries, the EMEA welcomed delegations and visitors from a number of non-EU countries in 2001 from Australia, China, Japan, Turkey, Ukraine and US.

1.8 European Department for the Quality of Medicines

Useful web site:

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

The programme for the sampling and testing of centrally authorised products continued in 2001, in collaboration with the European Department 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-EFTA Member States. A total of 30 products were tested in the 2001 programme. No major problems were identified during testing.

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.

The programme of testing for 2003 was agreed in 2001.

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 2001. EMEA staff also participated at the European Pharmacopoeia Commission sessions. 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.

1.9 Financial control

EMEA Financial controller, a.i.
Claus CHRISTIANSEN

Previous discussions regarding the transfer of financial control responsibilities for all EU decentralised bodies to the European Commission (COM(1997) 489 final, OJ C 335, 6.11.1997, p. 15) were superseded by the introduction of an internal audit function at the European Commission.

The intention is for financial control to also be replaced by an internal audit function at all EU decentralised bodies, including the EMEA. However, this will require a recasting of the financial regulation, initially by the European Commission and subsequently by the EMEA. It is currently estimated that this could take two to three years.

Meanwhile, the financial control function continued to be ensured by the Agency's interim financial controller together with an assistant during 2001.

The financial controller dealt with 9 867 transactions in 2001. The high quality of financial transactions continued in 2001, with 1.08 % of transactions returned by the financial controller compared to 1.05 % in 2000. Rejection was mainly for reasons of minor irregularities, which were all resolved prior to final approval.

- 91 % of submissions to financial control were handled within 2 days or less
- 99 % of submissions to financial control were handled within 5 days or less

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, Scientific advice and orphan drugs
Agnès SAINT RAYMOND

Head of Sector, Quality of medicines
John PURVES

Head of Sector, Safety and efficacy of medicines
Isabelle MOULON

Deputy Head of Sector, 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, Regulatory affairs and organisational support
Tony HUMPHREYS

Head of Sector, Pharmacovigilance and post-authorisation safety and efficacy of medicines
Noël WATHION (acting)

Deputy Head of Sector, 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
Fernando GARCIA ALONSO

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

Reorganisation of the Unit for the Evaluation of Medicinal Products for Human Use

One of the major tasks undertaken in 2001 was to complete the reorganisation of the Unit for the Evaluation of Medicinal Products for Human Use in two units, dealing with pre-and post-authorisation aspects respectively. This was done in order to increase the consistency of the operation of the centralised procedure both from a procedural and a scientific viewpoint.

The new structure came into force in January 2001 and was operational by mid-2001. The real impact of the reorganisation on the operation of the centralised procedure will only become fully apparent in 2002 once additional resources are available.

Priorities for medicines for human use in 2001 – progress report

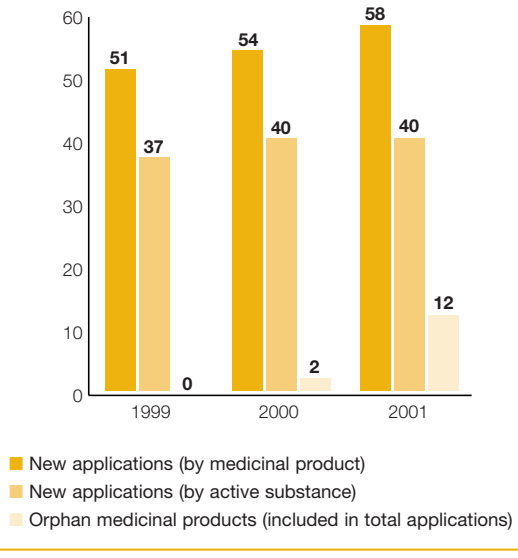
- Initial applications for marketing authorisation increased in 2001, including a noticeable percentage of orphan medicinal products as an effect of the number of products designated in 2000 and 2001
- The Agency's continuing efforts to strengthen the conduct of pharmacovigilance led to the implementation on 5 December 2001 of the EudraVigilance database and the data processing network, allowing the electronic transmission of individual case safety reports
- Provision of scientific advice to sponsors of medicinal products, improvements of the existing procedures and further developments for the particular needs of orphan medicinal products through the protocol assistance procedure required a sustained effort throughout 2001
- Activities relating to the Agency's responsibilities for orphan medicinal products, the support to the European Commission and completion of the implementation of the orphan drug regulation required significant resources in 2001
- Post-authorisation activities increased markedly during the year. Particular efforts were made in order to meet requirements of Commission Directive 1999/82/EC for demonstration of compliance of all centrally authorised products with the Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products
- The CPMP and COMP working parties and ad hoc groups provided the scientific committees with advice relating to specific medicinal products and produced a large number of guidance documents that were either published as final documents or released for consultation
- The secretariat has provided support for the activities of 9 new ad hoc groups and organised several workshops to meet the challenges of constantly developing science, new technologies, emerging therapies, ethical issues, public health issues including biological threats, and transparency and communication expectations of citizens and interested parties

2.1 Initial evaluation

The number of applications for marketing authorisations, including the number of new active substances, increased in 2001 compared to 2000. Numbers were below initial forecasts due to delays in submissions of planned applications for designated orphan medicinal products and fewer applications for more common diseases.

The effect of the implementation of the orphan medicines regulation became more visible with 12 applications submitted to the EMEA for designated products in 2001. Applications from designated orphan medicines represented 20 % of the total number of applications.

Initial evaluation applications 1999-2001



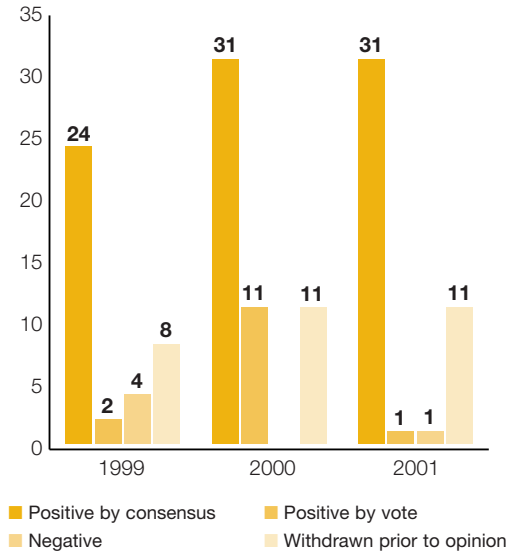
The first new applications using the new ICH common technical document (CTD) format were submitted simultaneously to the EMEA and the US Food and Drug Administration in 2001.

CPMP activities

The CPMP started a new 3-year mandate in January 2001. During its first meeting, Dr Daniel Brasseur was elected chairman and Dr Eric Abadie was elected vice-chairman of the Committee. The CPMP met 11 times and convened an extraordinary meeting in January 2001 to discuss a number of organisational issues.

The CPMP continued to discuss ways of improving its working practices and to prepare for the future, which will be characterised by a steady increase of the workload as well as by the need to address future technological advances in medicines such as gene therapy, cell therapy and medicinal products derived from transgenic animals and plants.

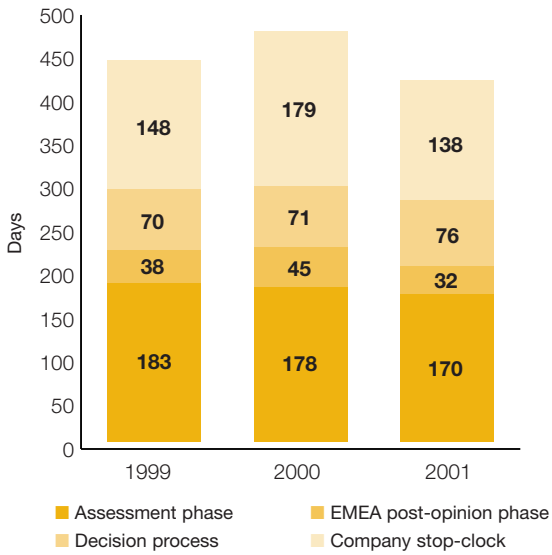
Initial evaluation opinions and withdrawals 1999-2001



Performance indicators

The average time for active EMEA scientific review and administrative tasks, in particular those activities relating to language review, decreased in 2001 compared to 2000. The average time from opinion to decision was 108 days.

Average number of days for centralised procedures 1999-2001



Two medicinal products were reviewed following an accelerated procedure, one of which was a designated orphan drug. Review times for these products were 119 and 83 days, benefiting patients with cancer and with HIV/AIDS.

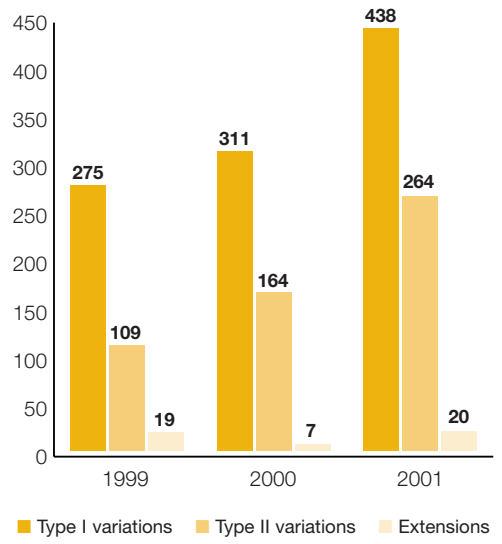
2.2 Post-authorisation activities

The number of post-authorisation applications and opinions adopted exceeded initial forecasts.

About 30 % of the minor variations (type I) correspond to changes in the manufacturing processes for authorised medicinal products or applications for new pharmaceutical forms. These changes are in many cases the result of marketing authorisation holders needing to comply with new regulatory standards or attempting to make manufacturing processes more efficient. About 60 % of the variations were related to the progress made by marketing authorisation holders in complying with the Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products.

The number of major variation (type II) applications in particular rose compared to previous years, mainly due to safety-related product changes.

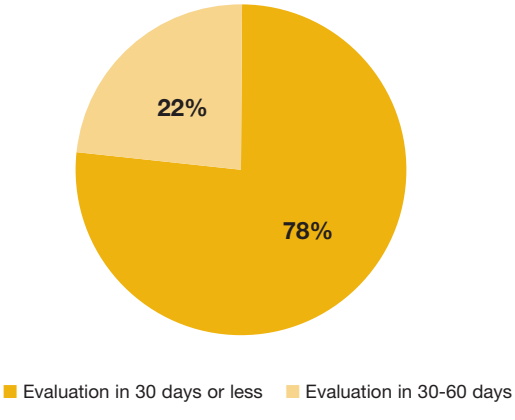
Post-authorisation opinions 1999-2001



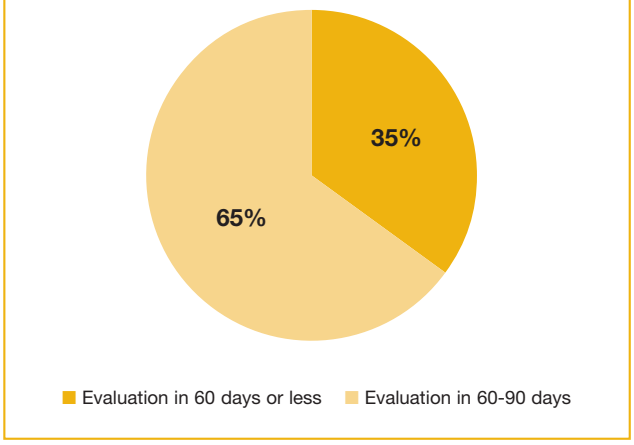
The management of post-authorisation activities improved in 2001, particularly at the level of the CPMP, through the introduction of a number of organisational changes designed to simplify the review process.

All variation applications were treated within the regulatory time frame. For type I variations, 78 % were handled in 30 days or less. In 22 % of cases additional information was required from marketing authorisation holders extending the evaluation time

Evaluation time for type I variations 2001



Evaluation time for type II variations 2001



to a maximum of 60 days. For type II variations, 35 % of applications received an opinion in 60 days or less, but in 65 % of cases complementary information was necessary before finalisation within the maximum 90 days time frame.

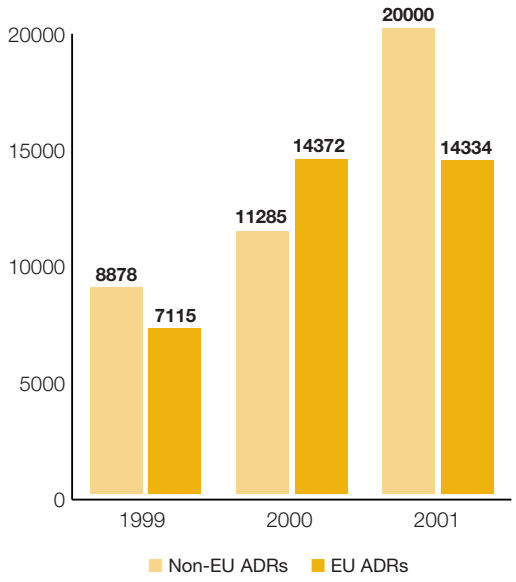
2.3 Pharmacovigilance and maintenance activities

The principal focus of pharmacovigilance and maintenance activities in 2001 was the implementation of the EudraVigilance database and the data processing network. These tools were made available on schedule on 5 December 2001, ready for the electronic transmission and management of individual case safety reports for all medicinal products authorised in the European Union. The medical dictionary for regulatory activities (MedDRA) was implemented as part of the EudraVigilance project.

During 2001 discussions were held in different forums at the EMEA to investigate how the conduct of pharmacovigilance in the EU could be strengthened. Topics addressed included the need for additional sources of pharmacovigilance information, for better regulatory compliance, to increase scientific expertise in the field and to improve communication and transparency.

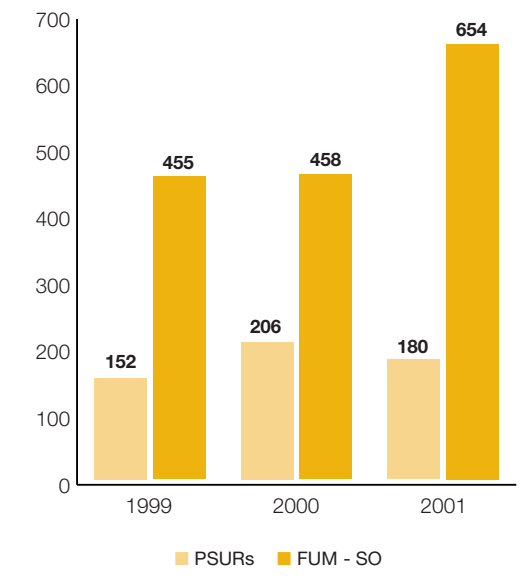
The number of adverse drug reaction reports continued to grow in 2001, underlining the importance of the database to ensuring a strengthened conduct of pharmacovigilance in the European Union.

EU and non-EU adverse drug reports 1999-2001



Post-marketing commitments, whether or not linked to marketing authorisations granted under exceptional circumstances, also showed a growing trend in 2001.

Periodic safety update reports, follow-up measures and specific obligations 1999-2001



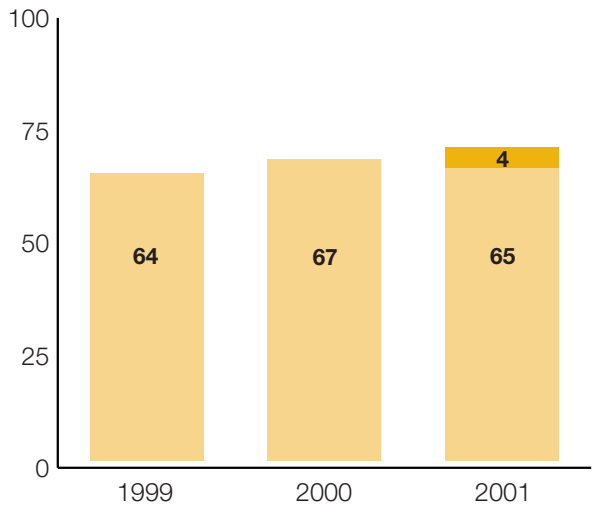
2.4 Scientific advice

The Scientific Advice Review Group, as a part of the CPMP, is responsible for providing advice to sponsors on quality, safety or efficacy-related aspects of medicinal products. Designated orphan medicinal products are entitled to receive scientific advice in the form of protocol assistance.

The procedure for protocol assistance was developed during 2001 and should be fully implemented in 2002. This procedure provides additional support from the Agency and its committees to sponsors of orphan medicinal products. Members of the COMP will directly contribute to this initiative aimed at encouraging the development of medicinal products for rare diseases.

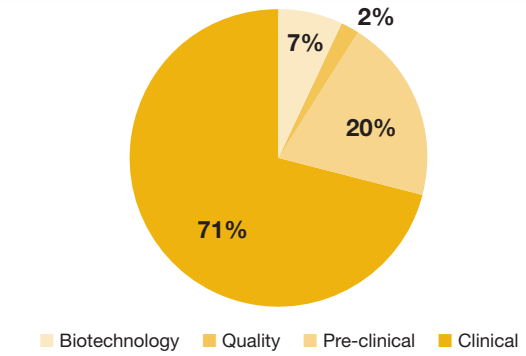
The number of protocol assistance started to rise in 2001 as a consequence of the increase in number of designated orphan drugs since 2000.

Scientific advice and protocol assistance given (including follow-up advice) 1999-2001

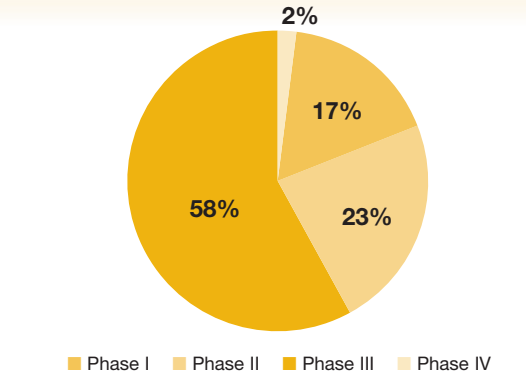


Of the requests for scientific advice and protocol assistance finalised in 2001, two-thirds related to the clinical aspects of the development of medicinal products. In 60 % of cases these requests related to phase III clinical trials.

Scientific advice requests by topic 2001

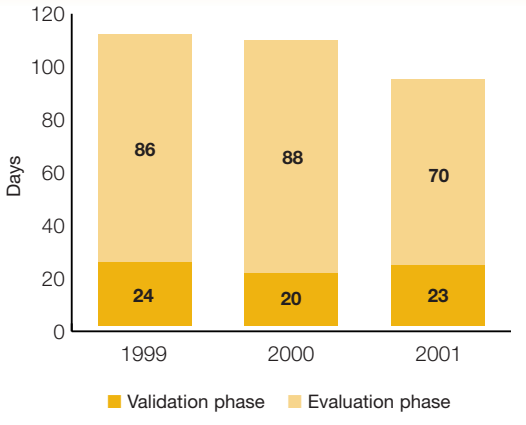


Clinical trial phases of scientific advice requests 2001



Agreed timelines for the scientific advice procedure were respected in 2001 and were below the 120 days time frame between submission of an application and availability of the advice letter.

Median number of days for scientific advice procedures 1999-2001



2.5 Arbitration and Community referrals

The workload relating to arbitrations and Community referrals increased considerably over 2000 levels.

Referrals to the EMEA under Article 10 of Council Directive 75/319/EEC and Article 7(5) of Commission Regulation (EC) No 541/95 arise in cases of disagreement between Member States on a medicinal product within the mutual recognition procedure.

Date of CPMP opinion	*International non-proprietary name (INN)*
Arbitration referrals	
Article 10 Council Directive 75/319/EEC	
27.6.2001	Captopril/hydrochlorothiazid
Ongoing	Dacarbazine
Ongoing	Alteplase
Article 7(5) Commission Regulation (EC) No 541/95	
20.9.2001	Desogestrel
Ongoing	Fenofibrate
Ongoing	Somatropin
Community harmonisation and pharmacovigilance referrals	
Article 11 Council Directive 75/319/EEC	
Ongoing	Fluoxetine
Ongoing	Fluroxamine
Ongoing	Captopril
Ongoing	Captopril/hydrochlorothiazide
Ongoing	Midazolam
Ongoing	Enalapril
Ongoing	Domperidone
Ongoing	Clozapine
Ongoing	Calcium folinate
Ongoing	Ranitidine
Article 12 Council Directive 75/319/EEC	
13.12.2001	Cisapride
Ongoing	Calcitonin
Ongoing	Human coagulation factor VIII
Article 15 Council Directive 75/319/EEC	
18.10.2001	Sertindole
Ongoing	Cerivastatin

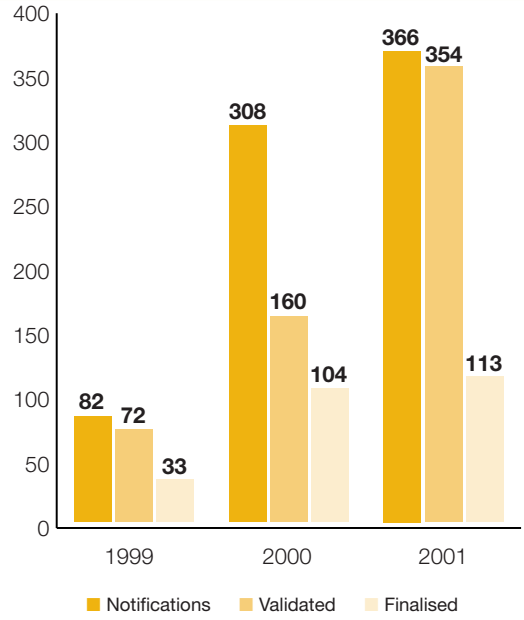
The objective of referrals under Article 11 is the harmonisation within the Community of the conditions of authorisation for products already approved by the Member States, in particular with regard to their therapeutic indications. The EMEA received 9 such referrals in 2001.

Referrals under Articles 12 and 15 of the Directive relate to pharmacovigilance concerns for products authorised through national procedures. There was 1 referral initiated under Article 12 and 1 referral under Article 15 in 2001. A number of referrals initiated in 2000 continued in 2001. These procedures required considerable resources to manage since they involve a large number of marketing authorisations and marketing authorisation holders.

The EMEA finalised its scientific review in 2001 on the risk of venous thromboembolism associated with the use of so-called 'third generation' combined oral contraceptives, with recommendations made concerning changes to the product information. The outcome of the scientific review was accompanied by a coordinated communication strategy by the EMEA and the national competent authorities.

2.6 Special services

Parallel distribution notifications 1999-2001



The number of parallel distribution notifications continued to grow in 2001. Discussions with interested parties were initiated in the second half of the year to investigate further improvements to the procedure.

The principal destinations of medicinal products in the notifications were United Kingdom, Germany and Sweden, with the main countries of origin being France, Italy, Spain and Greece.

2.7 International activities

The Agency continued its collaborative efforts in relation to the national competent authorities of central and eastern European authorities, in particular with regard to the management of the simplified procedure for the recognition of Community marketing authorisations by these authorities.

Within the PERF programme, CPMP members, experts and staff from the Units for the Pre and Post-authorisation evaluation of medicines for human use actively participated in a number of workshops relating to the implementation of Community pharmaceutical legislation, pharmacovigilance and dossier assessment.

Through the visiting expert programme, officials from a number of non-EU competent authorities were able to spend short periods of time with the Agency to better understand the European system.

The EMEA continued its interaction with the US Food and Drug Administration, not only through the work of the ICH process, but also as part of the US-EU Trans-Atlantic Business Dialogue. The regular programme of videoconferences between the CPMP Pharmacovigilance Working Party and the EMEA continued in 2001. Other authorities with which the EMEA worked in 2001 included Health Canada, the WHO Collaborating Centre for International Drug Monitoring and the WHO International Non-proprietary Name (INN) programme.

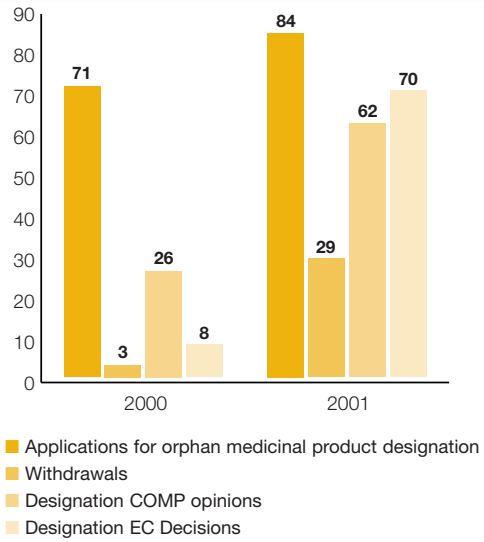
Within the European Community, the EMEA continued its work with the European Monitoring Centre for Drugs and Drug Addiction, a EU decentralised body based in Lisbon. Initial contacts were also established with the Office for Harmonization in the Internal Market (Trade marks and Designs), a EU decentralised body based in Alicante.

2.8 Orphan medicinal products

Applications for designation of orphan medicinal products exceeded initial forecasts by 15 %, showing a continuing interest on the part of sponsors to benefit from the new orphan drug regulation introduced in 2000. This was the first full year of implementation of the orphan drug Regulation (EC) 141/2000.

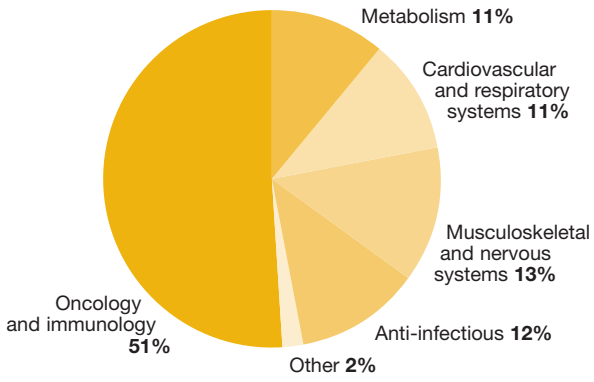
A total of 29 applications for designation were withdrawn in 2001 since the sponsors were not able to fully justify their requests.

Orphan medicinal product procedures 2000-2001



The COMP met 11 times in 2001. Membership of the Committee is given in Annex 4.

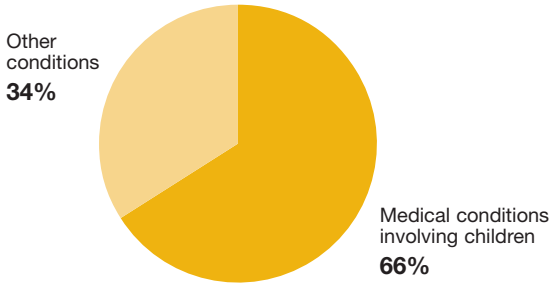
COMP opinions by therapeutic area 2001



Details of the designations recommended by the COMP in 2001 are given in Annex 9. More than half of the medicinal products that received a COMP opinion in 2001 are developed for the treatment of cancers, diseases of immunological origin and metabolic diseases of which a number are related to enzyme deficiencies.

Of the medicinal products that received an opinion from the COMP in 2001, 66 % are aimed at treating diseases affecting adults and children, or children only.

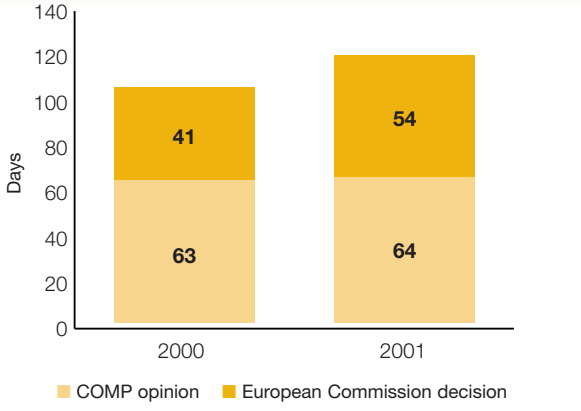
Orphan medicinal products for the treatment of children 2001



The average time taken by the COMP to adopt recommendations on the designation of orphan medicines in 2001 was comparable to 2000 and was below the target 90 days. The time taken for the decision on designation increased slightly. Overall the process remains within the target 120 days.

A total of 62 medicinal products received a positive opinion from the COMP in 2001 and the European Commission took 70 decisions on designation.

Average number of days for designation of orphan medicinal products 2000-2001



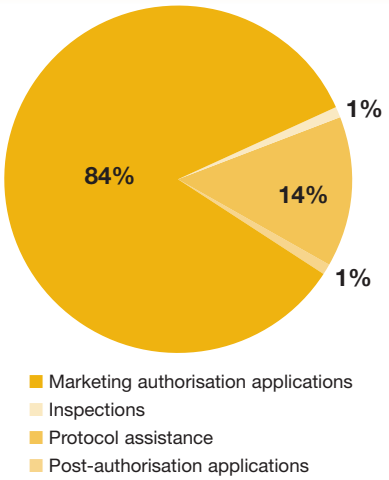
The COMP developed a number of guidance documents to facilitate the preparation of applications by sponsors. Details of these documents are given in Annex 10.

Two workshops were organised in 2001, with patient representative organisations and with sponsors and pharmaceutical industry organisations.

Designated orphan medicinal products are entitled to receive reductions on fees levied by the EMEA when applications are made for marketing authorisation or for other services. These reductions are allocated from a special contribution voted each year by the European Parliament and Council.

Fee reductions in 2001 have mainly be used for applications for marketing authorisation and for protocol assistance.

Use of EU special contribution for orphan medicines 2001



2.9 Working parties and ad hoc groups

The list of guidance documents published in 2001, together with their status, is given in Annex 10.

- **Biotechnology Working Party**

The Biotechnology Working Party met 9 times in 2001. The group was in charge of 33 guidance documents of which 12 were new and 5 were published. Activities related to transmissible and bovine spongiform encephalopathies were of particular importance.

- **Efficacy Working Party**

The Efficacy Working Party met 5 times in 2001 and was in charge of 37 guidance documents of which 15 were new and 31 were published.

- **Safety Working Party**

The Safety Working Party met 3 times in 2001 and had been in charge of 27 guidance documents of which 11 were new and 7 were published.

- **Pharmacovigilance Working Party**

The Pharmacovigilance Working Party met 8 times during 2001. It developed 1 new guidance document, contributed to the finalisation of 2 multidisciplinary guidance documents and revised 4 other guidance documents. The development of or contribution to a further 6 guidance documents is ongoing. A number of subgroups were created for the development of specific guidance documents and for the safety review of drug classes.

- **Joint CPMP/CVMP Quality Working Party**

The joint CPMP/CVMP Quality Working Party met on 4 times in 2001 and released 9 guidelines. The working party continued working on the implementation of the Common Technical Document and increased its collaboration with the European Pharmacopoeia in the framework of the Certification of Suitability scheme.

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

The ad hoc group met 3 times in 2001 and was in charge of 14 guidance documents of which 7 were new and 2 were published.

- **Herbal Medicinal Products Working Party**

The Working Party on Herbal Medicinal Products met three times in 2001. The working party collaborated with the ad hoc Meeting of good manufacturing practices (GMP) Inspection Services on the finalisation of a proposal for revision of Annex 7 to GMP provisions on herbal medicinal products. The working party also finalised its Points to consider on good agricultural and collection practice for starting materials of herbal origin.

The working party addressed a number of pharmacovigilance and safety issues associated with herbal products and liaised

with the Pharmacovigilance Working Party for an exchange of information and consideration of possible actions.

The working party prepared its work programme for 2002-2003 in the light of orientations given by the Management Board with regard to the adoption and publication of documents.

An annual hearing with relevant scientific European learned societies and associations in the field of herbal medicinal products was held in October 2001.

CPMP satellite groups

Invented Names Review Group

The group was established in November 1999 upon request of the CPMP and is composed of representatives of the Member States, the European Commission and EMEA. The group is chaired by an EMEA representative and meets once a month in the margins of the CPMP plenary meetings.

The main activity of the group was to maintain consistency in the review of the invented names proposed by applicants from a safety public health point of view, to establish rules and criteria and update the currently available guideline on acceptability of trade names for medicinal products processed through the centralised procedure. A workshop with interested parties was held on 11 December 2001 to present the revised guideline prior to its formal release by the CPMP.

CPMP Organisational Matters Group (ORGAM)

The ORGAM was established upon request of the new CPMP in January 2001. The group is chaired by the CPMP chairman and is composed of CPMP members and EMEA representatives. It held its first meeting in February 2001 and met regularly in 2001. The group focused on developing new and updated internal and external guidance on the centralised procedure. Its main aim is to improve the functioning of the CPMP and of the centralised procedure as a whole.

Documents published included an update of the accelerated review procedure, revised guidance on renewal of centralised marketing authorisations and on conduct of oral explanations. The group also participated in the review of the EMEA/CPMP performance indicators.

Meeting of the chairmen of CPMP and working parties

Composed of the chairman and vice-chairman of the CPMP, the chairmen of the CPMP working parties and EMEA representatives, this group was created in 2001 with the aim of discussing and coordinating multidisciplinary topics and work programmes of the working parties, and assist the EMEA in its planning process.

CPMP ad-hoc working groups

The following ad hoc groups were active in 2001:

- The ad hoc group on oncology, chaired by Dr Frances Rotblat, met once and focused on the development of medicinal products aiming at treating cancer in children and revised the current note for guidance on anti-cancer medicinal products in man
- The ad hoc group on anti-HIV, chaired by Dr Per Nilsson, met once and focused on updating of the guideline on medicinal products for treatment of HIV. The current points to consider document on the assessment of anti-HIV medicinal products was amended in order to introduce general principles on the clinical development of dual protease inhibitors
- The ad hoc group on comparability of biotechnology medicinal products, chaired by Dr Markku Toivonen met 3 times in 2001 in order to prepare recommendations on this topic

The following new ad hoc groups were created in 2001:

- The ad hoc group on paediatrics, chaired by Dr Daniel Brasseur, met twice in 2001 and began looking at the coordination of actions on the development and use of medicinal products used in children, and at ensuring availability of information to the EMEA and its scientific committees
- The ad hoc group on gene therapy, chaired by Dr Lincoln Tsang, held one meeting and focused on dose definition and standardisation of adenoviral vectors
- The ad hoc group on pharmacogenetics, chaired by Dr Eric Abadie, held two meetings in 2001 and prepared a position paper on terminology in pharmacogenetics

- The ad hoc group on xenogeneic cell therapy, chaired by Dr Pekka Kurki, met twice in 2001 and prepared a points to consider document on the quality and manufacturing aspects of cell therapy products.

COMP ad hoc working groups

The COMP created 3 ad hoc working groups in 2001 to support its activities.

- The ad hoc COMP Biotechnology Working Group, chaired by Prof. Jean-Hugues Trouvin and Dr Harrie Seeverens, provided the COMP with advice on the criteria for designation of biotechnology medicinal products, medicinal products derived from blood or emerging technologies and therapies. The group met 3 times in 2001
- The ad hoc COMP Working Group on Epidemiology, chaired by Dr Kalle Hoppu, prepared a guidance document on prevalence, in the context of the regulation on orphan drugs, which provides advice to sponsors on preparation of applications. The group met 2 times in 2001
- The ad hoc COMP Working Group with Interested Parties, chaired by Mr Yann Le Cam and Dr Patrick Le Courtois. The group prepared proposals and documents for the committee in the framework of its transparency, communication activities and support activities to the European Commission. The group is composed of representatives of patient and of pharmaceutical industry organisations, and work began to identify representatives of health professional and learned societies. The group met 3 times in 2001

2.10 Mutual recognition facilitation group

Useful web site:

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

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

The mutual recognition facilitation group (MRFG) is intended to coordinate and facilitate the operation of the mutual recognition procedure. The group met 11 times in 2001. Tomas Salmonson and Christer Backman chaired the meetings during the Swedish Presidency in the first half of 2001 and Natacha Grenier during the Belgian Presidency in the second half.

Two informal meetings of the MRFG were organised under the presidencies to discuss issues related to the mutual recognition procedure such as harmonisation projects and the ongoing review of pharmaceutical legislation.

Support from the EMEA to the operation of the MRFG continued in 2001, including the use of the improved meeting facilities at the Agency. The EMEA also organised a preparatory meeting for both Member States that held the EU presidency in 2001 and assisted the chairpersons in several meeting-related activities throughout the year.

A total of 36 breakout sessions were organised by reference Member States (referring to 29 new applications and 7 variations). In relation to the number of new applications, the number is lower than in 2000.

Mutual recognition procedure	Total submitted in 2001*	Under evaluation in 2001*	Ended positively in 2001*	Referrals started in 2001
New applications	484	101	443	1
Type I variations	1 611	179	1 487	-
Type II variations	544	219	474	3

**Figures are as at 31 December 2001 and include multiple procedures*

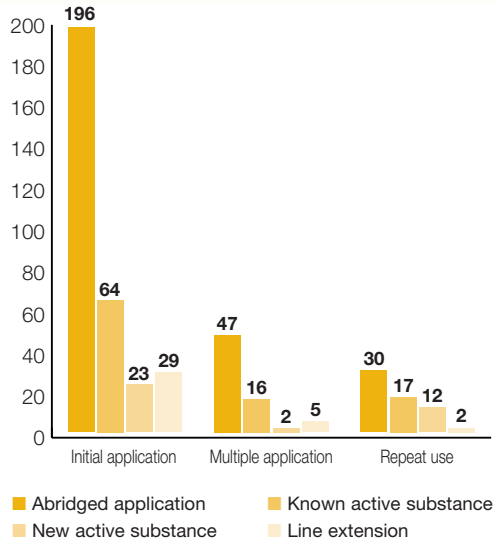
The total number of both submitted and completed applications increased, especially the number of type I variations. There was no noticeable change in the number of arbitrations arising from mutual recognition procedures (new applications/variations) compared to previous years.

The frequency of withdrawals of applications – 23 % – (at least one withdrawal per procedure) from individual Member States in the mutual recognition procedure continued to be an issue of concern in 2001. It should be noted, however, that out of 4 226 applications in the concerned Member States, 304 were withdrawn (7.2 %).

Press releases with statistics and adopted documents are published on the Heads of Agencies website, which was redesigned during 2001.

Further development of the EudraTrack tracking system was continued during the year 2001.

Mutual recognition applications ended positively in 2001 (1st and 2nd level of classification)



Mutual recognition applications ended positively in 2001 (3rd level of classification)

Full dossier	Informed consent	Bibliographic	Generic	Fixed combination	Different use, route or dose	Total
102	10	36	226	17	52	443

Mutual recognition applications ended positively in 2001 (4th level of classification)

Chemical substance	Biological: blood product	Biological: vaccine	Biological: other	Herbal	Total
424	3	8	8	-	443

Mutual recognition applications ended positively in 2001 (5th level of classification)

Prescription only	Non-prescription (including OTC)	Total
388	55	443

A number of guidance documents on using the mutual recognition procedure were published in 2001 to assist applicants and marketing authorisation holders. These include general information on national administrative processes in the mutual recognition procedure, a best practice guide for handling of renewals in the mutual recognition procedure, a recommendation for a mutual recognition procedure after finalisation of an arbitration procedure with a positive opinion by the CPMP and a positive decision by the European Commission and a proposal for a core summary of product characteristics for hormone replacement therapy.

In addition a number of specific guidance documents relating to transmissible spongiform encephalopathy were published by the MRFG during 2001 and several existing guidance documents were revised.

The MRFG advanced its work on a number of ongoing projects, in particular by promoting the preparation of harmonised summaries of product characteristics (SPC) for originator medicinal products. With a mandate given by the Heads of Agencies group, a Joint CPMP/MRFG Working Group on Harmonisation of SPCs was established for this purpose and 4 meetings chaired by Tomas Salmonson were held during the autumn 2001.

In addition, significant resources were allocated for monitoring of the withdrawals in mutual recognition procedure to identify reasons behind them and to prepare comprehensive reports to the Heads of Agencies.

In order to allow Member States more time for discussion in the course of mutual recognition procedure for new applications, the MRFG adopted a modified timetable after several months' pilot project. In the new agreed timetable the concerned Member States send their comments to the reference Member State within 50 days instead of 55 days.

Norway and Iceland participate as full members in the mutual recognition procedure and in meetings of the MRFG since the beginning of 2000. Since summer 2001, Liechtenstein also had the opportunity to participate in mutual recognition procedure. Two observers from central and eastern European countries and the representative of the European Commission also regularly attended MRFG meetings during 2001.

Two liaison meetings between the MRFG and interested parties took place in 2001. MRFG members also participated in conferences and seminars in the pharmaceutical field.

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
Stephen FAIRCHILD (until 15 April 2001)
Sheila KENNEDY (acting)

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

Availability of Medicines Task Force
Peter JONES

Priorities for veterinary medicines in 2001 – progress report

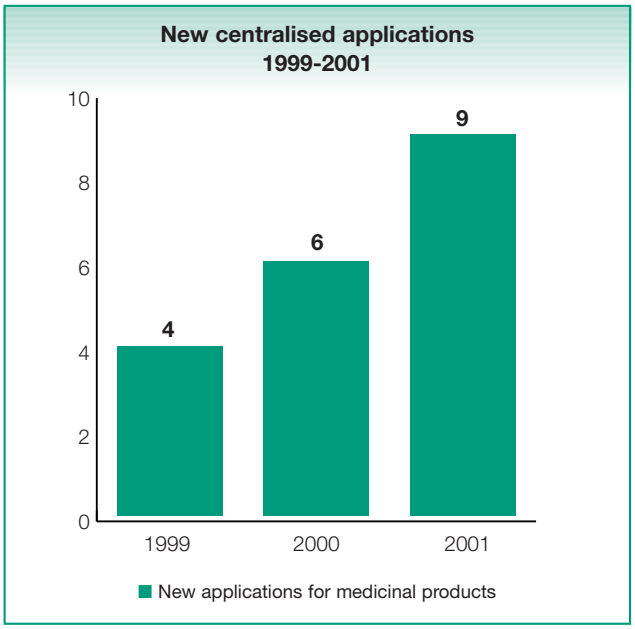
- The CVMP adopted the note for guidance on risk assessment in establishing maximum residue limits (MRLs) to facilitate extrapolation of MRLs from major species to minor species in support of the availability of medicines initiative during the first quarter of 2001. The Committee made substantial progress towards finalising procedures for applications for extrapolations
- The CVMP released for consultation two key guidelines as part of the risk management strategic plan on antimicrobial resistance. The first guideline covers pre-authorisation studies to assess the potential for resistance resulting from the use of antimicrobial veterinary medicinal products and the second concerns antimicrobials for general veterinary use in target animal species
- A second benchmarking study based on the joint EMEA-European Federation of Animal Health (FEDESA) questionnaire on the use of the centralised system of authorisation was completed in 2001. The study shows a high level of satisfaction on the part of the European veterinary pharmaceutical industry with the centralised system and the support from the EMEA, reflecting a consistency in full compliance with regulatory deadlines as in the past

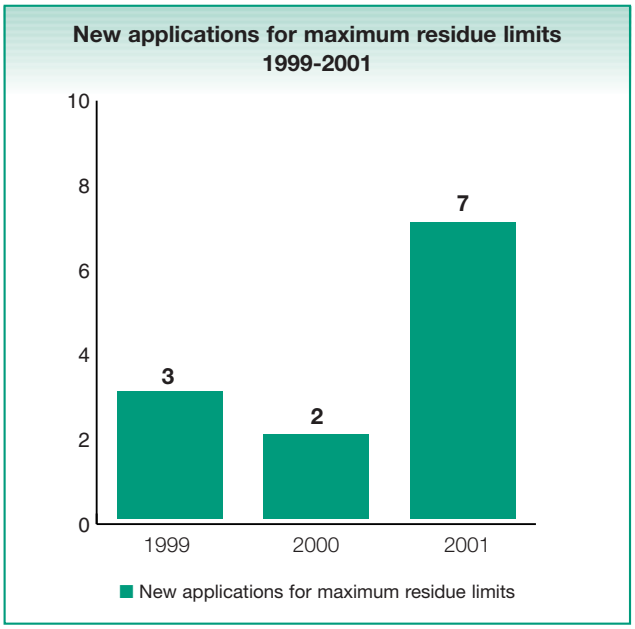
- The CVMP and marketing authorisation holders proceeded well with completion of demonstration of compliance with the Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products. By the end of 2001 all necessary procedures for centrally authorised veterinary medicines had either been completed or were nearing completion
- In cooperation with FEDESA, the publication of summaries of CVMP opinions on initial marketing authorisation applications and MRLs was introduced in 2001. The opinions are now published at the time of adoption. Summaries of opinions were introduced as part of the EMEA initiatives towards improving transparency within the regulatory process
- The routine use of checklists by EMEA project managers for full applications as well as for extensions and type I and type II variations has helped to ensure that as the workload has steadily increased all procedural steps are addressed in accordance with the agreed timetables. Standard operating procedures have now been drafted for variations to ensure that all applications are dealt with in a consistent manner
- The EMEA task force on the availability of veterinary medicines welcomed the publication at the beginning of 2001 of the Communication from the Commission to the Council and European Parliament on the availability of veterinary medicines (COM(2000) 806 final, 5.12.2000)
- Implementation of electronic reporting of adverse reactions for veterinary medicines was delayed because of further work to be completed in the VICH programme

3.1 Initial evaluation

The number of applications for initial evaluations ran close to the target of 10, with nine applications received for a range of new and innovative products. Three of the applications were made under Part A of the Annex to Council Regulation (EEC) No 2309/93 and six under Part B of the Annex.

Seven new applications for establishment of maximum residue limits (MRLs) for veterinary medicinal products for food animals were received, exceeding the forecast of five.





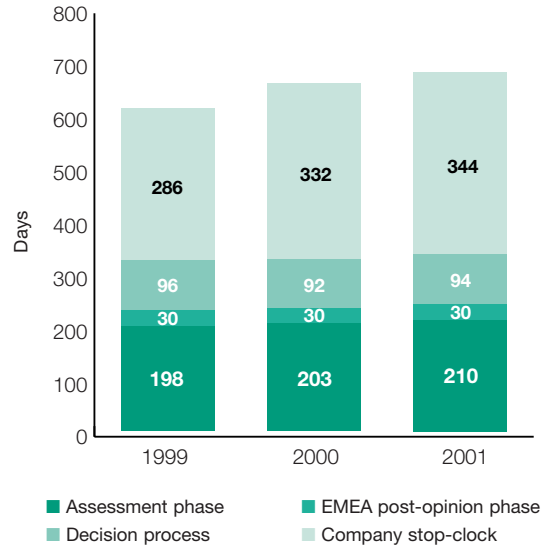
CVMP activities

The CVMP started a new 3-year mandate in January 2001. During its first meeting, Steve Dean was elected chairman and Gérard Moulin was elected vice-chairman of the Committee. The CVMP met 11 times and no extraordinary meetings were held. Details of membership of the CVMP are given in Annex 3.

A Strategic Planning Group was established under the chairmanship of the vice-chairman of the Committee, Gérard Moulin. Three meetings were held and addressed issues including:

- Fairer appointment of rapporteurs and co-rapporteurs
- Prevention of premature application to the centralised system
- More effective consultation processes for CVMP and working parties in reviewing early drafts of VICH guidelines
- Assessor training
- Compliance with post authorisation obligations

Average number of days for centralised procedures 1999-2001



Performance indicators

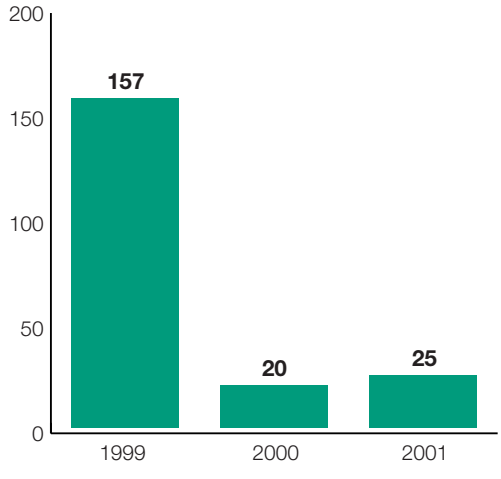
A second benchmarking study by the EMEA and the European Federation of Animal Health (FEDESA) was successfully completed in 2001. The results were presented at the EMEA-FEDESA Infoday on 17-18 May 2001. The survey covered 18 applications, which were current on 1 January 2000 and had received a Community marketing authorisation before 1 April 2001. Findings from the survey included:

- Pre-submission meetings had been held for 94 % of the products covered by the survey, compared to only 66% in 2000
- The assessment report from rapporteurs was received by day 70 for 94 % of the products, which was an improvement on the 78 % in 2000
- A steady and consistent improvement in the quality of summaries of product characteristics, package insert, labelling and translations in all areas. Comments from CVMP members had fallen by 25 % on the previous year, indicating more confidence in rapporteur and co-rapporteur assessment work
- The opportunity for an oral explanation was found useful by 75 % of respondents, which was encouraging since the first report in 2000 identified the oral explanation as an area for improvement

3.2 Establishment of maximum residue limits for old substances

Efforts continued to establish definitive MRLs for those old substances having provisional MRLs and placed in Annex III of Council Regulation (EC) No 2377/90. Twenty-five substances were reviewed in 2001 and finalised following final receipt of answers received to CVMP lists of questions. Thirteen substances remain pending.

Opinions for maximum residue limits for old substances 1999-2001



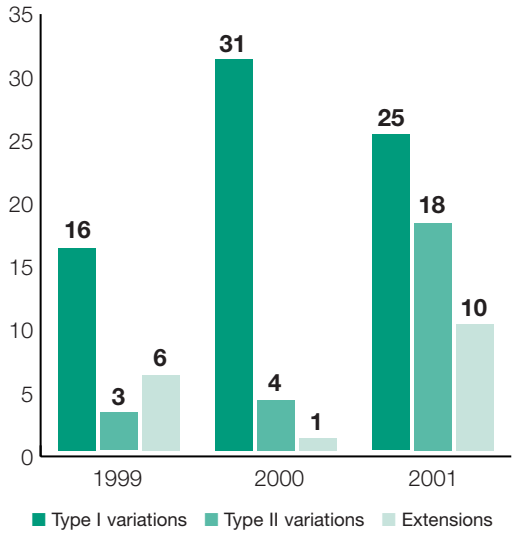
3.3 Post-authorisation activities

There was an increase in post-authorisation activities, in line with the increased number of centrally authorised veterinary medicinal products.

Applications for line extensions increased significantly with 10 applications, exceeding the forecast by 50 %. The number of applications for type I (minor) variations was below target with 25 applications. There were 18 applications for type II (major) variations, more than twice the forecast number.

The number of applications for extensions/modifications to MRLs was below target with 4 applications received. This is a disappointingly low number given the guideline on extrapolation of MRLs to minor species that was adopted by the CVMP in 2001. It had been anticipated that the guideline would be an incentive to industry to extend MRLs set for major species to minor ones.

Post-authorisation applications for centrally authorised medicinal product 1999-2001

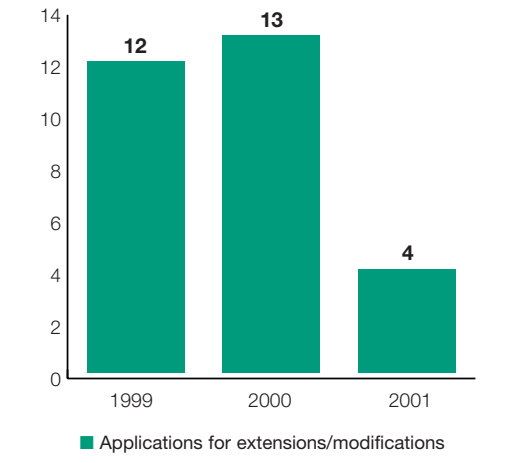


3.4 Pharmacovigilance and maintenance activities

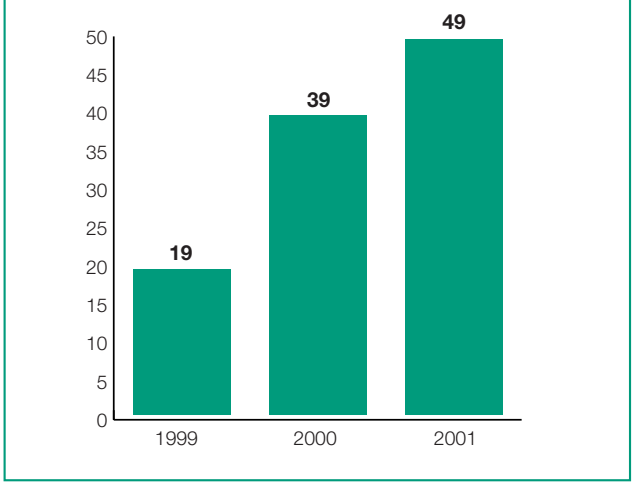
The number of periodic safety update reports (PSURs) for centrally authorised veterinary medicinal products steadily increased during 2001, slightly exceeding the forecast workload. The CVMP Pharmacovigilance Working Party increased the frequency of its meetings, reflecting this rise in reporting and the need for input into CVMP consideration of the issues involved.

Progress with the implementation of a Community pharmacovigilance system for veterinary medicinal products was delayed. Once of the main reasons is non-completion of pharmacovigilance reporting specifications within the VICH process. In addition, priority has been given for the selected contractor to finalise implementation for human medicines first.

Applications for extension/modification of maximum residue limits 1999-2001



Periodic safety update reports 1999-2001



3.5 Scientific advice

One request for scientific advice from the CVMP was made in respect of establishment of MRLs for a new veterinary medicinal product. This was in line with workload forecasts.

3.6 Arbitration and Community referrals

The first arbitration referral for a veterinary medicine under Article 18 of Council Directive 81/851/EEC under the mutual recognition procedure was made to the CVMP in May 2001 by The Netherlands. The referral related to operational safety for a live Newcastle Disease vaccine for poultry. The CVMP adopted its opinion at its September 2001 meeting. The Committee did not support the objection of The Netherlands to the summary of product characteristics agreed by the reference and other concerned Member States (OJ C 49, 22.2.2002, p. 6).

In October 2001 the CVMP considered a referral under Article 20 of Council Directive 81/851/EEC in respect of concerns relating to the inadequacy of withdrawal times for long-acting injectable formulations of benziathine penicillin resulting in tissue residues at slaughter in excess of the Community MRLs. The procedure is ongoing.

At its December 2001 meeting, the CVMP adopted a positive opinion recommending the lifting of the suspension of the marketing authorisation for Econor. The European Commission decision to suspend the authorisation was taken in December 2000 on the basis of adverse reactions and their impact on target animal safety.

3.7 Interested parties

The EMEA worked closely with FEDESA on improving transparency in the regulatory process. From April 2001 summaries of CVMP opinions on marketing authorisation were published 15 days after their adoption. From November 2001 summaries of opinions on marketing applications and MRLs were published on 'day 0' at the time of adoption.

Dialogue with interested parties on a number of current issues continued in 2001, including regular meetings between the CVMP and the interested parties. A successful joint EMEA-FEDESA Infoday was held in May 2001, looking at topical issues including antimicrobial resistance and the 2001 review of European pharmaceutical legislation.

A new approach to meetings with interested parties was introduced in November 2001. Experts from both the CVMP and interested parties were brought together as a focus group at the beginning of the consultation period for the new guidelines on minimising antimicrobial resistance. The format was considered to have been successful by participants and will be repeated for other mutually agreed topics.

3.8 International activities

The Unit and the CVMP participated in a number of workshops as part of the second Pan-European Regulatory Forum (PERF II) programme. Workshops successfully completed include:

- Immunologicals – veterinary vaccines*
  EMEA, September 2001
- Safety – veterinary medicines
  Prague, October 2001
- Efficacy – veterinary medicines*
  EMEA, October 2001
- Centralised and mutual recognition procedures
  EMEA, December 2001

** held in conjunction with CVMP working party meetings*

Preparations began for the secondment of pharmacovigilance experts from central and eastern European countries to EU Member State national competent authorities for training in veterinary pharmacovigilance.

The EMEA continued its active support of the International Conference on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH) and the VICH secretariat. The CVMP has worked to release several new VICH-derived guidelines, either for consultation or as final. Details of guidelines are given in Annex 10.

The EMEA hosted a meeting of the VICH Steering Committee on 27-28 June 2001 and also a number of VICH expert working groups during the course of the year.

The EMEA acted as a temporary expert to the World Health Organisation initiative on antimicrobial resistance. The Agency also participated, as part of the European Commission delegation, in the 13th Session of the Codex Committee on Residues of Veterinary Drugs in Foods that met in Charleston, USA in December 2001.

3.9 Working parties and ad hoc groups

The working parties of the CVMP largely met the targets set by the Committee. A total of 17 guidelines were drafted and released for consultation and 21 guidelines adopted. This is in line with the 15 forecasted. In addition the working parties participated in a number of workshops in support of the PERF II initiative. Details of all CVMP guidelines are given in Annex 10.

- **Efficacy Working Party**

The Efficacy Working Party met 3 times in 2001. In addition to a number of guidelines either finalised or released for consultation, the working party considered efficacy requirements for minor uses and minor species in the context of the availability of veterinary medicines with a view to finalisation in early 2002. As part of the risk management strategic plan for antimicrobial resistance, the working party also prepared papers on standard phrases for recommendations in the SPC for antimicrobials, as well as endorsing prudent use of antimicrobials in the veterinary sector within the European Union.

- **Immunologicals Working Party**

The Pharmacovigilance Working Party met 4 times in 2001 and completed preparation of 4 concept papers and guidelines. In addition, the working party worked closely with the CPMP Biotechnology Working Party in addressing issues relating to transmissible and bovine spongiform encephalopathies. An ad hoc group of experts on foot and mouth disease (FMD) was created in 2001. The purpose of the group is propose harmonisation of existing guidelines from the CVMP, the United Nations Food and Agriculture Organisation (FAO) and the EDQM, with the intent of evaluating FMD medicines so that the quality, safety and efficacy would be seen to be consistent with Community pharmaceutical legislation.

- **Pharmacovigilance Working Party**

The Pharmacovigilance Working Party met 6 times in 2001, an increase that reflects the additional work of pharmacovigilance support to the CVMP in respect of centrally and nationally authorised medicinal products. Further developments of the VEDDRA list of clinical terms to support the VEDDRA database were undertaken with endorsement by the CVMP at its October 2001 meeting. The working party supported the work of the EudraVigilance Telematics Implementation Group on further development and implementation of electronic transmission and management of electronic reporting of adverse drug reactions to be in compliance with Community legislation.

- **Safety Working Party**

The Safety Working Party met 5 times in 2001 and finalised 11 guidelines either in consultation or in draft form. The work on establishing definitive MRLs for those old substances that currently have provisional status in Annex III of Council Regulation (EEC) No 2377/90 progressed faster than expected, with the working party making recommendations to the CVMP on 25 substances.

Work on the requirements for analytical methods was finalised by the working party and the CVMP following the consultation phase.

- **Joint CPMP/CVMP Quality Working Party**

The Joint CPMP/CVMP Quality Working Party met 4 times in 2001. With regard to guidelines applicable to medicinal products for both human and veterinary use, the Working Party finalised 6 guidelines for adoption and 2 for release for consultation (one of which concerned veterinary medicinal products only). A further note was issued providing guidance to industry on the application of the VICH uideline on residual solvents to existing medicinal products. Guidance was also provided to the topic group leader on VICH guidelines. Rapporteurs were appointed to review the need to update guidelines.

- **ad hoc group on antimicrobial resistance**

The ad hoc group appointed by CVMP to consider pre-authorisation testing requirements for new antimicrobials met 3 times in 2001. The ad hoc group finalised the draft

guideline, which was adopted for consultation by CVMP at its October meeting. The expert group also advised the CVMP on its input into the VICH Expert Working Group addressing the same topic.

3.10 Veterinary mutual recognition facilitation group

Useful web site:

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

The veterinary mutual recognition facilitation group (VMRF) met 11 times in 2001. Christer Backman chaired the meetings during the Swedish Presidency in the first half of 2001 and Ferdy Sprangers and Françoise Falize during the Belgian Presidency in the second half.

The EMEA provided full secretariat and administrative support to the group. Observers were welcomed from central and eastern European countries and the three EEA-EFTA concerned States. Representatives from the European Commission attended some of the VMRF meetings during 2001 and will continue to do so in the future.

The number of mutual recognition procedures completed decreased from 47 in 2000 to 43 in 2001. Eight Member States acted as reference member state in the procedures.

In order to improve the procedure a follow-up of reasons for withdrawal was performed with a view to solving problems for future applications.

The first arbitration procedure for a veterinary medicinal product was initiated in 2001. It will be finalised in 2002.

The VMRF-FEDESA liaison group met regularly during 2001. The joint VMRF-FEDESA survey of the mutual recognition procedure was continued in 2001.

An index of products authorised through the mutual recognition procedure is published on the web site of the Heads of Veterinary Agencies (HEVRA). The index gives access to core information for each product, together with the English-language version of the summary of product characteristics (SPCs). Member States are encouraged to contribute SPCs in national languages.

A number of organisational issues were discussed and resolved. The best practice guide was modified to detail Member States' work and to allow more time to applicants to answer questions raised by concerned Member States. The best practice guide for handling renewals in the mutual recognition procedure was also finalised.

Companies were given the possibility of asking questions directly to the VMRF through the HEVRA web site and the answers to 9 questions relating to the mutual recognition procedure in 2001 were published on the HEVRA web site.

Chapter 4
Inspections

Overview

Head of Sector
Stephen FAIRCHILD (until 15 April 2001)
Sheila KENNEDY (acting)

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

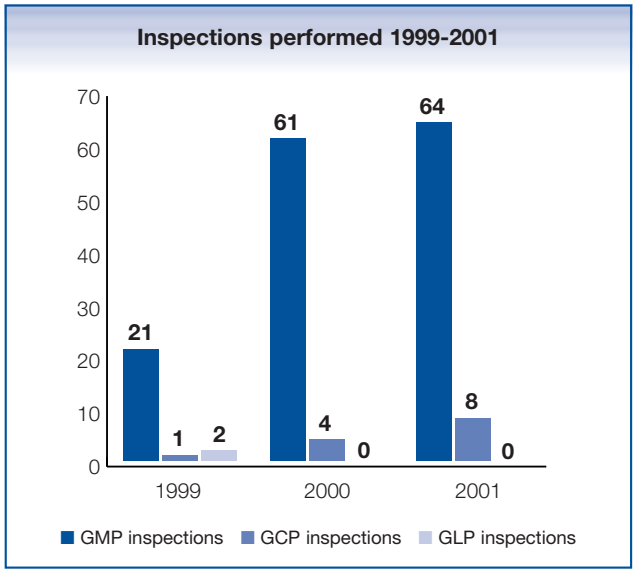
ad hoc Meeting of GCP inspection services
Fergus SWEENEY

The Sector for inspections was part of the Technical Coordination Unit until 31 August 2001, after which it was moved under the operational responsibility of the Unit for Veterinary medicines and inspections, as part of the reorganisation within the EMEA.

The Sector contributed to training activities within the PERF II programme and coordinated a number of joint inspections in central and eastern European countries.

Coordination of inspections for centralised procedures

The number of pre- and post-authorisation good manufacturing practice (GMP) inspections performed rose in 2001. The rate of increase shows signs of slowing compared to previous years.



This is in part due to the fact that an increasing number of manufacturing sites listed in new marketing authorisation applications have already been inspected in connection with other applications.

Work on the development of a database of sites used in the manufacture of centrally authorised products was progressed in 2001.

The ad hoc Meeting of GMP inspection services met on 5 occasions in 2001, and finalised a number of new and revised annexes to the EU GMP guide. The development of a joint audit programme to harmonise the conduct of inspections, handling of quality defect reports and authorisation of manufacturing sites through quality audits of inspection services was discussed. A revised compilation of EC inspection procedures was agreed. Observers from mutual recognition agreement (MRA) partners and central and eastern European countries attended technical parts of the meetings.

The number of good clinical practice (GCP) inspections requested for human medicinal products continued to increase, rising from 4 in 2000 to 8 in 2001. These inspections involve sponsor companies, investigators 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 clinical trials.

No GCP inspections for veterinary medicinal products have yet taken place. Preliminary discussions took place following implementation of the GCP guideline developed as part of the VICH process.

A first meeting was held with good laboratory practices (GLP) inspectors to formalise processes for GLP inspection request by the CPMP and CVMP.

A total of 11 reports on quality problems concerning centrally authorised products were received and monitored by the EMEA in 2001, leading to 4 batch recalls involving 3 medicinal products.

Preparation for implementation of the clinical trials directive

The ad hoc meetings of GCP and GMP inspection services were active in 2001 in the preparation of guidance documents required by Directive 2001/20/EC on the implementation of good clinical practice in the conduct of clinical trials on medicines for human use (OJ L 121, 01.05.2001, p. 34).

This work is ongoing and in particular involves drafting requirements for GMP of investigational medicinal products and detailed guidance on GCP inspections. The EMEA also participated in the European Commission working party for the preparation of other documents needed under the Directive.

Mutual recognition agreements

Mutual recognition agreement (MRA) implementation status

EC-Canada

The start of the operational phase was postponed for 12 months at the Joint Committee meeting in September 2001.

EC-United States

As part of the evaluation programme the EU performed a preliminary evaluation visit to the headquarters of the US Food and Drug Administration (FDA) in June 2001. Any further evaluation activities have been put on hold as the FDA only conducted their first on-site evaluation in the United Kingdom in November 2001. It became clear that the assessments of all the EU Member States would not be finished by the end of the transition period (November 2001). Discussions are still ongoing concerning the time and conditions to extend the transition period beyond the original 3-year period.

EC-Switzerland

The MRA is still awaiting ratification at Member State level and did not start as foreseen in early 2001. A new tentative date is the beginning of 2002.

EC-Japan

The Council of the European Union adopted the text of the MRA with Japan on 27 September 2001 and enters into force on 1 January 2002. The MRA will start with an 18-month preparatory phase. It covers human medicinal products only.

Agreements in force

EC-Australia

(human and veterinary medicinal products)

Activities in 2001 included the completion of the transition period for veterinary medicinal products for the 1 June 2001. The contents of the certificates of GMP compliance for manufacturers and batch certificates have been agreed with Australia.

EC-New Zealand

(human and veterinary medicinal products)

The GMP Annex is in operation since 1 January 1999 for human medicinal products as with the Australian MRA. For veterinary medicinal products the activities in the transition period are progressing well and it is expected to start the operational phase by the beginning of 2002.

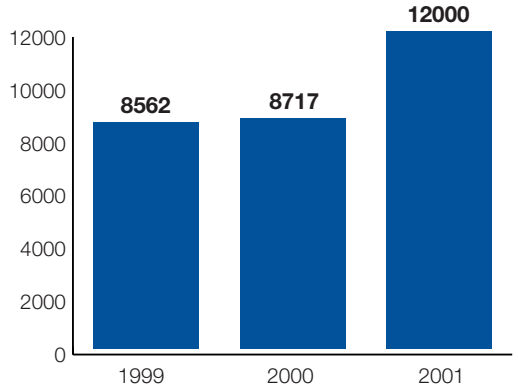
Certification of medicinal products

Demand for certificates increased significantly both relative to 2000 levels and budgeted projections for the year. The number of certificates requested rose to 12 000 compared to 8 717 in 2000. The rise is due to a combination of an increasing number of centrally authorised medicines and the number of variations, extensions and renewals for these authorisations.

The EMEA is working with trade associations and industry representatives to address items related to the EMEA certification scheme, including a review of the request forms, arrangements for payments and other ways to maximise the efficiency of the system.

The information package for certificates of medicinal products issued by the EMEA was updated in 2001. The package provides guidance on the certification of medicinal products in the EU in relation with the systems for authorisation.

Certificates of a medicinal product 1999-2001



Chapter 5
Administration and support activities

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 (acting)

Head of Sector for accounting
Gerard O'MALLEY

Communications and networking Unit

Head of Unit
Post vacant

Head of Sector for document management and publishing
Beatrice FAYL

Head of Sector for meeting management and conferences
Sylvie BÉNÉFICE

Head of Sector for project management
Tim BUXTON (acting)

Head of Sector for information technology
Michael ZOURIDAKIS

Deputy Head of Sector for information technology
David DRAKEFORD

5.1 Administration

The Administration Unit was reorganised in 2001 with the creation of a new sector responsible for the provision of infrastructure services. This brings together a range of internal services that had previously been in different areas of responsibility throughout the Agency.

Personnel and budget

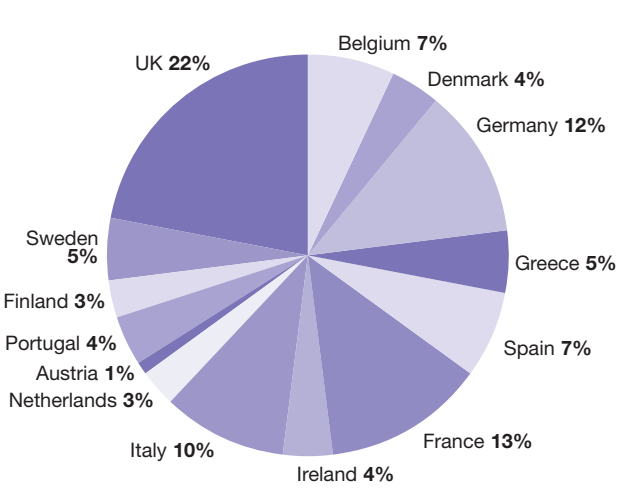
The year was characterised by a general increase in numbers of staff and recruitment procedures, the reshaping of the organisational structure of the EMEA and a complicated budgetary situation due to volatile fluctuations in the estimations of revenue income and workload. A total of 20 internal and external selection procedures were handled in 2001.

Work on the personal database system continued throughout the year and the introduction of a VAT neutral budget was prepared.

Key objectives achieved in 2001 include:

- Implementation of the 2001 budget in accordance with the financial regulations
- Regular budget reports to EMEA management and the Management Board;
- Preparation of the 2002 budget and follow up on the approval process for the European Community contribution
- Recruitment of new staff through selection procedures
- Administration of staff entitlements in accordance with the Staff Regulations
- Provision of information and assistance to new staff and the organisation and co-ordination of training programmes for all staff

EMEA staff members by nationality in 2002



(Luxembourg 0%)

Infrastructure services

The sector came into existence in September 2001 and provides facilities management, archiving, reprographics and mail room services.

Office and meeting space was a priority in 2001. New conference facilities on the third floor were completed at the beginning of 2001, together with new mailing and reprographics areas. Additional available space was identified and work began on procurement of architect and other services for the fitting out work to be carried out in 2002.

Work began on the preparation of a business contingency plan for the EMEA.

Improvements to the archiving and retrieval of EMEA documents were introduced in 2001 following an internal audit.

Accounting

The principal challenge for the Accounting Sector in 2001 was to absorb the increased level of operations due to the expansion of activities of the operational units, particularly in the areas of meetings and revenue, with a staffing level unchanged since 1996.

The sector handled approximately 33 000 transactions in 2001 compared to 27 150 in 2000.

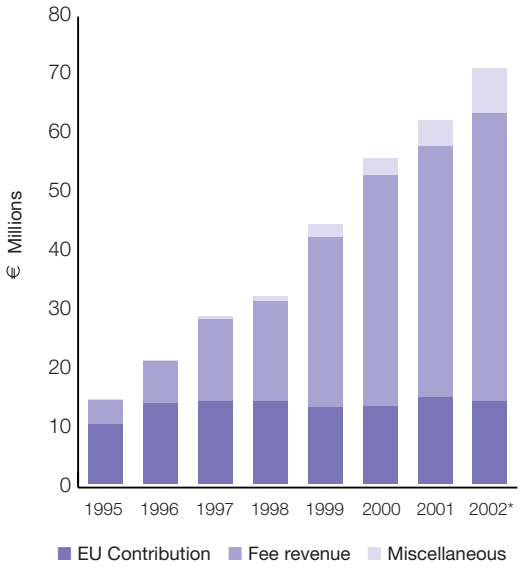
The sector contributed to the analytical and activity costing exercise for the EMEA. It also looked at a number of opportunities to implement electronic data exchange within EMEA accounting systems and also with third parties, such as suppliers and customers, in order to make productivity gains.

5.2 Document management and publishing

Document management

The project to introduce an electronic document management system (EDMS) at the EMEA aims to ensure transparency and integrity of the Agency's work processes by introducing a system to hold documents in a central repository, ensure that documents are forwarded to and accessible by all authorised staff; ensure the registration of documents to reflect their history; and ensure that staff always have access to the latest version of a document.

Evolution of the EMEA budget 1995-2002



** Budget for 2002 adopted by the Management Board 18 December 2001*

Following acceptance of the feasibility study commissioned at the end of 2000, work began on the implementation of the EDMS at the EMEA. Basic installation (servers, software, system configuration and testing) was completed in 2001, and implementation of the publishing process was progressed.

Electronic submission

Two projects were run in parallel in the area of electronic submissions: the definition of the electronic common technical document (eCTD) and the product information management (PIM) project.

- The eCTD defines a harmonised format (but not harmonised content) for the electronic submission of marketing authorisation applications in the European Union, Japan and the United States – the three regulatory partners in the ICH process. The eCTD is being defined as part of the ICH process in the M2 Electronic Standards for the Transfer of Regulatory Information Experts Working Group
- The specifications document for the eCTD was released for testing in May 2001. The expert group met by videoconference in October 2001 and expect to be able to recommend that the specifications be released for general consultation by the ICH Steering Committee early in 2002

- PIM is a joint initiative between the EMEA and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Its purpose is to develop an exchange standard for product information that is used in the summary of product characteristics, patient information leaflet and product packaging. In developing the standard, the project aims to ease the exchange of information between applicants and competent authorities, mostly through the automated reuse of data to eliminate multiple input and review of changes during the review cycle. A second prototype application was developed in 2001 in support of a revised exchange standard

The specification document and other work in progress relevant to the eCTD, together with information on other aspects of electronic submission, is available at the EMEA electronic submission web site: *http://esubmission.eudra.org*

Quality and coherence of regulatory documents

The Quality Review of Documents Group (QRD) continued its work with the increased use of secure electronic exchange of documents, requiring fewer meetings during the year.

A cross-Agency working group established to review the amount and timing of translation work carried out on product information submitted with marketing authorisation applications concluded, in consultation with a similar working group established within EFPIA, that it would be more efficient to work in the English-language only until the second phase of the assessment.

The heads of national competent authorities meeting in November 2001 endorsed this proposal and it is expected to become operational during 2002.

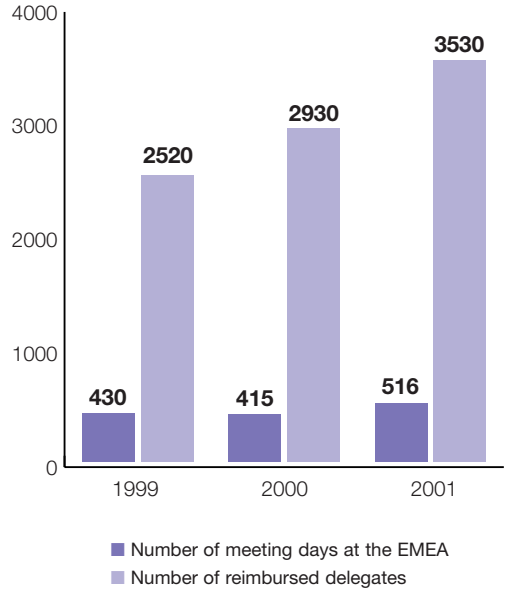
5.3 Meeting management and conferences

Meetings

The level of meeting-related activities in 2001 increased by some 30 % compared with 2000. The EMEA services organised a total of 327 meetings in 2001, with a total of 516 meeting days. A total of 3 530 delegates were reimbursed.

The new meeting facilities at the EMEA became operational in the second quarter of 2001, resulting in a doubling of the Agency's conference room capacity.

Meetings at the EMEA 1999-2001



Meeting management

The rules on reimbursement of delegates and experts attending meetings were revised by the Management Board in June 2001.

A number of aspects relating to meeting organisation were also revised in 2001, including internal procedures for requesting meetings, travel and accommodation bookings, invitations and other practical organisational issues. The first module of a computerised meeting management system was launched in November 2001. The system is designed to automate meeting room bookings and scheduling.

Partners

The provision and support of technical equipment and facilities for meeting rooms were reviewed, in particular as part of preparations for future enlargement of the EU.

As part of ongoing efforts to facilitate relations with external partners, the sector developed the provision of videoconferencing and teleconferencing facilities and the organisation of satellite meetings. This was in particularly important it the context of the organisation of the PERF programme.

5.4 Information technology

The role of the IT sector may be analysed as, on the one hand, the provision of information technology facilities and services to the EMEA internally, and the technical support of European initiatives and activities on the other.

IT services at the EMEA

Operations

The sector, in continuing its commitment to effective IT support to the Agency, has met its target of operational system availability and quality of service support with almost 100% availability over the complete range of information technology systems during the year.

Development

The IT sector has made a significant contribution to the development of two major systems at the Agency during 2001, namely the pharmacovigilance application named EudraVigilance and the electronic document management system. In addition, the sector has continued the development and implementation of the main drug approvals tracking system called SIAMED in consultation with WHO and completed the first module of the meetings management system. The sector undertook the development and implementation of a number of new mainstream projects including a new EMEA personnel system, new security system and a range of upgrades to user workstations.

Project management

Project management support to priority projects of the EMEA was supplied during the year. This support included technical assistance for the implementation of the electronic document management system, for the definition of the electronic common technical document (eCTD), and for the product information management (PIM) project.

European initiatives and activities

European initiatives have been prioritised by the European Commission in conjunction with the establishment of the new management structure for pan-European IT projects. The priorities, which were set after consultation with stakeholders in the European regulatory system, are communication, pan-European databases and electronic submission of data. These priorities have been set in the context of an overall requirement for better access to harmonised data for all competent authorities.

The priorities have been translated into four projects:

- Development and maintenance of the EudraNet
- Development and implementation of the EuroPharm database
- Development and implementation of the EudraVigilance system
- Development and implementation of the electronic common technical document (eCTD) in the context of work done by the M2 Experts Working Group of the International Conference on Harmonisation

The IT sector has played an active role at all levels in co-ordination and management of Eudra IT projects in the pharmaceutical sector, with regular participation and attendance at Telematics Management Committee and the Telematic Implementation Groups for all four major areas within this domain identified above. Within this context preparations have been undertaken and good progress made in the initiation of the planning required for the new responsibilities that the EMEA will assume for Eudra IT projects in 2003.

The Sector participated fully in the management activities relating to the EudraNet and provided technical and management support in the development and implementation of the EudraVigilance application. Work on the eCTD has been supported through membership of the European Community delegation to the ICH M2 Experts Working Group as well as technical support for the testing of the eCTD carried out during the middle of 2001.

Since 1 September 2001, responsibility for the European initiatives and project management functions has been shared with the new Sector for Project management.

European Commission Joint Research Centre: Support to pharmaceutical regulation

The Unit for Support to pharmaceutical legislation (JRC-SPR) is part of the European Commission Joint Research Centre's Institute for Health and Consumer Protection. Based at the EMEA in London, the group supports the IT network that connects the national competent authorities, European Commission and the EMEA itself.

The JRC-SPR Unit replaces the former ETOMEP Unit (European technical office for medicinal products).

The mission of the JRC-SPR in 2001 has changed to take into account the policy decision to transfer all telematic services and developments to EMEA from January 2003. The EudraTrack system that supports the mutual recognition process is not included in the transfer.

The Unit was charged with the preparation and execution of the transfer of the Eudra system at the beginning of 2001. An implementation plan was prepared and involves the reinforcement of the JRC presence in London to take into account changes in personnel. The plan foresees an in depth reorganisation of the current EudraNet architecture by achieving a separation between the Eudra systems and the Agency's own IT network.

A new workspace platform was introduced for the EudraRoom cooperation tool and the new cooperation space has been renamed as EudraWorkspace. EudraSafe – the secure document exchange service – was also reorganised with improved users account management and increased security.

Operation of EudraMail, web hosting and network services continued as planned.

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	Paul WEISSENBERG, Bertrand CARSIN
	Alternate: Philippe BRUNET
Belgium	André PAUWELS, Frans GOSSELINCKX
Denmark	Ib VALSBORG, Jytte LYNGVIG
Germany	Hermann Josef PABEL, Gerhard Josef KOTHMANN, *Vice-chairman*
Greece	Marios MARSELOS, Elias MOSSIALOS
Spain	María Victoria de la CUESTA GARCÍA, Ramón PALOP BAIXAULI
France	Philippe DUNETON, Martin HIRSCH
Ireland	Tom MOONEY, Michael C GAYNOR
Italy	Nello MARTINI, Romano MARABELLI
Luxembourg	Mariette BACKES-LIES
Netherlands	John A LISMAN, Frits PLUIMERS
Austria	Alexander JENTZSCH, Ernst LUSZCZAK
Portugal	Miguel ANDRADE, Rogério GASPAR
Finland	Pekka JÄRVINEN, Hannes WAHLROOS
Sweden	Birgitta BRATTHALL, Anders BROSTRÖM
United Kingdom	Roy ALDER, Michael RUTTER

Observers

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

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) [1]
- Michalis AVGERINOS (Greece)
- Rolf BASS (Germany)
- Geert DE GREEF (Belgium)
- Jens ERSBØLL (Denmark)
- Silvio GARATTINI (Italy)
- Fernando GARCIA ALONSO (Spain)
- Jacqueline GENOUX-HAMES (Luxembourg)
- Lars GRAMSTAD (Norway)
- Manfred HAASE (Germany)
- Else HØIBRAATEN (Norway)
- Magnús JÓHANNSSON (Iceland)
- Pekka KURKI (Finland)
- Frits LEKKERKERKER (Netherlands) [2]
- David LYONS (Ireland)
- Pieter NEELS (Belgium) [3]
- Per NILSSON (Sweden)
- Antonia PANTOUVAKI (Greece)
- Heribert PITTNER (Austria)
- Jean-Louis ROBERT (Luxembourg)
- Pasqualino ROSSI (Italy)
- Frances ROTBLAT (United Kingdom)
- Patrick SALMON (Ireland)
- Tomas SALMONSON (Sweden)
- Cristina SAMPAIO (Portugal)
- Beatriz SILVIA LIMA (Portugal)
- Josef SUKO (Austria)
- Sigurdur THORSTEINSSON (Iceland)
- Markku TOIVONEN (Finland)
- Jean-Hugues TROUVIN (France)
- Barbara VAN ZWIETEN-BOOT (Netherlands)

* The country of the nominating Member State is given for information purposes only.

1 Replaced Alasdair BRECKENRIDGE as of the April 2001 meeting.

2 Replaced Hans van BRONSWIJK as of the September 2001 meeting.

3 Replaced Daniel BRASSEUR as of the February 2001 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) [1]
- 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)
- Paul-Pierre PASTORET (Belgium)
- Halldór RUNÓLFSSON (Iceland)
- Jean-Claude ROUBY (France)
- Liisa SIHVONEN (Finland)
- Marc WIRTOR (Luxembourg)

* The country of the nominating Member State is given for information purposes only.

[1] Replaced Steve DEAN as of the February 2001 meeting.

Annex 4

Members of the Committee for Orphan Medicinal Products

Chairman	Josep TORRENT i FARNELL

Members

Belgium	André LHOIR
Denmark	Heidrun BOSCH-TRABERG [1]
Germany	Rembert ELBERS
Greece	George STRATHOPOULOS
Spain	José Félix OLLOLA MARAÑÓN
France	François MEYER
Ireland	Brendan BUCKLEY
Italy	Domenica TARUSCIO
Luxembourg	Henri METZ
Netherlands	Harrie SEEVERENS
Austria	Hans Georg EICHLER
Portugal	José Manuel GIÃO TOSCANO RICO
Finland	Kalle HOPPU
Sweden	Kerstin WESTERMARK
United Kingdom	Rashmi SHAH [2]
Patient organisation representatives	Moisés ABASCAL ALONSO, Yann LE CAM, *Vice-chairman*, Alastair KENT
EMEA representatives	Eric ABADIE [3], Gianmartino BENZI, David LYONS [4]

Observers

Iceland	Sigurdur THORSTEINSSON
Norway	Randi NORDAL

1 Replaced Jan RENNEBERG as of the January 2001 meeting.

2 Was replaced by Alex NICHOLSON as of the May 2001 meeting and re-appointed as of October 2001.

3 Replaced Jean-Michel ALEXANDRE as of the March 2001 meeting.

4 Replaced Mary TEELING as of the March 2001 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 2000 - 2002

The summarised comparative budget statements for 2000 to 2002 are as follows: (Amounts expressed in euro)

	2000 [1] (31.12.2000)		2001 [2] (31.12.2001)		2002 [3] (18.12.2001)	
Revenue						
Fees	39 154 000	70.82%	45 771 000	69.49%	49 000 000	69.46%
General EU contribution	13 200 000	23.88%	14 700 000	22.32%	14 000 000	19.84%
Special EU orphan medicinal product contribution	1 000 000	1.81%	600 000	0.91%	3 300 000	4.68%
Contribution from EEA	245 220	0.44%	287 640	0.44%	310 000	0.44%
Contribution from EU programmes (PERF)	217 000	0.39%	2 314 360	3.51%	1 632 000	2.31%
Other	1 471 000	2.66%	2 193 000	3.33%	2 305 000	3.27%
TOTAL REVENUE	**55 287 220**	**100.00%**	**65 866 000**	**100.00%**	**70 547 000**	**100.00%**
Expenditure						
Staff						
Salaries	18 493 000	33.45%	20 615 000	31.30%	24 952 000	35.37%
Interim and other support persons	1 058 000	1.91%	1 414 000	2.15%	1 905 000	2.70%
Other staff-related expenditure	1 350 000	2.44%	1 683 640	2.56%	1 776 000	2.52%
Total title 1	20 901 000	39.80%	23 712 640	36.00%	28 633 000	40.59%
Building/equipment						
Rent/charges	5 212 220	9.43%	5 149 000	7.82%	5 936 000	8.41%
Expenditure on data processing	2 423 500	4.38%	4 293 000	6.52%	2 570 000	3.64%
Other capital expenditure	2 353 000	4.26%	1 658 000	2.52%	1 170 000	1.66%
Postage and communications	480 000	0.87%	617 000	0.94%	394 000	0.56%
Other administrative expenditure	1 593 000	2.88%	1 829 000	2.78%	1 925 000	2.73%
Total title 2	12 061 720	21.82%	13 546 000	20.57%	11 995 000	17.00%
Operational expenditure						
Meetings	3 270 000	5.92%	4 110 000	6.24%	4 320 000	6.12%
Evaluations	18 682 500	33.79%	21 308 000	32.35%	23 333 000	33.07%
Translation	p.m.	0.00%	428 000	0.65%	359 000	0.51%
Studies and consultants	5 000	0.01%	225 000	0.34%	85 000	0.12%
Publications	150 000	0.27%	190 000	0.29%	190 000	0.27%
EU programmes	217 000	0.39%	2 346 360	8.20%	1 632 000	2.31%
Total title 3	22 324 500	40.38%	28 607 360	43.43%	29 919 000	42.41%
TOTAL EXPENDITURE	**55 287 220**	**100.00%**	**65 866 000**	**100.00%**	**70 547 000**	**100.00%**

Notes

[1] Final appropriations for 2000. [2] Final appropriations for 2001. [3] Budget for 2002 as adopted by the Management Board on 18.12.2001.

Annex 7

CPMP opinions in 2001 on medicinal products for human use

Product • Brand name • INN • Part A/B	Marketing authorisation holder	Therapeutic area • ATC code • Indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Foscan** • **temoporfin** • **Part B**	• Scotia Pharmaceuticals	• L01XX • Treatment of squamous cell carcinoma of head and neck	• 21.10.1999 • 25.01.2001 • 215 days • 238 days	• 20.08.2001 • 24.10.2001 • 26.10.2001 • OJ C 336, 30.11.2001, p. 13
• **Uprima** • **apomorphine** • **Part B**	• Abbott Laboratories	• G04BE • Treatment of erectile dysfunction	• 03.01.2000 • 25.01.2001 • 156 days • 227 days	• 01.03.2001 • 28.05.2001 • 30.05.2001 • OJ C 183, 26.06.2001, p. 7
• **Ixense** • **apomorphine** • **Part B**	• Takeda Europe R&D Centre Ltd	• G04BE • Treatment of erectile dysfunction	• 03.01.2000 • 25.01.2001 • 156 days • 227 days	• 01.03.2001 • 28.05.2001 • 30.05.2001 • OJ C 183, 26.06.2001, p. 7
• **HBVAXPRO** • **recombinant Hepatitis B virus small surface antigen (HbsAg)** • **Part A**	• Aventis Pharma S.A.	• J07BC01 • Active immunisation against hepatitis B virus infection caused by all known subtypes in children and adolescents	• 30.10.2000 • 25.01.2001 • 68 days • 17 days	• 05.03.2001 • 27.04.2001 • 04.05.2001 • OJ C 158, 31.05.2001, p. 2
• **Taluvian** • **apomorphine** • **Part B**	• Abbott S.p.A	• G04BE • Treatment of erectile dysfunction	• 31.10.2000 • 25.01.2001 • 60 days • 26 days	• 01.03.2001 • 28.05.2001 • 30.05.2001 • OJ C 183, 26.06.2001, p. 7
• **Nespo** • **darbepoetin alfa** • **Part A**	• Amgen Europe B.V.	• B03XA02 (temporary) • Treatment of anaemia associated with chronic renal failure	• 21.01.2000 • 01.03.2001 • 202 days • 199 days	• 21.03.2001 • 08.06.2001 • 11.06.2001 • OJ C 183, 26.06.2001, p. 7
• **Aranesp** • **darbepoetin alfa** • **Part A**	• Amgen Europe B.V.	• B03XA02 (temporary) • Treatment of anaemia associated with chronic renal failure	• 21.01.2000 • 01.03.2001 • 202 days • 199 days	• 21.03.2001 • 08.06.2001 • 11.06.2001 • OJ C 183, 26.06.2001, p. 7
• **Nonafact** • **human coagulation factor IX** • **Part A**	• Sanquin	• B02BD04 • Treatment and prophylaxis of bleeding in patients with haemophilia B	• 18.02.2000 • 01.03.2001 • 202 days • 171 days	• 03.04.2001 • 03.07.2001 • 05.07.2001 • OJ C 209, 27.07.2001, p. 6
• **Fabrazyme #** • **agalsidase beta** • **Part A**	• Genzyme B.V.	• A16AB04 (temporary) • Long-term replacement therapy in patients with a confirmed diagnosis of Fabry disease	• 18.07.2000 • 29.03.2001 • 187 days • 64 days	• 02.05.2001 • 03.08.2001 • 07.08.2001 • OJ C 243, 31.08.2001, p. 2
• **Ceprotin** • **protein C** • **Part A**	• Baxter AG	• B01AX • Indicated in purpura fulminans and coumarin induced skin necrosis in patients with severe congenital protein C deficiency	• 21.01.2000 • 29.03.2001 • 185 days • 243 days	• 03.05.2001 • 16.07.2001 • 17.07.2001 • OJ C 209, 27.07.2001, p. 6
• **INOmax** • **nitric oxide** • **Part B**	• AGA AB	• R07AX • Treatment of newborns with hypoxic respiratory failure	• 18.02.2000 • 29.03.2001 • 199 days • 202 days	• 11.05.2001 • 01.08.2001 • 06.08.2001 • OJ C 243, 31.08.2001, p. 2

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

Product • Brand name • INN • Part A/B	Marketing authorisation holder	Therapeutic area • ATC code • Indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **MabCampath** • **alemtuzumab** • **Part A**	• Millenium & Ilex UK Ltd	• L01XC • Second-line treatment of chronic lymphocytic leukaemia	• 14.04.2000 • 29.03.2001 • 203 days • 142 days	• 30.04.2001 • 06.07.2001 • 10.07.2001 • OJ C 209, 27.07.2001, p. 6
• **Ketek** • **telithromycin** • **Part B**	• Aventis Pharma S.A.	• J01 • Treatment of community-acquired pneumonia, acute exacerbation of chronic bronchitis, acute sinusitis and tonsillitis/pharyngitis	• 14.04.2000 • 29.03.2001 • 164 days • 181 days	• 02.05.2001 • 09.07.2001 • 10.07.2001 • OJ C 209, 27.07.2001, p. 6
• **Levviax** • **telithromycin** • **Part B**	• Aventis Pharma S.A.	• J01 • Treatment of community-acquired pneumonia, acute exacerbation of chronic bronchitis, acute sinusitis and tonsillitis/pharyngitis	• 14.04.2000 • 29.03.2001 • 164 days • 181 days	• 02.05.2001 • 09.07.2001 • 10.07.2001 • OJ C 209, 27.07.2001, p. 6
• **Depocyte** • **cytarabine** • **Part B**	• SkyePharma PLC	• L01BC01 • Intrathecal treatment of lymphomatous meningitis	• 21.10.1999 • 29.03.2001 • 176 days • 313 days	• 02.05.2001 • 11.07.2001 • 12.07.2001 • OJ C 209, 27.07.2001, p. 6
• **Replagal** # • **agalsidase alfa** • **Part A**	• TKT Europe-5S AB	• A16AB03 (temporary) • Long-term replacement therapy in patients with a confirmed diagnosis of Fabry disease	• 18.07.2000 • 29.03.2001 • 200 days • 49 days	• 02.05.2001 • 03.08.2001 • 07.08.2001 • OJ C 243, 31.08.2001, p. 2
• **Liprolog** • **insulin lispro** • **Part A**	• Eli Lilly Nederland B.V.	• A10AB04 • Diabetes mellitus	• 30.01.2001 • 25.04.2001 • 86 days • 0 days	• 07.06.2001 • 01.08.2001 • 03.08.2001 • OJ C 243, 31.08.2001, p. 2
• **Caspofungin MSD** • **caspofungin** • **Part B**	• Merck Sharp & Dohme	• J02AX04 • Secondline treatment of invasive aspergillosis	• 31.10.2000 • 26.07.2001 • 207 days • 59 days	• 20.08.2001 • 24.10.2001 • 25.10.2001 • OJ C 336, 30.11.2001, p. 13
• **Travatan** • **travoprost** • **Part B**	• Alcon Laboratories (UK) Ltd	• S01EX • Treatment of elevated intraocular pressure (second-line)	• 26.12.2000 • 26.07.2001 • 152 days • 58 days	• 22.08.2001 • 27.11.2001 • 29.11.2001 • OJ C 371, 28.12.2001, p. 8
• **Glivec** # • **imatinib mesilate** • **Part B**	• Novartis Europharm Ltd	• L01XX28 (temporary) • Treatment of patients with chronic myeloid leukemia (CML)	• 27.03.2001 • 26.07.2001 • 119 days • 0 days	• 23.08.2001 • 07.11.2001 • 12.11.2001 • OJ C 336, 30.11.2001, p. 13
• **Viread** • **tenofovir** • **Part B**	• Gilead Science International Ltd	• J05A • Treatment of HIV infected patients with early virological failure in combination with other anti HIV products	• 22.05.2001 • 18.10.2001 • 83 days • 63 days	• • • •
• **Protopy** • **tacrolimus** • **Part B**	• Fujisawa GmbH	• D11AX14 (temporary) • Treatment of moderate to severe atopic dermatitis	• 16.08.2000 • 18.10.2001 • 204 days • 218 days	• • • •
• **Trisenox** # • **arsenic trioxide** • **Part B**	• Cell Therapeutics (UK) Ltd	• L01XX27 (temporary) • Induction for induction of remission and consolidation in adult patients with relapsed/ refractory acute promyelocytic leukaemia (APL)	• 27.02.2001 • 18.10.2001 • 180 days • 51 days	• • • •

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

Product • Brand name • INN • Part A/B	Marketing authorisation holder	Therapeutic area • ATC code • Indication	EMEA/CPMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Protopic** • **tacrolimus** • **Part B**	• Fujisawa GmbH	• D11AX14 (temporary) • Treatment of moderate to severe atopic dermatitis	• 16.08.2000 • 18.10.2001 • 204 days • 218 days	• • • •
• **Kineret** • **anakinra** • **Part A**	• Amgen Europe	• L04AA14 • Treatment of the signs and symptoms of rheumatoid arthritis	• 18.07.2000 • 15.11.2001 • 204 days • 273 days	• • • •
• **Xapit** • **parecoxib** • **Part B**	• G D Searle & Co Ltd	• M01AH • For the short-term treatment of postoperative pain	• 31.10.2000 • 15.11.2001 • 204 days • 171 days	• • • •
• **Dynastat** • **parecoxib** • **Part B**	• G D Searle & Co Ltd	• M01AH • For the short-term treatment of postoperative pain	• 31.10.2000 • 15.11.2001 • 204 days • 171 days	• • • •
• **Rayzon** • **parecoxib** • **Part B**	• G D Searle & Co Ltd	• M01AH • For the short-term treatment of postoperative pain	• 31.10.2000 • 15.11.2001 • 204 days • 171 days	• • • •
• **Lumigan** • **bimatoprost** • **Part B**	• Allergan Sales Ltd	• S01EX • Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension	• 26.12.2000 • 15.11.2001 • 192 days • 127 days	• • • •
• **Arixtra** • **fondaparinux** • **Part B**	• Sanofi-Synthelabo	• B01AE • Prevention of venous thromboembolic events in patients undergoing major orthopaedic surgery	• 27.02.2001 • 13.12.2001 • 205 days • 78 days	• • • •
• **Quixidar** • **fondaparinux** • **Part B**	• NV Organon	• B01AE • Prevention of venous thromboembolic events in patients undergoing major orthopaedic surgery	• 27.02.2001 • 13.12.2001 • 205 Days • 78 Days	• • • •
• **Dynepo** • **epoetin delta** • **Part A**	• Aventis Pharma SA France	• B03XA • Treatment of anaemia in patients with chronic renal failure	• 26.09.2000 • 13.12.2001 • 206 Days • 238 days	• • • •
• **Vfend** • **Voriconazole** • **Part B**	• Pfizer Ltd	• J02AC • Antifungal agent	• 28.11.2000 • 13.12.2001 • 203 days • 169 days	• • • •

Annex 8

CVMP opinions in 2001 on medicinal products for veterinary use

Centralised applications

Product • Brand name • INN • Part A/B	Marketing authorisation holder	Therapeutic area • Target species • Indication	EMEA/CVMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision • Notification • Official Journal
• **Poulflox** • **difloxacin** • **Part B**	• Virbac	• Poultry • Antibacterial for systemic use	• 09.12.99 • 21.06.00 • 152 days • 43 days	• 21.07.00 • 16.11.00 • 20.11.00 • OJ C 2, 05.01.2001, p. 3
• **Porcilis AR-T DF** • **inactivated vaccine** • **Part A**	• Intervet International	• Pigs • Vaccine against atrophic rhinitis	• 12.01.99 • 19.07.00 • 204 days • 336 days	• 18.08.00 • 13.11.00 • 20.11.00 • OJ C 2, 05.01.2001, p. 3
• **Pruban** • **rescortol butyrate** • **Part B**	• Intervet International	• Dogs • Anti-inflammatory for cutaneous inflammatory disorders	• 15.09.98 • 19.07.00 • 196 days • 477 days	• 18.08.00 • 16.11.00 • 20.11.00 • OJ C 2, 05.01.2001, p. 3
• **Bayovac CSF Marker** • **live vaccine** • **Part A**	• Bayer	• Pigs • Marker vaccine against Classical Swine Fever	• 16.12.98 • 19.07.00 • 210 days • 309 days	• 29.11.00 • 02.02.01 • 06.02.01 • OJ C 53, 20.02.2001, p. 2
• **Pirsue** • **pirlimycin** • **Part B**	• Pharmacia Upjohn	• Dairy cattle • Clinical & sub-clinical mastitis	• 12.01.99 • 11.10.00 • 210 days • 428 days	• 10.11.00 • 29.01.01 • 31.01.01 • OJ C 53, 20.02.2001, p. 2
• **Zubrin** • **tepoxalin** • **Part B**	• Schering Plough	• Dogs • Treatment of pain & inflammation	• 18.05.99 • 08.11.00 • 210 days • 330 days	• 08.12.00 • 13.03.01 • 14.03.01 • OJ C 127, 27.04.2001, p. 2
• **Eurican Herpes 205** • **inactivated vaccine** • **Part B**	• Merial	• Dogs • Vaccine against canine herpes	• 13.07.99 • 08.11.00 • 209 days • 274 days	• 08.12.00 • 26.03.01 • 29.03.01 • OJ C 127, 27.04.2001, p. 2
• **Metacam** • **meloxicam** • **Part B extension**	• Boehringer Ingelheim	• Cattle • Diarrhoea/respiratory infections	• 14.09.99 • 10.01.01 • 184 days • 301 days	• 09.02.01 • 23.04.01 • 25.04.01 • OJ C 158, 31.05.2001, p. 2
• **Virbagen Omega** • **feline interferon** • **Part A**	• Virbac	• Dogs • To reduce mortality and clinical signs of canine parvovirosis	• 21.12.99 • 11.07.01 • 210 days • 358 days	• 10.08.01 • 06.11.01 • 08.11.01 • OJ C 336, 30.11.2001, p. 13
• **Eurifel RCP-FelV** • **vaccine** • **Part A**	• Merial	• Cats • Vaccine against feline rhinotracheitis, calcivirus, panleucopenia and leukaemiac	• 19.12.00 • 05.12.01 • 210 days • 141 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
• **Linear dodecyl benzene sulfonic acid**	• Bovine	• 22.01.99 • 19.07.00 • 195 days • 321 days	• 18.08.00 • 25.04.01 • OJ L118, 27.04.2001, p. 6
• **Phoxim (extension)**	• Ovine	• 19.01.00 • 19.07.00 • 120 days • 0	• 18.08.00 • 25.04.01 • OJ L118, 27.04.2001, p. 6
• **Florfenicol (extension)**	• Fish	• 29.01.96 • 11.11.00 • 212 days • 1504 days	• 08.11.00 • 29.06.01 • OJ L177, 30.06.2001, p. 52
• **Meloxicam (extension)**	• Porcine	• 07.09.00 • 06.12.00 • 90 days • 0	• 04.01.01 • 27.06.01 • OJ L175, 28.06.2001, p. 14
• **Tilmicosin (extension)**	• Turkeys	• 07.09.00 • 06.12.00 • 90 days • 0	• 04.01.01 • 27.06.01 • OJ L175, 28.06.2001, p. 14
• **Doramectin (extension)**	• Reindeer	• 11.12.97 • 10.01.01 • 203 days • 923 days	• 09.02.01 • 18.07.01 • OJ L195, 19.07.2001, p. 32
• **Rafoxanide**	• Bovine and ovine	• 11.02.97 • 10.01.01 • 193 days • 1236 days	• 09.02.01 • 18.07.01 • OJ L195, 19.07.2001, p. 32
• **Tiludronate**	• Equine	• 12.10.00 • 10.01.01 • 90 days • 0	• 09.02.01 • 18.07.01 • OJ L195, 19.07.2001, p. 32
• **Moxidectin (extension)**	• Bovine milk	• 09.10.00 • 14.02.01 • 90 days • 0	• 16.03.01 • 30.07.01 • OJ L205, 31.07.2001, p. 16
• **Tosychloramide sodium (extension)**	• Dairy cows	• 20.01.00 • 14.03.01 • 120 days • 298 days	• 06.04.01 • 22.08.01 • OJ L227, 23.08.2001, p. 33
• **Deltamethrin (extension)**	• Fin fish	• 09.11.99 • 13.06.01 • 177 days • 404 days	• 06.07.01 • 07.11.01 • OJ L291, 08.11.2001, p. 9
• **Bronopol (extension)**	• Salmonidae	• 15.03.01 • 13.06.01 • 90 days • 0	• 06.07.01 • 07.11.01 • OJ L291, 08.11.2001, p. 9

Annex 9

COMP opinions in 2001 on designation of orphan medicinal products

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **Xaliproden hydrochloride**	• Sanofi-Synthélabo	• Treatment of amyotrophic lateral sclerosis	• 07.08.2000 • 25.08.2000 • 21.11.2000 • 89 days	• 23.11.2000 • 17.01.2001
• **Arsenic trioxide**	• Pharmacie Centrale des Hôpitaux de Paris	• Treatment of acute promyelocytic leukaemia	• 08.08.2000 • 22.09.2000 • 21.11.2000 • 61 days	• 23.11.2000 • 17.01.2001
• **Lusupultide**	• Byk Gulden Lomberg Chemische Fabrik GmbH	• Treatment of acute respiratory distress syndrome	• 01.09.2000 • 22.09.2000 • 21.11.2000 • 61 days	• 23.11.2000 • 17.01.2001
• **L-Lysine-N-Acetyl-L-Cysteinate**	• SMB Technology S.A.	• Treatment of cystic fibrosis	• 09.08.2000 • 22.09.2000 • 19.12.2000 • 89 days	• 03.01.2001 • 14.02.2001
• **Ibuprofen**	• Orphan Europe Sarl	• Treatment of patent ductus arteriosus	• 02.05.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Recombinant human acid α-glucosidase**	• Genzyme B.V.	• Treatment of glycogen storage disease type II (Pompe's disease)	• 10.08.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Pegvisomant**	• Pharmacia Enterprises S.A	• Treatment of acromegaly	• 11.08.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Bosentan**	• Actelion Registration Ltd	• Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	• 21.08.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Ribavirin**	• ICN Pharmaceuticals Ltd	• Treatment of haemorrhagic fever with renal syndrome	• 06.09.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Laronidase**	• Genzyme B.V.	• Treatment of mucopolysaccharidosis type I	• 08.09.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Imatinib mesylate**	• Novartis Europharm Ltd	• Treatment of chronic myeloid leukaemia	• 03.10.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001

Product INN	Sponsor	Therapeutic area • ATC code • Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **N-acetylglactos amine-4-sulfatase**	• ClinTrials Research Ltd	• Mucopolysaccharidosis type VI (Maroteaux-Lamy Syndrome)	• 04.10.2000 • 19.10.2000 • 19.12.2000 • 62 days	• 03.01.2001 • 14.02.2001
• **Ibuprofen**	• Orphan Europe Sarl	• Prevention of patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age	• 02.05.2000 • 19.10.2000 • 15.01.2001 • 89 days	• 19.01.2001 • 05.03.2001
• **Inolimomab**	• Opi Orphan Pharma International	• Treatment of Graft versus Host disease	• 05.09.2000 • 19.10.2000 • 15.01.2001 • 89 days	• 18.01.2001 • 05.03.2001
• **Ribavirin**	• ICN Pharmaceuticals Ltd	• Treatment of adenovirus infection in immunocompromised patients	• 06.09.2000 • 19.10.2000 • 15.01.2001 • 89 days	• 18.01.2001 • 08.03.2001
• **Ranpirnase**	• Dr. Erika Morgenstern	• Treatment of malignant mesothelioma	• 20.10.2000 • 22.12.2000 • 09.02.2001 • 50 days	• 13.02.2001 • 29.03.2001
• **Gusperimus trihydrochloride**	• Euro Nippon Kayaku GmbH	• Treatment of Wegener's granulomatosis	• 27.10.2000 • 13.11.2000 • 09.02.2001 • 89 days	• 13.02.2001 • 29.03.2001
• **Arsenic trioxide**	• Cell Therapeutics (UK) Ltd	• Treatment of myelodysplastic syndromes	• 02.10.2000 • 22.12.2000 • 09.02.2001 • 50 days	• 13.02.2001 • 29.03.2001
• **Arsenic trioxide**	• Cell Therapeutics (UK) Ltd	• Treatment of multiple myeloma	• 02.10.2000 • 22.12.2000 • 09.02.2001 • 50 days	• 13.02.2001 • 29.03.2001
• **8-cyclopentyl-1,3-dipropyl xanthine**	• SciClone Pharmaceuticals Italy S.r.l.	• Treatment of Cystic fibrosis	• 07.12.2000 • 22.12.2000 • 09.02.2001 • 50 days	• 13.12.2001 • 29.03.2001
• **Levodopa and carbidopa (Gastroenteral Use)**	• NeoPharma Production AB	• Treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations and not responding to oral treatment	• 04.10.2000 • 22.12.2000 • 20.03.2001 • 89 days	• 26.03.2001 • 10.05.2001
• **Recombinant human C1-inhibitor**	• Pharming NV	• Treatment of angioedema caused by C1 inhibitor deficiency	• 09.10.2000 • 22.12.2000 • 20.03.2001 • 89 days	• 26.03.2001 • 11.05.2001
• **Anti-HM1.24 monoclonal antibody (AHM)**	• Chugai Pharma Europe Ltd	• Treatment of Multiple myeloma	• 08.02.2001 • 23.02.2001 • 20.03.2001 • 26 days	• 26.03.2001 • 10.05.2001

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **Fomepizole**	• Idis Ltd	• Treatment of methanol poisoning	• 15.12.2000 • 11.01.2001 • 10.04.2001 • 90 days	• 11.04.2001 • 30.05.2001
• **Human engineered monoclonal antibody specific for Transforming Growth Factor β2**	• Cambridge Antibody Technology Ltd	• Prevention of scarring in glaucoma filtration surgical procedures	• 18.12.2000 • 11.01.2001 • 10.04.2001 • 90 days	• 11.04.2001 • 30.05.2001
• **Retroviral γc cDNA containing vector**	• Génopoïétic S.A.	• Treatment of Severe Combined Immunodeficiency (SCID)-XI Disease	• 29.11.2000 • 23.02.2001 • 10.04.2001 • 47 days	• 11.04.2001 • 30.05.2001
• **Human Milk Fat Globule 1 / Human Milk Fat Globule 1-S-p-isothiocyanatobenzyl-diethylenetriaminepentaacetic acid for use with ^{90}Yttrium**	• Antisoma plc	• Treatment of ovarian cancer	• 04.12.2000 • 23.02.2001 • 10.04.2001 • 47 days	• 11.04.2001 • 30.05.2001
• **Ecteinascidin 743**	• Pharma Mar AS	• Treatment of soft tissue sarcoma	• 05.02.2001 • 23.02.2001 • 10.04.2001 • 47 days	• 11.04.2001 • 30.05.2001
• **Recombinant human alpha-1-antitrypsin (Respiratory Use)**	• Bayer AG	• Treatment of emphysema secondary to congenital alpha-1-antitrypsin deficiency	• 06.12.2000 • 23.02.2001 • 10.04.2001 • 47 days	• 11.04.2001 • 30.05.2001
• **Betaine anhydrous**	• Orphan Europe Sarl	• Treatment of homocystinuria	• 02.05.2000 • 15.03.2001 • 23.05.2001 • 70 days	• 28.05.2001 • 09.07.2001
• **Thalidomide**	• Laboratoires LAPHAL	• Treatment of multiple myeloma	• 01.06.2000 • 23.02.2001 • 23.05.2001 • 90 days	• 28.05.2001 • 09.07.2001
• **Thalidomide**	• Laboratoires LAPHAL	• Treatment of graft-versus-host disease	• 01.06.2000 • 23.02.2001 • 23.05.2001 • 90 days	• 28.05.2001 • 09.07.2001
• **Alpha$_1$-Proteinase Inhibitor (Respiratory use)**	• Aventis Behring GmbH	• Treatment of emphysema secondary to congenital alpha$_1$-antitrypsin deficieny	• 02.10.2000 • 15.03.2001 • 23.05.2001 • 70 days	• 28.05.2001 • 09.07.2001
• **Ziconotide (Intraspinal Use)**	• Elan Pharma International Ltd	• Treatment of chronic pain requiring intraspinal analgesia	• 04.12.2000 • 23.02.2001 • 23.05.2001 • 90 days	• 28.05.2001 • 09.07.2001
• **Ramoplanin**	• Biosearch Italia S.p.A	• Prevention of invasive infections due to Vancomycin resistant enterococci (VRE) in colonised patients deemed at risk of infection	• 10.08.2000 • 23.02.2001 • 23.05.2001 • 90 days	• 28.05.2001 • 09.07.2001

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **1,3-Propanedisulfonic acid, disodium salt (Fibrillex)**	• Quintiles Ltd	• Treatment of Systemic Secondary Amyloidosis	• 10.10.2000 • 13.11.2000 • 12.06.2001 • 116 days #	• 18.06.2001 • 31.07.2001
• **Seocalcitol**	• Leo Pharmaceutical Products	• Treatment of hepatocellular carcinoma	• 05.01.2001 • 20.04.2001 • 12.06.2001 • 54 days	• 18.06.2001 • 31.07.2001
• **Zinc acetate dihydrate**	• Orphan Europe Sarl	• Treatment of Wilson's disease	• 02.05.2000 • 20.04.2001 • 12.06.2001 • 54 days	• 18.06.2001 • 31.07.2001
• **Sinapultide, dipalmitoylphos-phatidylcholine, palmitoyl-oleoyl phosphatidylglyc-erol and palmitic acid (Surfaxin)**	• Discovery Laboratories, Inc	• Treatment of Meconium Aspiration Syndrome (MAS)	• 27.03.2001 • 20.04.2001 • 18.07.2001 • 90 days	• 25.07.2001 • 19.09.2001
• **Beraprost sodium**	• Aventis Pharma SA	• Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	• 21.05.2001 • 11.06.2001 • 18.07.2001 • 38 days	• 25.07.2001 • 18.09.2001
• **Cladribine**	• Lipomed GmbH	• Treatment of indolent non-Hodgkin lymphoma	• 01.03.2001 • 20.04.2001 • 18.07.2001 • 90 days	• 25.07.2001 • 18.09.2001
• **Recombinant human acid sphingomyelinase**	• Genzyme BV	• Treatment of Niemann-Pick disease, type B	• 26.02.2001 • 11.06.2001 • 18.07.2001 • 38 days	• 25.07.2001 • 19.09.2001
• **Repertaxin L-lysine salt**	• Dompé s.p.a.	• Prevention of delayed graft function in organ transplant	• 05.04.2001 • 20.04.2001 • 18.07.2001 • 90 days	• 25.07.2001 • 19.09.2001
• **Porcine lung surfactant**	• Leo Pharmaceutical Products	• Treatment of Acute Lung Injury	• 23.05.2001 • 11.06.2001 • 18.07.2001 • 38 days	• 25.07.2001 • 19.09.2001
• **Dexrazoxane**	• TopoTarget A/S	• Treatment of anthracycline extravasations	• 24.05.2001 • 11.06.2001 • 18.07.2001 • 38 days	• 25.07.2001 • 19.09.2001
• **Pemetrexed disodium**	• Eli Lilly Nederland B.V.	• Treatment of malignant mesothelioma	• 25.05.2001 • 11.06.2001 • 18.07.2001 • 54 days	• 25.07.2001 • 17.09.2001
• **Deoxyribose phosphorothioate (5'-tct-ccc-agc-gtg-cgc-cat-3')**	• Voisin Consulting SARL	• Treatment of chronic lymphocytic leukaemia	• 23.05.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001

Includes time for appeal

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **Idebenone**	• Laboratoires Takeda	• Treatment of Friedreich's ataxia	• 12.07.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001
• **Imatinib mesilate**	• Novartis Europharm Ltd	• Treatment of malignant gastrointestinal stromal tumours	• 13.07.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001
• **Celecoxib**	• Pharmacia-Pfizer EEIG	• Treatment of Familial Adenomatous Polyposis (FAP)	• 04.04.2001 • 11.06.2001 • 07.09.2001 • 89 days	• 17.09.2001 • 20.11.2001
• **Phenylephrine hydrochloride**	• S.L.A Pharma (UK) Ltd	• Treatment of ileal pouch anal anastomosis (IPAA) related faecal incontinence	• 29.09.2001 • 11.06.2001 • 07.09.2001 • 89 days	• 17.09.2001 • 20.11.2001
• **Thalidomide**	• Pharmion Ltd	• Treatment of multiple myeloma	• 13.07.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001
• **Thalidomide**	• Pharmion Ltd	• Treatment of erythema nodosum leprosum (ENL) or type II lepra reactions	• 13.07.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001
• **Abetimus sodium**	• ICON Clinical Research UK Ltd	• Treatment of lupus nephritis	• 25.05.2001 • 11.06.2001 • 07.09.2001 • 89 days	• 17.09.2001 • 20.11.2001
• **Deoxyribose phosphorothioate (5'-tct-ccc-agc-gtg-cgc-cat-3')**	• Voisin Consulting SARL	• Treatment of multiple myeloma	• 23.05.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 20.11.2001
• **Recombinant human monoclonal antibody to hsp90**	• NeuTec Pharma plc	• Treatment of invasive fungal infections	• 11.04.2001 • 11.06.2001 • 07.09.2001 • 89 days	• 17.09.2001 • 05.12.2001
• **Apomorphine**	• Orion Corporation	• Treatment of off-periods in Parkinson's disease not responding to other oral treatment	• 25.05.2001 • 11.06.2001 • 07.09.2001 • 89 days	• 17.09.2001 • 05.12.2001
• **Stiripentol**	• Laboratoires BIOCODEX	• Treatment of severe myoclonic epilepsy in infancy	• 04.06.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 05.12.2001
• **Halofuginone hydrobromide**	• PPD Global Ltd	• Treatment of systemic sclerosis	• 12.07.2001 • 30.07.2001 • 26.10.2001 • 89 days	• 05.11.2001 • 11.12.2001

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• **Denileukin diftitox (Onzar)**	• Ligand Pharmaceuticals	• Treatment of cutaneous T-cell Lymphoma	• 12.07.2001 • 30.07.2001 • 26.10.2001 • 89 days	• 05.11.2001 • 11.12.2001
• **Octovalent *Pseudomonas aeruginosa* O-polysaccharide-toxin A conjugate vaccine**	• Orphan Europe SARL	• Prevention of *Pseudomonas aeruginosa* infections in patients with cystic fibrosis	• 20.07.2001 • 24.08.2001 • 26.10.2001 • 64 days	• 05.11.2001 • 11.12.2001
• **gly^2-Recombinant human glucagon-like peptide**	• Pharm Research Associates (UK) Ltd	• Treatment of short bowel syndrome	• 09.08.2001 • 24.08.2001 • 26.10.2001 • 64 days	• 05.11.2001 • 11.12.2001
• **Iduronate-2-sulfatase**	• TKT UK Ltd	• Treatment of Mucopolysaccharidosis type II (Hunter Syndrome)	• 05.09.2001 • 20.09.2001 • 26.10.2001 • 37 days	• 05.11.2001 • 11.12.2001
• **Thalidomide**	• Kendle International Ltd	• Treatment of multiple myeloma	• 23.05.2001 • 30.07.2001 • 07.09.2001 • 40 days	• 17.09.2001 • 19.12.2001
• †	• †	• Treatment of acute lung injury	• 27.03.2001 • 24.08.2001 • 21.11.2001 • 90 days	• † • †
• †	• †	• Treatment of diarrhoea associated with intestinal microsporidial infection	• 29.05.2001 • 20.09.2001 • 21.11.2001 • 63 days	• † • †
• †	• †	• Treatment of acute lymphoblastic leukaemia	• 09.08.2001 • 24.08.2001 • 21.11.2001 • 90 days	• † • †
• †	• †	• Treatment of systemic sclerosis	• 28.08.2001 • 20.09.2001 • 21.11.2001 • 62 days	• † • †
• †	• †	• Treatment of high-grade glioma with subsequent use of ganciclovir sodium	• 04.09.2001 • 20.09.2001 • 21.11.2001 • 62 days	• † • †
• †	• †	• Treatment of myelodysplastic syndromes	• 05.09.2001 • 20.09.2001 • 21.11.2001 • 62 days	• † • †
• †	• †	• Treatment of glioma	• 12.10.2001 • 26.10.2001 • 18.12.2001 • 54 days	• † • †

† Awaiting adoption of European Commission decision

Product INN	Sponsor	Indication	EMEA/COMP • Validation • Opinion • Active time • Clock stop	European Commission • Opinion received • Date of decision
• †	• †	• Treatment of Pseudomonas aeruginosa lung infection (including colonisation) in cystic fibrosis	• 06.09.2001 • 26.10.2001 • 18.12.2001 • 54 days	• † • †
• †	• †	• Treatment of Familial Adenomatous Polyposis (FAP)	• 09.08.2001 • 26.10.2001 • 18.12.2001 • 54 days	• † • †
• †	• †	• Treatment of high-grade dysplasia in Barrett's Esophagus	• 11.10.2001 • 26.10.2001 • 18.12.2001 • 54 days	• † • †

† Awaiting adoption of European Commission decision

Annex 10

Guidelines and working documents in 2001

CPMP Biotechnology Working Party

Reference number	*Document title*	*Status*
CPMP/BWP/269/95 Rev. 3	Note for guidance on plasma-derived medicinal products	Released for consultation January 2001
CPMP/BWP/2490/00	Note for guidance on cell culture inactivated influenza vaccines – Annex to Note for guidance on harmonisation of requirements for influenza vaccines CPMP/BWP/214/96	Released for consultation January 2001
CPMP/BWP/3088/99	Note for guidance on the quality, pre-clinical and clinical aspects of gene transfer medicinal products	Adopted April 2001
EMEA/410/01 Rev. 1	Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products	Adopted by CPMP and CVMP May 2001
CPMP/BWP/3207/00	Note for guidance on comparability of medicinal products containing biotechnology-derived proteins as drug substance	Adopted September 2001

CPMP Blood and Plasma Working Group

Reference number	*Document title*	*Status*
EMEA/CPMP/BPWG/283/00	Note for Guidance on the clinical investigation of human normal immunoglobulin for subcutaneous and intramuscular use	Released for consultation March 2001
EMEA/CPMP/BPWG/1089/00	Note for guidance on the clinical investigation of plasma derived fibrin sealants	Released for consultation December 2001

CPMP Efficacy Working Party

Reference number	*Document title*	*Status*
EMEA/CPMP/EWP/552/95 rev. 1	Note for guidance on postmenopausal osteoporosis in women	Adopted January 2001
EMEA/CPMP/EWP/49/01	Concept paper on the development of an Appendix to the CPMP Note for guidance on the clinical investigation of medicinal products in the treatment of schizophrenia, on methodology of clinical trials concerning the development of depot preparations of approved medicinal products in schizophrenia	Adopted March 2001

Reference number	*Document title*	*Status*
EMEA/CPMP/EWP/18/01	Concept paper on the development of a CPMP Note for guidance on the clinical investigation of medicinal products for the treatment of urinary incontinence in women	Adopted March 2001
CPMP/EWP/567/98 rev. 1	Note for guidance on clinical investigation of medicinal products for the treatment and prevention of bipolar disorder	Adopted April 2001
CPMP/EWP/205/95 rev. 1	Note for guidance on evaluation of anticancer medicinal products in man	Adopted May 2001
EMEA/CPMP/EWP/1045/01	Concept paper on the revision of the CPMP/BWP Note for guidance (CPMP/BWP/214/96) on harmonisation of requirements for influenza vaccines	Adopted May 2001
EMEA/CPMP/EWP/967/01	Concept paper on the development of a CPMP Note for guidance on the evaluation of medicinal products indicated for thrombolysis in acute myocardial infarction	Adopted May 2001
EMEA/CPMP/EWP/512/01	Concept paper on the development of a CPMP Note for guidance on the evaluation of medicinal products for the treatment of dyslipoproteinaemia	Adopted May 2001
EMEA/CPMP/EWP/788/01	Concept paper on the development of a CPMP Note for Guidance on the evaluation of medicinal products for treatment of migraine	Adopted May 2001
EMEA/CPMP/EWP/2330/99	Points to consider on application with 1) meta-analyses and 2) one pivotal study	Adopted May 2001
EMEA/CPMP/EWP/2284/99	Points to consider on clinical investigation of medicinal products for the management of Crohn's disease	Adopted June 2001
EMEA/CPMP/EWP/PhVWP/1417/01	Joint PhVWP/EWP Concept paper on the development of a CPMP Note for guidance on the use of medicinal products during pregnancy: need for post-marketing data	Adopted June 2001
EMEA/CPMP/EWP/1343/01	Concept paper on the development of a CPMP Points to consider document on the evaluation of new anti-fungal agents for invasive fungal infections	Adopted July 2001
CPMP/EWP/QWP/1401/98 rev. 1	Note for guidance on the investigation of bioavailability and bioequivalence	Adopted July 2001
EMEA/CPMP/EWP/561/98	Note for guidance on clinical investigation of medicinal products for the treatment of multiple sclerosis	Adopted July 2001

Reference number	*Document title*	*Status*
EMEA/CPMP/EWP/1533/01	Concept paper on the development of an addendum on acute cardiac failure to the CPMP Note for guidance on clinical investigation of medicinal products in the treatment of acute cardiac failure	Adopted July 2001
EMEA/CPMP/EWP/560/98	Points to consider on Clinical investigation of medicinal products for the treatment of acute stroke	Adopted September 2001
EMEA/CPMP/EWP/2747/00	Note for guidance on co-ordinating investigator signature of clinical study reports	Adopted October 2001
EMEA/CPMP/EWP/2991/01 draft 2	Concept paper on the development of an addendum on the clinical requirements of modified release medicinal products submitted as a line-extension of an existing marketing authorisation to the CPMP Note for guidance on modified release oral and transdermal dosage forms: section II (pharmacokinetic and clinical evaluation) (CPMP/EWP/280/96)	Adopted November 2001
EMEA/CPMP/EWP/1119/98	Points to consider on the evaluation of diagnostic agents	Adopted November 2001
EMEA/CPMP/EWP/1776/99	Points to consider on missing data	Adopted November 2001
EMEA/CPMP/602/95 rev. 3	Points to consider on the assessment of anti-HIV medicinal products	Adopted December 2001
CPMP/EWP/1776/99 draft 5	Points to consider on missing data	Released for consultation January 2001
CPMP/EWP/908/99	Points to consider on multiplicity issues in clinical trials	Released for consultation July 2001
CPMP/EWP/2863/99	Points to consider on adjustment for baseline covariates	Released for consultation December 2001
CPMP/602/95 rev. 3	Points to consider on the assessment of anti-HIV medicinal products	Released for consultation May 2001
CPMP/EWP/518/97 rev. 1	Note for guidance on clinical investigation of medicinal products in the treatment of depression	Released for consultation April 2001
CPMP/EWP/1080/00	Note for guidance on clinical investigation of medicinal products in the treatment of diabetes mellitus	Released for consultation July 2001
CPMP/EWP/18/01	Note for guidance on the clinical investigation of medicinal products for the treatment of urinary incontinence in women	Released for consultation November 2001
CPMP/EWP/612/00 draft 7	Note for guidance on clinical investigation of medicinal products for treatment of pain	Released for consultation November 2001
CPMP/EWP/2922/00 draft 6	Note for guidance on the clinical investigation of medicinal products in the treatment of asthma	Released for consultation November 2001

CPMP Pharmacovigilance Working Party

Reference number	*Document title*	*Status*
CPMP/PhVWP/1618/01	Position paper on compliance with pharmacovigilance regulatory obligations	Adopted November 2001
CPMP/EWP/PhVWP/1417/01	Concept paper on the development of a CPMP Note for guidance on the use of medicinal products during pregnancy: Need for post-marketing data	Adopted June 2001
CPMP/SWP/373/01	Concept paper on the development of a CPMP Note for guidance on risk assessment of medicinal products on human reproductive and development toxicities: From data to labelling	Adopted June 2001
CPMP/PhVWP/175/95	Note for guidance on the procedure for competent authorities on the undertaking of pharmacovigilance activities	Published by the European Commission in December 2001 in volume 9 of the 2001 edition of the Rules governing medicinal products in the European Union
CPMP/183/97	Note for guidance on the conduct of pharmacovigilance for centrally authorised products	Published by the European Commission in December 2001 in volume 9 of the 2001 edition of the Rules governing medicinal products in the European Union
CPMP/PhVWP/108/99	Notice to marketing authorisation holders - pharmacovigilance guidlines	Published by the European Commission in December 2001 in volume 9 of the 2001 edition of the Rules governing medicinal products in the European Union

CPMP Safety Working Party

Reference number	*Document title*	*Status*
CPMP/SWP/2145/00	Update of Note for guidance on non-clinical local tolerance testing of medicinal products	Adopted March 2001
CPMP/SWP/372/01	Points to consider document on the non-clinical assessment of the carcinogenic potential of insulin analogues	Adopted November 2001
CPMP/SWP/2877/00	Update of Note for guidance on carcinogenic potential	Released for consultation January 2001
CPMP/SWP/4447/00	Discussion paper on environmental risk assessments for pharmaceuticals	Released for consultation January 2001
CPMP/SWP/446/00	Note for guidance on specification limits for residues of heavy metal catalysts in medicinal products	Released for consultation January 2001

Reference number	*Document title*	*Status*
CPMP/SWP/398/01	Note for guidance on photosafety testing	Released for consultation March 2001
CPMP/SWP/2600/01	Points to consider document on the need for reproduction studies in the development of insulin analogues	Released for consultation September 2001

EMEA Herbal Medicinal Products Working Party

Reference number	*Document title*	*Status*
EMEA/18123/00	Compilation of general quality questions answered by the Herbal Medicinal Products Working Party	Endorsed in March 2001
EMEA/HMPWP/31/99 Rev 1	Points to consider on good agricultural and collection practice for starting materials of herbal origin	Released for consultation July 2001

CVMP Efficacy Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/016/00	Conduct of bioequivalance studies for veterinary medicinal products	Adopted January 2001
EMEA/CVMP/005/00 Rev 1	Testing and evaluation of the efficacy of antiparasitic substances for the treatment of tick and flea infestations in dogs and cats	Adopted February 2001
CVMP/VICH/833/99	Efficacy of anthelmintics: Specific recommendations for equines	Adopted July 2001
CVMP/VICH/834/99	Efficacy of anthelmintics: Specific requirements for porcines	Adopted July 2001
CVMP/VICH/835/99	Efficacy of anthelmintics: Specific requirements for canines	Adopted July 2001
CVMP/VICH/545/00	Efficacy of anthelmintics: Specific requirements for feline	Adopted July 2001
CVMP/VICH/546/00	Efficacy of anthelmintics: Specific requirements for poultry	Adopted July 2001
EMEA/CVMP/237/01	Conduct of efficacy studies for non-steroidal anti-inflammatory drugs	Adopted December 2001
EMEA/CVMP/816/00	Statistical principles for veterinary clinical trials	Adopted December 2001

Reference number	*Document title*	*Status*
EMEA/CVMP/237/01	Conduct of efficacy studies for non-steroidal anti-inflammatory drugs	Released for consultation March 2001
EMEA/CVMP/411/01	Efficacy testing of ectoparasiticides for cattle, sheep and goats	Released for consultation May 2001
EMEA/CVMP/627/01	Revised guideline: Antimicrobials for general veterinary use	Released for consultation October 2001
EMEA/CVMP/612/01	SPC for antimicrobial products	Released for consultation October 2001

CVMP Immunologicals Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/852/99	Field trials with veterinary vaccines	Adopted October 2001
EMEA/CVMP/743/00	Requirements and controls applied to bovine serum used in the production of immunological veterinary medicinal products	Adopted October 2001
EMEA/CVMP/743/00	Requirements and controls applied to bovine serum used in the production of immunological veterinary medicinal products	Released for consultation February 2001
CVMP/VICH/095/01	Biologicals: Testing of residual formaldehyde	Released for consultation February 2001
CVMP/VICH/096/01	Biologicals: Testing of residual moisture	Released for consultation July 2001

CVMP Pharmacovigilance Working Party

Reference number	*Document title*	*Status*
CVMP/VICH/646/01	Pharmacovigilance of veterinary medicinal products: Management of periodic summary update reports (PSUs)	Released for consultation July 2001
CVMP/VICH/647/01	Pharmacovigilance of veterinary medicinal products: Controlled list of terms	Released for consultation July 2001
EMEA/CVMP/695/01	Processing of renewals in the centralised procedure	Released for consultation October 2001

CVMP Safety Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/187/00	Risk analysis approach for residues of veterinary medicinal products in food of animal origin	Adopted January 2001
EMEA/410/01	Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products	Adopted February 2001
CVMP/VICH/525/00	Safety studies for veterinary drug residues in human food: Reproduction studies	Adopted July 2001
CVMP/VICH/526/00	Safety studies for veterinary drug residues in human food: Genotoxicity studies	Adopted July 2001
EMEA/CVMP/234/01	Safety evaluation of antimicrobial substances regarding the effects on human gut flora	Released for consultation April 2001
CVMP/VICH/644/01	Guidance on pre-approval information for registration of new veterinary medicinal products for food producing animals with respect to antimicrobial resistance	Released for consultation July 2001
CVMP/VICH/645/01	Studies to evaluate the safety of residues of veterinary drugs in human food: Carcinogenicity testing	Released for consultation July 2001
EMEA/CVMP/244/01	Pre-authorisation studies to assess the potential for resistance resulting from the use of antimicrobial veterinary medicinal products	Released for consultation October 2001

Joint CPMP/CVMP Quality Working Party

Reference number	*Document title*	*Status*
EMEA/CVMP/598/99	Process validation	Adopted February 2001
EMEA/CVMP/271/01	Limitations to the use of ethylene oxide in the manufacture of medicinal products	Adopted April 2001
EMEA/CVMP/453/01	Start of shelf-life of the finished dosage form	Adopted May 2001
EMEA/CVMP/814/00	Quality of herbal medicinal products	Adopted July 2001
EMEA/CVMP/815/00	Specifications: Test procedures and acceptance criteria for herbal drugs, herbal drug preparations and herbal medicinal products	Adopted July 2001
EMEA/CVMP/115/01	Quality of water for pharmaceutical use	Adopted November 2001

Reference number	*Document title*	*Status*
EMEA/CVMP/115/01	Quality of water for pharmaceutical use	Released for consultation February 2001
EMEA/CVMP/424/01	In-use stability testing of veterinary medicinal products	Released for consultation May 2001
EMEA/CVMP/961/01	Use of near infra-red spectroscopy by the pharmaceutical industry and the data to be forwarded in part II of the dossier for a marketing authorisation	Released for consultation November 2001

Committee for Orphan Medicinal Products

Reference number	*Document title*	*Status*
EMEA/14220/00	Procedure for orphan medicinal product designation - general principles	Revised January 2001
EMEA/2677/01	Procedure for a sponsor to appeal a negative COMP opinion	Finalised February 2001
EMEA/189/01	Guideline on the format and content of annual reports	Released for consultation September 2001
EMEA/436/01	Points to consider on the calculation and reporting of prevalence of a condition for orphan designation	Released for consultation November 2001

Annex 11

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:

Noël WATHION
Direct telephone (44-20) 74 18 85 92
E-mail: noel.wathion@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:

Francisco PEÑARANDA FERNANDEZ
Fax number for defective product rapid alerts:
(44-20) 74 18 85 90
E-mail: francisco.penaranda@emea.eu.int

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:

Subscription Service
European Agency for the Evaluation of Medicinal Products
7 Westferry Circus
Canary Wharf
UK - London E14 4HB

A subscription service is available for all EMEA public documents, distributing documents electronically or in paper form.

Further information can be obtained from the above address or from:

Iro MAVROPOULOS
Direct telephone (44-20) 74 18 85 82
E-mail: subscriptions@emea.eu.int

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

The list of European experts is available for examination on request at the EMEA offices. Requests may be made either in writing to the EMEA or sent to the following e-mail addresses:

Human medicines' experts list: **human_experts@emea.eu.int**

Veterinary medicines' experts list: **vet_experts@emea.eu.int**

Inspectors' experts list: **inspectors_experts@emea.eu.int**

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