

**THE EUROPEAN AGENCY  
FOR THE EVALUATION OF  
MEDICINAL PRODUCTS**

**THIRD  
GENERAL  
REPORT**

**1997**

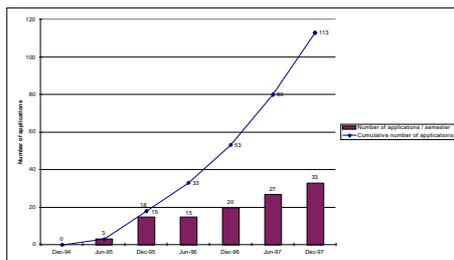
## EMEA mission statement

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

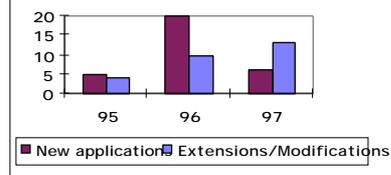
- mobilising scientific resources from throughout the European Union to provide high quality evaluation of medicinal products, to advise on research and development programmes and to provide useful and clear information to users and health professionals,
- developing efficient and transparent procedures to allow timely access by users to innovative medicines through a single European marketing authorisation,
- controlling the safety of medicines for humans and animals, particularly through a pharmacovigilance network and the establishment of safe limits for residues in food-producing animals.

## EMEA performance indicators

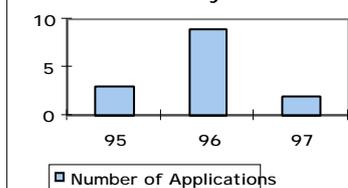
**Total Number of Human Applications received 1995-1997**



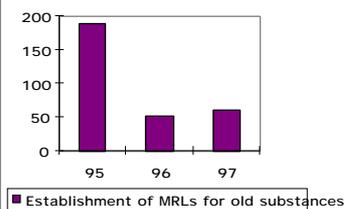
**New MRL applications**



**Centralised Procedures for Veterinary Products**



**Establishment of Old MRLs**



**THIRD GENERAL REPORT  
ON THE ACTIVITIES OF THE EUROPEAN  
AGENCY FOR THE EVALUATION OF  
MEDICINAL PRODUCTS**

**1997**

*Adopted by the Management Board on 3 December 1997*

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## FOREWORD

by  
**Strachan Heppell**  
Chairman of the Management Board

*{Graphic: Photo  
of Strachan  
Heppell}*

1997 has been the last year of the three-year transition from the pre-1995 national system of approval for new medicines to the new European system. As from the beginning of 1998, all new medicines will have to be evaluated under the new European system, except where a medicine is only to be marketed in a single Member State.

If the new system has started well, and I am glad to say that is a widely held view, the credit should be shared by all those who have made a substantive contribution. This includes not just the EMEA and the national authorities but the many national experts, the regulatory affairs staff in pharmaceutical companies and the European institutions, especially the European Commission.

But a good start is no more than that. What is important for the future is to have in place mechanisms to ensure that performance continues to improve. Such mechanisms are particularly important for an independent and free-standing regulatory authority like the EMEA.

The key to securing high quality performance lies in proper accountability. To achieve such accountability, any organisation needs to set clear and realistic performance targets and then measure whether those targets are met. Alongside that, the organisation needs to be open and transparent about its decisions and about the outcome of its performance measurement.

From the start the Management Board has laid great emphasis on the Agency's accountability and transparency. We have made good progress on both fronts in 1997, as the Executive Director explains in his report. We must build on this in the years to come.

# INTRODUCTION

by  
**Fernand Sauer**  
Executive Director

*{Graphic: Photo  
of Fernand  
Sauer}*

## Increasing skills and building for the future

During 1997 the EMEA has made particular effort to:

- re-evaluate the real needs and workload of the European approval system, measuring performance and the costs of the centralised system;
- consolidate on experience by re-designing procedures and their documentation, reinforcing technical support and improving transparency at all levels;
- improve the provision of scientific advice to companies, optimising management of human and financial resources and implement an IT platform fully compatible with EMEA partners.

At the end of the three-year transition period, I am proud to see that the EMEA is now firmly established and recognised as a major partner in the international regulatory system, due to the joint efforts of the different components of the EMEA: Management Board, scientific committees, working parties and staff.

The achievements of the European authorisation system and of the EMEA described in this Annual Report are also a direct result of the commitment of our many partners. The national competent authorities have responded positively to the increasing demands placed on them. Equally, the European Parliament and Commission have continued to support the work of the EMEA; in particular the Commission has identified the possibility for reducing the time required for the granting of Community marketing authorisations.

The continuing commitment of EMEA staff must receive special recognition. I take this opportunity to thank both the staff who have worked so hard since the beginning of the Agency and newer staff who have adapted quickly during such a fast moving year.

One of the key challenges continues to be the multicultural aspects of the work of the EMEA, in particular the quality of information given to users of medicinal products.

A second challenge is the consolidation of achievements to date. Many members of staff have participated in the quality management system project begun in April 1997 and this involvement will be extended to all staff and aspects of EMEA functions during 1998.



# 1. EMEA IN 1997

## END OF THE TRANSITION PERIOD

This Annual Report is presented by the Executive Director in accordance with Article 55(3) of Council Regulation (EEC) No 2309/93 of 22 July 1993 (OJ L 214, 24.8.1993, p.1).

The first two years of activities are described in the 1995 and 1996 Annual Reports of the EMEA (published by the Office for Official Publications of the European Communities, ISBN 92-827-7491-0 and 92-9155-002-7).

This annual report covers activities of the EMEA in 1997. This Chapter sets out the activities of the Management Board and the Agency's partnership with national competent authorities. General activities of the EMEA are described in Chapter 2, including performance indicators, transparency and international activities.

The operational and technical work of the EMEA in 1997 are reported in Chapter 3 on human medicines, Chapter 4 on veterinary medicines and Chapter 5 on technical co-ordination, including the work of the European Technical Office for Medicinal Products (ETOMEP). Administration and budget matters are described in Chapter 6.

The report, in accordance with Article 15c(1) of Council Directive 75/319/EEC, as amended, and Article 23c(1) of Council Directive 81/851/EEC, as amended, also summarises the operation of the decentralised procedure during 1997.

### 1.1 Overview of the EMEA

Since 1995 the new European system for the authorisation of medicinal products for human and veterinary use has made considerable progress. Designed to promote both public health and the free circulation of pharmaceuticals, access to the European market is facilitated for new and better medicines – benefiting users and European pharmaceutical research. In the case of veterinary medicinal products, animal health is protected and consumer health is promoted through the fixing of maximum residue limits in food-producing animals.

The new European system is based on co-operation between the national competent authorities of the Member States and the EMEA. The EMEA acts as the focal point of the new system, co-ordinating the scientific resources made available by Member State national authorities, including a network of 2 112 European experts.

### 1.1 Overview of the EMEA

### 1.2 The Management Board in 1997

### 1.3 Scientific resources at the disposal of the EMEA

Picture "Building EMEA"

Based in London, the EMEA is located in Canary Wharf, midway between the City of London and City Airport. The Agency occupies three floors of 7 Westferry Circus, covering an area of about 6 500 m<sup>2</sup>, including three conference rooms with interpretation and facilities for national delegates attending meetings.

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The new European system offers two routes for authorisation of medicinal products:

- a centralised procedure, with applications made directly to the EMEA leading to the granting of a European marketing authorisation by the Commission. Use of this procedure is compulsory for products derived from biotechnology, and optional for other innovative medicinal products.
- a decentralised procedure, which is applicable to the majority of conventional medicinal products. Applications are made to the Member States selected by the applicant and the procedure operates by mutual recognition of national marketing authorisations. Where this is not possible, the EMEA is called on to prepare a binding arbitration.

Purely national authorisations are still available for medicinal products to be marketed in one Member State.

## 1.2 The Management Board in 1997

### *Meetings of the Management Board*

The second mandate of the Management Board began in 1997, with some new members joining the Board. Mr Strachan Heppell and Dr Romano Marabelli were unanimously re-elected Chairman and Vice-Chairman for their second term of office. Membership of the Board in 1997 is given in Annex 1.

The Board met four times in 1997 on 5 February, 4 June, 1 October and 3 December. Part of the June meeting was given over to a brainstorming session which examined the regulatory challenges facing the EMEA for the millennium for both human and veterinary medicines. The Board also looked at the role of the EMEA in supporting the international relations of the EU, the identification and management of regulatory costs, and also at the role of information technology and quality standards in modern regulatory management.

Other subjects considered by the Management Board in 1997 include the EMEA information technology platform, paediatric clinical trials and the creation of new advisory scientific committees by the European Commission. The Board also noted the Joint Action adopted by the EU Council of Ministers on 16 June 1997 on risk assessment of new synthetic drugs (OJ L 167, 26.6.1997).

## *Work priorities*

One of the first matters addressed by the Board was the adoption at its February meeting of a work programme for 1997-98, setting out nine overall priorities for the EMEA and specific activities of the Units and Sectors (published by the Office for Official Publications of the European Communities, ISBN 92-9155-006-X).

### ***EMEA work priorities in 1997-1998***

1. centralised applications for marketing authorisations for medicinal products
2. maintenance and pharmacovigilance activities
3. establishment of maximum residue limits for substances in veterinary medicinal products
4. arbitrations and other Community referral procedures
5. scientific advice to future applicants and the EU institutions
6. information to health care professionals and public
7. technical support to international harmonisation initiatives (ICH, VICH, etc.)
8. support for the mutual recognition national authorisations, as requested
9. support for certain European policies at the request of the Commission or European Parliament

## *Budgetary decisions*

Following the opinion of the EU Court of Auditors, the Board adopted a decision at its February meeting granting discharge to the Executive Director for the execution of the 1994 and 1995 budgets. The Board also granted discharge to the EMEA accounting officers for the 1994 and 1995 budgets on 1 October 1997.

The Board granted discharge to the Executive Director and the accounting officer for execution of the 1996 budget at its meeting of 3 December 1997 further to the opinion of the EU Court of Auditors.

The initial draft budget for 1997 of ECU 28.2 million was adopted on 4 December 1996. A number of internal budgetary transfers of appropriations were adopted by the Board during the year. A supplementary and amending budget was adopted by the Board at its meeting of 3 December to ECU 28.53 million, reflecting additional income.

Budget summaries for 1995 to 1997 are presented in Annex 6.

A carry-forward from the 1996 budget to 1997 of ECU 1.62 million was approved by the Board at its February meeting. This in particular allowed an increase in the fund for orphan medicinal products to ECU 800 000 for 1997 and also reinforced investment in information technology amounting to a total of ECU 1.1 million.

The Board adopted the preliminary draft budget of ECU 33.9 million for 1998

*Picture "Management Board"*

at its meeting in February 1997, with a request for contribution of ECU 14 million. The EU budgetary authorities finally reduced this contribution to ECU 12 million. This led the Management Board to adjust the 1998 budget at its December meeting to ECU 31.9 million.

### *EMEA financial control*

During 1997 the work of the EMEA Financial Controller focused on consolidation of financial procedures and structures. The Financial Controller also contributed to the costing and analytical accounting exercise, and the implementation of the future computer budget and accounting system.

Considerable improvement was seen throughout the year in the quality of transactions presented to Financial Control for approval. At the beginning of the year, almost 10 per cent of transactions had to be revised for procedural or, in a small number of cases, material errors before being executed. This fell to 3 per cent by the end of the year.

The internal target of dealing with 85 per cent of routine transactions within one day was attained and surpassed within the first quarter of the year. The secondary target of dealing with 100 per cent of routine transactions within 5 days was respected in 1997.

The EMEA Financial Controller, Birgit Snoeren, left the Agency midway through 1997. The Management Board appointed Claus Christiansen as interim financial controller at its June meeting.

At the request of the European Parliament, the Commission brought forward proposals (OJ C 335, 6.11.1997) which would transfer the financial control responsibilities of all recently created decentralised EU bodies to the Commission – including that of the EMEA. A presentation of the Commission's proposal concerning arrangements for the EMEA was made by the European Commission Financial Controller at the 1 October meeting of the Management Board.

Close contacts were maintained with the European Commission during 1997 to ensure smooth transition of financial control in 1998.

## **1.3 Scientific resources at the disposal of the EMEA**

*Picture "EWP"*

The Committee for Proprietary Medicinal Products (CPMP) and Committee for Veterinary Medicinal Products (CVMP) are made up of 30 members each. Members were nominated by Member States in 1995 for a term of three years, chosen by reason of their role and expertise in the evaluation of medicinal products. Membership of the CPMP and CVMP is given in Annexes 2 and 3.

When acting as members of the scientific committees they act independently of their nominating authority. Their independence is similarly guaranteed by a publicly available declaration of interests and curriculum vitae.

## *European experts*

European experts continue to be an important part of the contribution of national competent authorities to the operation of the centralised procedure. The partnership between the EMEA and national competent authorities is a vital part of the functioning of the centralised procedure. These contributions extend beyond acting as rapporteur, co-rapporteur or provision of inspection service for individual applications, work for which national authorities receive partial compensation.

Participation in the work of the scientific committees and their working parties represents a significant workload for all national competent authorities. No compensation is made for this aspect of Member State participation in the work of the EMEA. This contribution has been of special importance in 1997 given additional support work to mutual recognition and international harmonisation work, involving in particular the Biotechnology, Efficacy, Pharmacovigilance, Quality and Safety Working Parties.

The EMEA list of European experts was updated continuously during 1997. There was a total of 2 112 at the end of 1997, most of whom also work for the national agencies and are made available to the EMEA. The list contains 1 659 experts in the field of human medicines and 453 for veterinary medicinal products.

These experts participate not only in the evaluation teams which support the work of rapporteurs and co-rapporteurs, but also participate in CPMP and CVMP working parties and the activities of the International Conferences for Harmonisation (ICH and VICH).

The full list of European experts, together with their declarations of interests, was constantly updated during 1997 and is available to the public at the EMEA.

## *Partnership agreement with national competent authorities*

A formal basis for this relationship was agreed at the end of 1996 and finalised at the beginning of 1997 in the form of a partnership agreement. Implementation of this formal agreement began in March 1997 with the conclusion between national competent authorities and the EMEA of contracts for the provision of evaluation and inspection services (Statement of principles governing the partnership between the national competent authorities and the EMEA; EMEA/MB/013/97).

The contracts set out the responsibilities and positions of parties, and provide a guarantee of quality of rapporteur and inspection assessment reports.

Contact addresses of the national competent authorities are given in Annex 4.

### *Summary of standard contract:*

- Conditions for provision of assessment and inspection reports (time limits and quality of report)
- Obligations on national competent authority to provide necessary resources for drawing up of the assessment report
- Guarantee of independence of rapporteurs, experts and inspectors
- Obligations of confidentiality
- Compensation of national competent authorities for resources made available to EMEA
- Dispute settlement

### *The costing exercise and preparation for fee reform*

Based on the results of a costing exercise carried out at the request of the European Commission during 1996, the Board finalised its position at its February meeting on the reform of fees payable by industry to the EMEA (EMEA/MB/057/96.Public). This was forwarded to the Commission as a contribution to the preparation of a proposal for a new Council Regulation on fees.

The report in particular highlights the contributions made by Member State national authorities to the operation of the centralised procedure. For example, for 1997 the report estimated the resource requirements for work in the veterinary medicines sector at 584 working days or about 2.75 full-time equivalent people. For the human medicines sector the estimated contribution rises to 1 092 working days, approximately 5 full-time equivalent people.

## 2. GENERAL ACTIVITIES OF THE EMEA

### 2.1 Transparency and public access

A major consultation exercise was carried out in the first half of 1997 on transparency and access to documents of the EMEA. This consultation took place in the joint context of the Management Board review of relations with interested parties and also the recommendations adopted by the European Ombudsman relating to rules on access to documents of all EU institutions and decentralised bodies.

Provisional rules on access to documents of the EMEA were adopted on 30 April 1997 and were distributed with a consultation paper to some 100 interested parties and dissemination points. The paper was also made available on the Internet.

Responses to the consultation paper and the rules on access to documents formed the basis for a workshop on transparency and access to documents of the EMEA held on 30 October 1997.

The meeting was a first opportunity for a number of national competent authorities and representatives from a wide range of consumer, patient, pharmaceutical industry and media groups to discuss issues of transparency. Representatives of the European Ombudsman, European Parliament and US Food and Drug Administration, together with the Nordic Council on Medicines, also participated at this workshop.

On the basis of a report from Professor Henschler, rapporteur for the transparency workshop, the Management Board confirmed the Decision on rules on access to documents of the EMEA and requested the Executive Director to continue to explore with the CPMP and CVMP, further initiatives towards greater transparency in the operations of the EMEA.

### 2.2 Performance and quality management initiatives

#### *EMEA performance*

As part of the performance indicators initiative taken by the Management Board at the end of 1996, the Executive Director set a number of goals and targets for the EMEA for 1997 (EMEA/MB/062/96).

**2.1 Transparency and public access**

**2.2 Performance and quality management initiatives**

**2.3 Contacts with European institutions and interested parties**

**2.4 International relations**

Standards of service:  
publication of improved tables,  
timely publication of EPARs and  
MRL assessment reports,  
EFPIA/EMEA questionnaire

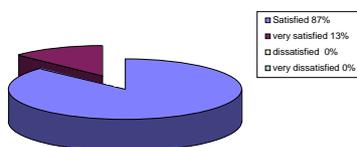
Efficiency and costs: costing  
exercise in fee report, ActiTrak

Improving the quality of the  
system: ATS, QMS, good  
financial standards

#### a. Standards of service

- Improved tables summarising marketing authorisations granted under the centralised procedure were constantly updated and published every month in 1997. These tables outline the time taken for both the EMEA evaluation and Commission decision-taking (see Annexes 7 and 8).
- European public assessment reports (EPARs) continued to be published in a timely manner in 1997, including being made available on the EMEA Internet web site.
- In addition to EPARs for medicinal products, summary assessment reports for maximum residue limits (MRLs) for substances used in veterinary medicines continued to be made available. Some 322 MRL summary reports for old and new veterinary substances were completed by the end of 1997.
- Another important initiative was the creation of a dedicated service within the EMEA to deal with the dissemination of information and publications. A document subscription service was also launched.
- A questionnaire jointly prepared by EMEA and the European Federation of Pharmaceutical Industries' Associations (EFPIA) was finalised at the beginning of 1997. It was distributed to all applicants for and holders of Community marketing authorisations during the course of the year. Recipients were asked to assess the performance of the rapporteurs, CPMP and EMEA secretariat at each stage of the centralised procedure.

EMEA/EFPIA Survey on the Centralised Procedure  
Degree of Satisfaction of Rapporteurs/Co-Rapporteurs



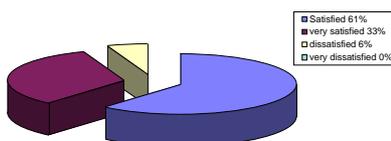
The questionnaire covered new applications for the period June 1995 to September 1997. A preliminary assessment of results was carried out on 15 May 1997, followed by presentation of the full results at an Info-Day jointly organised by the EMEA and EFPIA on 23 October 1997.

The overall findings were positive, with a high level of satisfaction of all parties involved in procedures dealt with by the CPMP. Some specific areas for improvements were identified by the questionnaire, including preparation by companies for oral hearings, quality of translations as well as the mechanism for their submission and assessment, and clarification on how questions from the CPMP are dealt with by companies.

#### b. Efficiency and costs

- The survey of costs of the EMEA Secretariat and national competent authorities continued in 1997. As part of the attempt to identify and understand the regulatory costs of the centralised system better, alternative analytical costing methods were applied to Secretariat costs (EMEA/MB/002/97).
- Development progressed during 1997 on a time recording system (ActiTrak) for the EMEA Secretariat. Its implementation was however delayed by the change of the IT platform which was completed at the end of the year.
- Work also continued in 1997 on the development of a computerised accounting and budgetary system. Co-developed with other EU decentralised bodies, the system is expected to be operational in 1998.

EMEA/EFPIA Survey on the Centralised Procedure  
Degree of Satisfaction of Applicants



### *c. Improving the quality of the system*

- The joint development of an application tracking system (ATS) progressed well in 1997. Aimed at integrating IT into EMEA daily activities, the system has been tested in 1997 and is expected to be fully operational in 1998.
- The EMEA Financial Regulation (EMEA/MB/011/97) was amended on 5 February 1997 as part of the harmonisation of financial standards of all decentralised EU bodies. Implementing rules were similarly adopted to ensure transparency and uniformity of application of the Financial Regulation (EMEA/MB/012/97).
- A quality management system was launched in the EMEA in April 1997. It is composed of training and management improvement initiatives. Building on the findings of two groups - Culture Team and Process Team - nine improvement teams were set up to look at the key processes and functions of the EMEA:
  - Strategic business planning
  - Information management
  - Scientific opinions
  - Quality product information
  - EMEA quality manual and internal audits
  - Scorecards
  - Europartnership
  - Training and appraisals
  - Implementation of management actions

## **2.3 Contacts with European institutions and interested parties**

The primary institutional partner of the EMEA is the European Commission, in particular Directorates-General III (Industry), VI (Agriculture), XII (Science, research and development), XXIV (Consumer policy and consumer health protection) and the Joint Research Centre.

During 1997, the EMEA participated in all meetings of the Commission's Pharmaceutical Committees for human and veterinary medicines, together with the working groups established by the Pharmaceutical Committees. These committees and working groups are managed by Directorate-General III. To facilitate contacts with the Commission, increasing use was made in 1997 of video-conferencing facilities.

In the light of the creation of new scientific committees under the management of Directorate-General XXIV, contacts have been established in order to prevent possible overlap of activities with those of the EMEA scientific committees.

The EMEA continued its contacts with the European Parliament, in particular with the Committee on Environment, consumer protection and public health, and also the Committee on Budgets. Members of Parliament attended various meetings during 1997 and a special meeting was held at the EMEA in November with representatives of the Environment Committee, led by Mr Ken Collins, MEP. EMEA representatives also attended meetings of the

informal European Parliament Intergroup on pharmaceuticals, chaired by Professor Umberto Scapagnini, MEP.

The EMEA participated in the work of the European Pharmacopoeia through meetings in Strasbourg as part of the EU delegation. The European Pharmacopoeia Secretariat also regularly attended meetings of EMEA working parties as observers. A procedure for the sampling and testing of products covered by the centralised authorisation system was commenced in collaboration with the European Department for the Quality of Medicines and the EU members of the Network of Official Medicines Control Laboratories, under the aegis of the European Pharmacopoeia.

#### *Interested parties*

The pattern of quarterly meetings with interested parties continued in 1997, including representatives from consumer, patient, industry and health care professional groups. A number of Info-Days, attended by 100 - 200 representatives from industry, were also jointly hosted either at the EMEA or nearby with EFPIA, FEDESA and AESGP.

Attempts were made to widen the scope of interested parties and particular attention was paid to establishing contacts with patient groups and also building relationships with the wider scientific community and international and European learned societies. Examples of groups invited during 1997 to EMEA meetings are given in the table.

A number of technical workshops on specific topics, e.g. scientific opinions, decision-making procedure, pharmacovigilance, performance indicators and export certificates, were organised with interested parties in 1997.

#### *Interested parties invited to CPMP quarterly meetings:*

Bureau Européen des Unions de Consommateurs (BEUC)  
European Federation of Pharmaceutical Industries' Associations (EFPIA)  
Association Européenne des Spécialités Pharmaceutiques Grand Public (AESGP)  
European Generic manufacturers' Association (EGA)  
Standing Committee of European Doctors  
Groupement des Pharmaciens de l'Union Européenne (GPUE)

#### *Interested parties invited to CVMP quarterly meetings:*

Bureau Européen des Unions de Consommateurs (BEUC)  
Fédération de la Santé Animale (FEDESA)  
Committee of Agricultural Organisations in the EU/General Committee of Agricultural Co-operation in the EU (COPA COGECA)  
Groupement des Pharmaciens de l'Union Européenne (GPUE)  
Federation of Veterinarians in Europe (FVE)

#### *Other groups invited to EMEA meetings in 1997:*

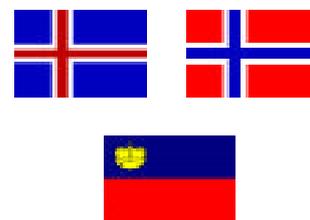
Drug Information Association (DIA)  
European Association of Genetic Support Groups (EAGS)  
Health Action International (HAI)  
International Federation of Associations of Pharmaceutical Physicians (IFAPP)  
International Society of Drug Bulletins (ISDB)  
Pan-European Federation of Regulatory Affairs Societies (PEFRAS)

## 2.4 International relations

The role of the EMEA in supporting European Commission international activities increased greatly in 1997.

Observers from the Nordic Council on Medicines already participate in certain meetings at the EMEA, in particular the Inspectors' Working Group.

Within the framework of the European Economic Area Agreement, it is anticipated that Iceland and Norway will participate directly in the work of the EMEA in 1998. A meeting with foreign ministry and national competent authority representatives of the States concerned, together with the EFTA Secretariat, was held in November 1997 at the EMEA. It is hoped that Liechtenstein will also be able to participate in the work of the EMEA at a later date.



Participation in the International Conferences on Harmonisation (ICH) for human and veterinary medicines remained a priority area of activity in 1997. Begun in 1990, the ICH is a tripartite science-driven initiative bringing together the regulatory authorities and industry representatives of the EU, Japan and US.

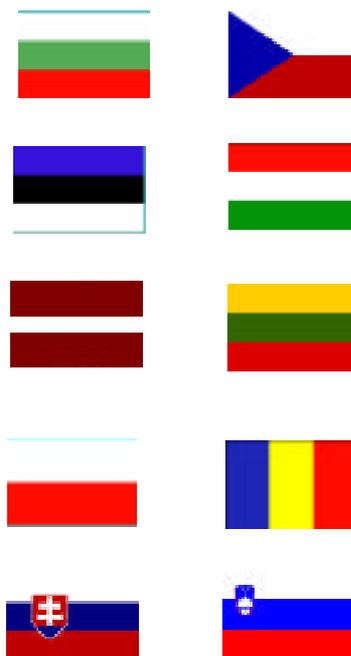
The ICH process reached a crucial point on 16-18 July 1997 at its Fourth Conference held in Brussels. It was attended by over 1 600 representatives of EU, Japanese, US and other observers from regulatory authorities and industry. Considerable progress has been made since 1991 with 46 trilateral positions now completed, covering 16 quality topics, 13 safety topics, 14 efficacy topics and 3 multidisciplinary topics.



Discussions have begun in 1997 on the Common Technical Dossier – the so-called global application dossier. This will be a major challenge for ICH in the coming years and will undoubtedly mobilise considerable resources at EMEA and national competent authorities level.

Inspired by the success of the ICH process, a similar initiative was launched in 1996 for veterinary medicines – VICH. The Steering Committee met for a second time in August 1997 in Paris and two VICH working groups met at the EMEA in London. Two VICH guidelines have already been released for consultation.

Under the auspices of the World Health Organisation, a conference with national authorities of the new independent states of the former Soviet Union was held at the EMEA in October 1997, with representatives of the drug regulatory authorities of Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, the Russian Federation, Turkmenistan, Ukraine and Uzbekistan.



The EMEA participated at the first meeting of the national regulatory authorities of central and eastern European countries (CEECs) in June 1997 in Sofia, Bulgaria. This was followed by a joint Commission and EMEA meeting in November 1997 at the EMEA attended by representatives of the drug regulatory authorities of Bulgaria, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, the Slovak Republic and Slovenia.

The major points of discussion were harmonisation with EU legislation, adaptation of their national authorities and the strategy to be adopted prior to possible accession to the European Union. The EMEA will be associated with pre-accession co-operation activities and is ready to offer technical assistance to all CEECs.

The interest of third countries in the operation of the centralised procedure continued in 1997. The EMEA received a number of delegations from national authorities during the year, including from Australia, Canada, China, Hungary, Japan, Korea, New Zealand and Ukraine.

In addition, a meeting of Latin American national authorities from Argentina, Bolivia, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay and Venezuela was hosted at the EMEA on the initiative of the Spanish authorities in February 1997.

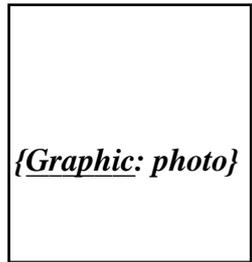
Outside the field of pharmaceuticals, the EMEA played host to meetings of the International Grains Council and the plenary session of the International Sugar Organisation. Both are part of the United Nations family of international organisations and, like the EMEA, also have their seat in Canary Wharf.

The EMEA also became actively involved in 1997 with mutual recognition agreements, a number of which have now been initialled or are under discussion. Once in force they will provide for mutual recognition of pharmaceutical inspections, easing access to international markets for European industry.

At the request of the European Commission the EMEA took over direct responsibility for managing the implementation and operation of the pharmaceutical aspects of the EU-Canada Mutual Recognition Agreement. This has involved co-ordination within the EU during the transitional phase ('confidence building') and providing secretarial support and joint chairmanship of the Joint Sectoral Group with Health Canada, the Canadian national authority.

Preparation also began in 1997 for the eventual implementation of the mutual recognition agreement with the USA.

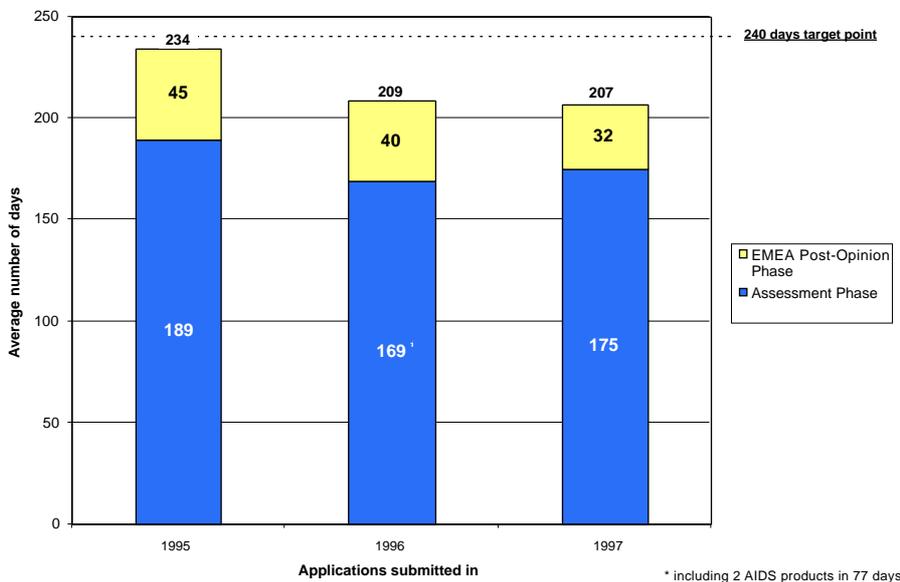
# 3. MEDICINAL PRODUCTS FOR HUMAN USE



Professor Jean-Michel Alexandre  
Chairman, Committee for Proprietary Medicinal Products

- 3.1 Unit for the Evaluation of Medicinal Products for Human Use
- 3.2 Operation of the centralised procedure
- 3.3 Other CPMP core activities
- 3.4 CPMP Working Parties
- 3.5 Mutual recognition

Mean EMEA Processing Time for Human Medicinal Products submitted 1995-1997



### 3.1 Unit for the Evaluation of Medicinal Products for Human Use

During 1997, the pattern of work undertaken in the centralised procedure has changed, compared with that in 1996. In addition to the review of new applications for marketing authorisations, there has been a substantial increase in follow-up work and on the maintenance of authorisations including, for example, specific obligations, follow-up measures, variations, annual assessment reports, periodic safety update reports and other safety-related issues.

Information on the number of marketing authorisations and variation applications received, and opinions granted in 1997 are shown in Annex 7, together with a full list of Community authorisation Decisions, as approved by the Commission in 1997. Despite this considerable increase in work-load, the EMEA co-ordinated the work such that the time limits, laid down in Council Regulation (EEC) No 2309/93, were met and improved on where appropriate.

### 3.2 Operation of the centralised procedure

Centralised procedures	1995	1996	1997			1995 -97 TOTAL
			1st half	2nd half	Total by Part A & B	
<b>Applications received</b>						
Part A	17	12	8	12	20	131
Part B	19	23	19	21	40	
<b>Opinions given by product</b>						
Part A	6	14	3	3	6	63
Part B	3	15	10	9	19	
<b>Opinions given by substance</b>						
Part A	5	11	3	3	6	50
Part B	3	12	7	6	13	
<b>Type I Variations</b>						
Part A	0	14	24	33	57	136
Part B	0	13	19	33	52	
<b>Type II Variations</b>						
Part A	1	3	7	12	19	64
Part B	0	13	11	17	28	
<b>Extension &amp; Abridged applications</b>						
Part A	0	3	0	32	32	39
Part B	0	2	0	2	2	
<b>Withdrawal</b>	2*	4**	1	4	5	11

\* ex-concertation procedures

\*\* including 2 ex-concertation procedures

### *Withdrawals*

Over the period 1995 - 97, eleven applications for centralised procedures (3 part A and 8 part B) have been voluntarily withdrawn by the applicants (5 in 1997). Four procedures concerned converted 'ex-concertation procedures' and seven new centralised applications.

Most withdrawals were linked to specific safety problems which might have led to a negative benefit-risk assessment by the CPMP. For example, five withdrawals were due to lack of proper efficacy and safety data to support the full indication claimed. Two withdrawals were due to manufacturing-related aspects.

### *Rapporteurships*

As in 1995 and 1996, the choice of Rapporteur and Co-Rapporteur for centralised applications has continued to be determined by taking into consideration preferences of applicants and the availability and expertise of CPMP members.

Applicants have helped ensure a balanced distribution of work amongst CPMP members by proposing three or four different CPMP members as requested by the Committee.

Delegates from	Rapporteur		Co-rapporteur		Total
	List A	List B	List A	List B	
<b>Austria</b>	0	5	0	4	9
<b>Belgium</b>	2	0	1	3	6
<b>Denmark</b>	6	3	3	2	14
<b>Finland</b>	1	3	0	4	8
<b>France</b>	1	6	3	7	17
<b>Greece</b>	0	0	1	1	2
<b>Germany</b>	8	2	2	3	15
<b>Ireland</b>	2	3	4	5	14
<b>Italy</b>	2	2	5	2	11
<b>Luxembourg</b>	0	0	0	4	4
<b>Netherlands</b>	3	6	4	3	16
<b>Portugal</b>	0	3	0	1	4
<b>Spain</b>	1	2	1	2	6
<b>Sweden</b>	2	6	2	7	17
<b>United Kingdom</b>	4	8	6	1	19
<b>Total</b>	32	49	32	49	112

### *Scientific advice*

The EMEA standard operating procedure on the scientific advice to be given by the CPMP for innovative medicinal products (EMEA/SOP/002/95) was first implemented in 1996. The experience gained with the procedure in 1997 led to a reorganisation of the work in order to optimise the procedure. This reorganisation ensured the better use of expertise provided by the CPMP working parties and the European network of experts and was helped by the wider availability of staff for expediting the progress of requests.

In 1997, 31 new requests for scientific advice including 4 follow-ups were submitted by pharmaceutical companies. Final advice was given for 25 requests. Two requests were withdrawn by the company, and in 3 cases the request was considered not acceptable by the CPMP. The scope of the advice given by the CPMP was related to quality (1 case), biotechnology (2 cases), safety (5 cases), clinical development (18 cases).

In 6 cases, the company was invited to meet the consultation group. Following several requests for advice on the development of medicinal products in the same therapeutic area, a 'Points to Consider' paper on Clinical investigation of medicinal products in the treatment of patients with acute respiratory distress syndrome (CPMP/EWP/504/97) was prepared and issued, addressing the key points in the clinical development of such medicinal products.

### *Operational matters*

The EMEA has continued to review and to improve its operational procedures. The consistent and high scientific quality of CPMP opinions prevented further scientific discussions during the Standing Committee phase. This facilitated the issuing of Commission Decisions granting Community marketing authorisations.

To improve further the review of centralised applications, the EMEA has encouraged companies to come to the Agency for pre-submission meetings in the pre-authorisation and post-authorisation phases (follow-up, variations, pharmacovigilance).

The objectives of such meetings are to address regulatory, technical and procedural questions as well as inspections in advance of the submission of applications and thereby minimise problems arising at the stage of validation or at any step of the procedure thereafter. The number of pre-submission meetings increased during 1997 and reached 60. Similar meetings were held at the EMEA with rapporteurs and co-rapporteurs to consider technical matters.

The EMEA Secretariat improved the provision of regulatory and legal advice to the CPMP and its working parties as well as to industry. The aim in the advice is to ensure compliance with EU legislation in the procedural management of dossiers both in the application and post-authorisation phase. This also helps the operation of the centralised procedure.

To this effect, standard operational procedures are constantly being developed by the EMEA Secretariat for consideration and adoption by the CPMP, for example on "Annual re-assessment of the specific obligations and the benefit/risk profile of medicinal products authorised under exceptional circumstances" (CPMP/SOP/657/97).

The responsibility for the checking of mock-ups and specimens of packaging and patient information leaflets became a heavy task for the Unit in 1997. Internal workshops have been organised to establish internal procedures dealing with linguistic matters, translations and the processing of opinions prior to transmission to the Commission.

### 3.3 Other CPMP core activities

#### Referrals

In 1995 and 1996 a total of 5 referrals were made to the CPMP concerning 17 products for which Opinions were given (see table).

In 1997 one referral was initiated in accordance with Article 12 of Council Directive 75/319/EEC for terfenadine-containing medicinal products.

An Article 12 referral initiated, in the interest of the Community, in 1996 for chlormezanone-containing medicinal products, related to serious skin reactions, was finalised. The Commission Decision resulted in the withdrawal of chlormezanone-containing medicinal products.

Three referrals for five active substances were initiated in 1997, in accordance with Article 15a of the same Directive. For one of them the CPMP adopted a majority Opinion. For the same product, the CPMP adopted an opinion for an Article 12 referral.

Two arbitrations for mutual recognition procedures were carried out following divergent positions of national authorities on an application for marketing authorisation (Article 10 of Council Directive 75/319/EEC) and on a type II variation procedure for a product authorised under the ex-‘concertation procedure’ (Article 7(5) of Commission Regulation (EC) No 541/95).

One Article 11 referral for the resolution of divergent national decisions initiated in 1996 by the marketing authorisation holder for an interferon a-containing product resulted in a Commission Decision amending the existing national marketing authorisations.

Type of referral Council Directive 75/319/EEC	Date of CPMP final Opinion	International non-proprietary name (INN)
<b>National authorisations</b>		
<b>Article 12</b>	19 October 1995	Naftidrofuryl
	19 December 1995	Sparfloxacin
	17 July 1996	Anorectics : Clobenzorex; Norpseudoephedrine; Phentermine; Fenproporex; Mazindol; Amfepramone; Phendimetrazine; Phenmetrazine; Mefenorex; Dexfenfluramine; Fenfluramine; Propylhexedrine; Fenbutrazate
	14 May 1997	Chlormezanone
	<i>ongoing</i>	<i>Terfenadine</i>
<b>Article 15a</b>	<i>ongoing</i>	<i>Dexfenfluramine; Fenfluramine</i>
	<i>ongoing</i>	<i>Phentermine; Amfepramone</i>

Type of Referral Council Directive 75/319/EEC	Date of CPMP final Opinion	International non-proprietary name (INN)
<b>Mutual recognition/Decentralised procedure</b>		
<b>Article 10 New applications</b>	17 April 1996	Glimepiridum
	18 December 1996	Mizolastine
	<i>ongoing</i>	<i>Fluoxetine</i>
<b>Article 11</b>	18 December 1996	Interferon a-2b
<b>Article 15a</b>	16 April 1997	Haemophilus influenzae type B conjugate
<b>Article 12</b>	24 September 1997	Haemophilus influenzae type B conjugate
<b>Article 7(5) Type II variations</b>	<i>ongoing</i>	<i>Epoetinum alfa</i>
	18 December 1996	Somatotropin

### 3.4 CPMP Working Parties

The CPMP working parties (Pharmacovigilance Working Party, Biotechnology Working Party, Efficacy Working Party and Safety Working Party), as well as the joint CPMP/CVMP Quality Working Party continued to meet in 1997 at regular intervals.

The working parties continued to provide recommendations to the CPMP, mainly in the form of CPMP and ICH guidelines. The status of guidelines discussed in 1997 is given in the tables provided for each working party. Quality guidelines are presented in Chapter 5 which deals with the Technical Co-ordination Unit.

Whereas biotechnology guidelines relate primarily to the centralised procedures (future, ongoing or earlier ones), guidelines for chemical quality, pre-clinical safety and clinical efficacy also support ongoing or future mutual recognition procedures.

#### *Pharmacovigilance activities and Pharmacovigilance Working Party*

The Pharmacovigilance Working Party (PhVWP), chaired by Dr S. Wood, met on 8 occasions in 1997. The main topics discussed were product-related issues, either at the request of the CPMP or the national authorities, as well as organisational matters such as the revision of Chapter V of the Notice to Applicants and existing guidelines in the field of pharmacovigilance activities. Furthermore discussions took place on pharmacovigilance for mutually recognised products. In liaison with the Pharmacovigilance Working Party the involvement of the CPMP in the field of pharmacovigilance for centrally-authorised products increased significantly.

In April, the CPMP adopted the document "Conduct of Pharmacovigilance for Centrally Authorised Products" (CPMP/183/97). This document is very important for the handling of safety concerns for medicinal products processed through the centralised procedure. The roles and responsibilities of all partners and of their involvement in these pharmacovigilance activities are clearly described, as well as the co-operation between the rapporteur and the EMEA Secretariat.

In order to deal in a rapid and efficient way with crisis situations related to pharmacovigilance or quality defects involving a centrally authorised product, the CPMP adopted in September a document on “Crisis management plan regarding centrally authorised products for human use” (CPMP/388/97). The document outlines the procedures to be followed and highlights the management structures and systems to be set up.

In 1997 an increased number of suspected serious unexpected adverse drug reactions (non-EU) were notified to the EMEA. In total 1 812 such adverse drug reactions were received.

Following the agreement by Member States in January 1997 to send, by e-mail every two weeks, to the EMEA Secretariat a line-listing (CIOMS II format) of serious adverse drug reactions occurring in their territory, a total of 3 069 EU adverse drug reactions reports were received.

### *Biotechnology Working Party*

The Biotechnology Working Party (BWP), chaired by Professor G. Vicari, met on 10 occasions in 1997. It is responsible for giving specialist technical assistance to the CPMP on manufacture and control of biotechnological and biological medicinal products including products derived from blood and plasma, and of immunological products. Guidelines adopted or released for consultation by the CPMP in 1997 are outlined in the table.

The ICH activities of this Working Party were co-ordinated by Professor J. H. Trouvin.

Furthermore, the Biotechnology Working Party has provided, at the request of the Mutual Recognition Facilitation Group, scientific advice relating to general (for example influenza vaccines) and some product specific matters.

Reference number	Title of guideline	Status
CPMP/BWP/214/96	Harmonisation of requirements for influenza vaccines	Adopted in March 1997
CPMP/BWP/859/95	Core SPC for human immunoglobulin	Adopted in March 1997
CPMP/ICH/295/95 (Q5A)	Quality of biotechnological products: viral safety evaluation of biotechnological products derived from cell lines of human or animal origin	Adopted in April 1997
CPMP/ICH/294/95 (Q5D)	Quality of biotechnological/biological products: derivation and characterisation of cell substrates used for production of biotechnological/biological products	Adopted in September 1997
CPMP/ICH/302/95 (S6) (in collaboration with SWP)	Preclinical safety evaluation of biotechnology-derived pharmaceuticals	Adopted in September 1997
CPMP/BWP/877/96	Minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products	Adoption pending
CPMP/BWP/477/97	Pharmaceutical and biological aspects of combined vaccines	Released for consultation in June 1997
CPMP/BWP/269/95 (revision 2)	Plasma derived medicinal products	Released for consultation in July 1997

During 1997 extensive scientific discussion continued on the revision of existing notes for guidance concerning vaccines (requirements for influenza and combination vaccines), medicinal products derived from blood and plasma (clotting factor concentrates, albumin and immunoglobulin) and issues on the potential risk of transmission of spongiform encephalopathy via medicinal products.

### *Efficacy Working Party*

The Efficacy Working Party (EWP), chaired by Professor A. Hildebrandt and co-chaired by Dr B. van Zwieten-Boot, who was also the co-ordinator for ICH matters, met 4 times in 1997.

It is responsible for drafting new methodological guidelines in established therapeutic areas as well as 'Points to consider' papers on specific clinical aspects in emerging or fast moving therapeutic areas. Upon request of the CPMP, core Summaries of Product Characteristics for particular medicinal products can be prepared. The group also provides a continuous input concerning efficacy topics within the ICH-process. Moreover, the Efficacy Working Party continuously updates existing guidelines in accordance with scientific progress.

In 1997, the following efficacy guidelines and 'Points to Consider' documents were adopted or released for consultation by the CPMP:

Reference number	Title of guideline	Status
CPMP/EWP/462/95	Clinical investigation of medicinal products in children	Adopted in March 1997
CPMP/EWP/558/95	Evaluation of new anti-bacterial medicinal products	Adopted in April 1997
CPMP/EWP/238/95	Clinical investigation of medicinal products in the treatment of hypertension	Adopted in May 1997
CPMP/EWP/520/96	Pharmacodynamic section of the SPC for anti-bacterial medicinal products	Adopted in June 1997
CPMP/EWP/553/95	Clinical investigation of medicinal products in the treatment of Alzheimer's disease	Adopted in July 1997
CPMP/ICH/287/95 (E2B)	Clinical safety data management: data elements for transmission of individual case safety reports	Adopted in September 1997
CPMP/ICH/291/95 (E8)	General considerations for clinical trials	Adopted in September 1997
CPMP/EWP/552/95	Involitional osteoporosis in women	Adopted in September 1997
CPMP/EWP/559/95	Clinical investigation of medicinal products in the treatment of schizophrenia	Released for consultation in February 1997
CPMP/EWP/560/95	Investigation of drug interactions	Released for consultation in March 1997
CPMP/EWP/281/96	Clinical investigation of medicinal products used in weight control	Released for consultation in March 1997
CPMP/ICH/289/95 (E5)	Ethnic factors in the acceptability of foreign clinical data	Released for consultation in March 1997
CPMP/ICH/363/96 (E9)	Statistical principles for clinical trials	Released for consultation in February 1997
CPMP/EWP/504/97	Points to Consider: Clinical evaluation of medicinal products in the treatment of patients with acute respiratory distress syndrome	Adopted in October 1997

The group is working on the following therapeutic areas: Parkinson's disease, prolonged and modified release formulations, extension of the anti-bacterial guideline, arthritis, combined vaccines, antidepressive agents, oral contraceptives.

Co-operation and exchange of scientific information with other CPMP working parties has notably increased during the year. Thus the clinical safety information requirements in line with CIOMS III were discussed with the Pharmacovigilance Working Party. Clinical requirements for combined vaccines and gene therapy/DNA vaccines were shared with the Biotechnology Working Party. Preclinical requirements for Osteoporosis were discussed with the Safety Working Party.

The need to update some particular aspects of bioequivalence testing and pharmacokinetic aspects of modified released formulations including transdermal patches has been recognised and a joint ad hoc group of experts of the Efficacy Working Party and Quality Working Party has been convened to deal with these issues under the chairmanship of Professor J. Guimaraes Morais.

On the basis of the CPMP new mandate on scientific advice, a more active contribution from the Efficacy Working Party is now required, relating both to the overall clinical development programme and to specific questions concerning the design of clinical trials.

#### *Safety Working Party*

The Safety Working Party (SWP), chaired by Dr P. Sjöberg, held three meetings to discuss pre-clinical, pharmacological and toxicological issues, in liaison with other working parties as appropriate. The SWP also gives advice on safety matters raised by the CPMP, upon request.

The Safety Working Party provides a continuous support to the safety topics within the ICH process. The ICH co-ordinator for safety was Dr J. W. Van der Laan.

Furthermore, specific questions on development and requirements have been addressed by the SWP including anti-cancer medicinal products, vaccines, gene therapy, assessment of the potential for QT interval prolongation by non-cardiovascular medicinal products.

The SWP is also involved in the preparation of CPMP scientific advice on pre-clinical matters and provides a forum for exchange of information on specific medicinal concerns when needed.

The following safety guidelines or points to consider documents were adopted or released for consultation in 1997:

Reference number	Title of guideline	Status
CPMP/ICH/299/95 (S1B)	Carcinogenicity: testing for carcinogenicity of pharmaceuticals	Adopted in September 1997
CPMP/ICH/366/95 (S1C (R))	Addendum to 'Dose selection for carcinogenicity studies of pharmaceuticals': addition of a limit dose and related notes of pharmaceuticals	Adopted in September 1997

Reference number	Title of guideline	Status
CPMP/ICH/174/95 (S2B)	Genotoxicity: a standard battery for genotoxicity testing of pharmaceuticals	Adopted in September 1997
CPMP/ICH/302/95 (S6) (in collaboration with BWP)	Preclinical safety evaluation of biotechnology-derived pharmaceuticals	Adopted in September 1997
CPMP/ICH/286/95 (M3)	Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals	Adopted in September 1997
CPMP/ICH/283/95 (Q3C) (in collaboration with QWP)	Impurities: residual solvents	Adopted in September 1997
CPMP/SWP/465/95	Pre-clinical pharmacological and toxicological testing of vaccines	Adopted in December 1997
CPMP/ICH/300/95 (S4)	Duration of chronic toxicity testing in animals (rodent and non rodent toxicity testing)	Released for consultation in September 1997
CPMP/986/96	Points to Consider: The assessment of the potential for QT interval prolongation by non-cardiovascular medicinal products	Adopted in December 1997

#### *Ad hoc CPMP Groups*

The ad hoc expert group on third generation oral contraceptives and cardiovascular risks, chaired by Professor K. Strandberg, met twice in 1997. The discussion resulted in the adoption by the CPMP of a revised Position Statement on oral contraceptives containing desogestrel or gestodene (CPMP/073/97, Rev.2), providing information as to the risk of venous thromboembolism associated with the use of oral contraceptives.

The ad hoc group on transmissible spongiform encephalopathies (TSE), chaired by Professor D. Dormont, was convened in order to revise the CPMP guideline on TSE.

The ad hoc influenza vaccine expert group, chaired by Dr J. Wood, met to discuss the choice of strains and the content of the application dossier.

The ad hoc group of experts on anti-retrovirals, chaired by Professor K. Strandberg, revised the 'Points to Consider' document concerning the requirements for registration of new anti-retroviral medicinal products taking into account the biomedical advances made in this field (CPMP/602/95-Rev.1).

The ad hoc group on 'Summary of Product Characteristics', chaired by Dr M. Teeling, was convened by the CPMP in order to revise the extent of quality, safety and clinical information which should be included in the summary of product characteristics. This task is performed in co-operation with all permanent CPMP working parties.

A round table of experts organised in collaboration with the European Commission on 18 December 1997, chaired by the chairman of the CPMP, was convened in order to discuss the use of new medicinal products in children.

### *Ad hoc Working Group on herbal medicinal products*

In 1997 an ad hoc Working Group on herbal medicinal products was created within the EMEA at the request of the European Commission in agreement with the Management Board. The mandate for this working group was limited to three meetings in 1997.

Under the chairmanship of Dr K. Keller, the working group met in June, September and November 1997 to address the issue of quality, safety and efficacy of herbal medicinal products. It reviewed existing legislation and guidelines to ensure among Member States a common understanding of current criteria for the assessment of such products.

In its report to the European Commission and to the EMEA, the group made recommendations for the development of further guidance/assessment criteria to prove sufficiently the quality, safety and efficacy of these products. It also gave recommendations for an appropriate use of the available scientific literature as well as existing European Pharmacopoeia, WHO and ESCOP monographs.

The Management Board considered the report from the Group at its December 1997 meeting and approved the continuation of the Group on an ad hoc basis in 1998.

### **3.5 Mutual recognition**

The mutual recognition or decentralised procedure is the second and complementary part of the single Community system which is being established in Europe with co-operation between the Member States, the EMEA and the European Commission.



The mutual recognition procedure has made considerable progress during 1997. The use of the procedure in 1997 was:

<b>Mutual recognition procedure</b>	<b>Total submitted in 1997 *</b>	<b>Under evaluation in 1997 *</b>	<b>Ended positively in 1997 *</b>	<b>Arbitrations in 1997 *</b>
<b>New applications</b>	190	51	147	1
<b>Type I variations</b>	139	16	99	0
<b>Type II variations</b>	215	66	152	1

\* Mid-December

The number of applications both submitted and completed has risen significantly during 1997, compared with 10 procedures completed in 1995 and 84 in 1996. The very low level of arbitrations is another encouraging feature. The adoption of the Best Practice Guide in September 1996 and its subsequent endorsement by the Heads of Agencies has helped to improve the time both for initiating a mutual recognition procedure and the granting of national marketing authorisations.

The development of a complementary best practice guide by the European Federation of Pharmaceutical Industries' Associations has been particularly

welcomed and this should help to improve the procedure further.

The Mutual Recognition Facilitation Group (MRFG) continues to meet at the EMEA in parallel with the meetings of the CPMP. The MRFG met under the chairmanship of Dr Truus Janse-de Hoog of the Netherlands from January to September 1997 and Dr David Jefferys of the United Kingdom for the remainder of the year until June 1998. The MRFG and the Member States have been particularly grateful for the support of the EMEA in providing meeting rooms for the Group and for the break-out sessions. The EMEA has also provided the Secretariat to support the MRFG. The recent decision of the Commission to attend the MRFG meetings has also been valuable.

In 1997 a total of 84 break-out sessions were organised by reference Member States and held at the EMEA. The MRFG has agreed a protocol for the handling of break-out sessions and is currently undertaking a diagnostic review of the best uses of these meetings.

One issue of concern is the frequency of withdrawals of applications from individual Member States during the mutual recognition procedure. This may be a feature of the transition period which will resolve itself next year, but it is being closely monitored and the reasons for withdrawal are being analysed.

During the year the MRFG has elaborated a validation report form, a response document form and a procedure for handling post-authorisation commitments.

The introduction of the tracking system 'EudraTrack' in October was a significant step forward. It should allow more statistical information to be generated which can be made available in the published monthly MRFG report and will also improve the monitoring of the procedure. During the year the MRFG significantly expanded its press release and is now making available more information on its deliberations and on the operation of the system.

During the year an increasing number of Member States acted as reference Member State and nine have now undertaken this important role. The number of finalised procedures by type is given in the table:

<b>Total number of finalised procedures by type August 1995 to December 1997*</b>		
	Number	Percentage
New active substance	77	31.5%
Generics	45	18.4%
Line extensions	29	11.9%
Fixed combination	20	8.2%
OTC	6	2.6%
Herbal	2	0.8%
Others	65	26.6%

\* The number includes multiple procedures (total = 244)

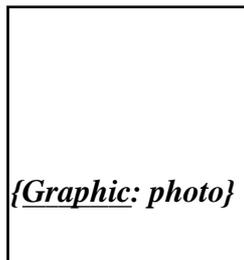
It is encouraging to see the wide range of applications now using the mutual recognition procedure, also that similar applications are using both Community procedures.

The MRFG has identified several areas where there is a need for existing CPMP guidelines to be updated or new guidance to be elaborated. These requests have been put to the CPMP to be addressed by its Working Parties. The issues identified by the MRFG for further work include the areas of hormone replacement therapy, paediatric medicines, oncology products, anti-infectives and revision of the guidance on bioequivalence testing. The MRFG has developed a procedure with the European vaccine manufacturers for handling influenza vaccines through the mutual recognition procedure for the influenza season 1998-99.

Significant issues remain to be addressed in the mutual recognition procedure but good progress has been achieved during 1997. The close co-operation between all the stakeholders in the system provides an encouraging platform for the rapid expansion in the number of procedures which can be expected over the next two years.



# 4. MEDICINAL PRODUCTS FOR VETERINARY USE



Preface by **Professor Dr Reinhard Kroker**  
Chairman, Committee for Veterinary Medicinal Products

*In the year 1997 the workload of the CVMP increased considerably although the number of submissions in the centralised procedure was less than expected and moreover, the deadline for the finalisation of MRL procedures was extended until 1 January 2000. Despite this extension, the main burden of the CVMP remains the establishment of MRLs for old substances. In this field the Safety of Residues Working Party under the chairmanship of Dr Beechinor has made great progress and provided an increasing number of proposals to the CVMP. The work on different guidelines should also be highlighted and a significant number of new guidance notes on priority topics have been adopted by the Committee.*

*Whilst the forecasted number of applications through the centralised procedure did not fully materialise, the expected amendment of Part B of Council Regulation (EEC) No 2309/93 to new substances in companion animals is expected to lead to an increase in the number of applications in the coming year.*

*The current structure of the CVMP meetings running from lunch-time on day 1 to lunch time on day 3 has been welcomed by the majority of the members and allows meetings of the Veterinary Mutual Recognition Facilitation Group, rapporteurs and quarterly meetings with interested parties to be co-ordinated around the plenary session of the Committee.*

*At the end of my first 3 year period in office I wish to express my deepest thanks to the members of the CVMP for their excellent co-operation and their efforts to hold the meetings in a convivial, positive and professional atmosphere. Many thanks also to the Agency and its staff for the great support of the work of the CVMP and myself. I am confident that the new CVMP will continue to fulfil its tasks as well as the old one did.*

- 4.1 Unit for the Evaluation of Medicinal Products for Veterinary Use
- 4.2 Operation of the centralised procedure
- 4.3 Other core CVMP activities
- 4.4 CVMP Working Parties and ad hoc Groups
- 4.5 Mutual recognition

## 4.1 Unit for the Evaluation of Medicinal Products for Veterinary Use

Good progress has been made in meeting the targets set out in the 1997 work programme, and details are provided in the sector reports below. However, the number of applications for authorisation through the centralised procedure, and for the establishment of maximum residue limits for new substances, has been fewer than expected. Progress in setting maximum residue limits for old substances has continued satisfactorily, although the accommodation of approximately 100 homeopathic substances and herbal remedies in the work programme, at the request of the European Commission, has added significantly to the task.

The recruitment of a new Head of Sector for the CVMP & Veterinary Procedures Sector was completed satisfactorily with the appointment of Dr Jill Ashley-Smith in July.

The CVMP has spent some considerable time in addressing two critical issues of importance which are currently attracting significant attention from society at large. The Committee has established an ad hoc working group of experts to evaluate the extent of the risk of anti-microbial resistance developing in animals as a result of the use of antibiotics in veterinary medicine and its potential transfer to man. Being aware of the ongoing developments with regard to transmissible spongiform encephalopathies the CVMP has continued to review the situation, in liaison with the CPMP.

## 4.2 Operation of the Committee for Veterinary Medicinal Products

### *Authorisations under the Centralised Procedure*

The goal of achieving full compliance with regulatory deadlines for completion of marketing authorisation applications has been achieved. The CVMP has reached a positive opinion in respect of 6 products during the year, 5 being pharmaceuticals eligible under Part B of the Annex to Council Regulation (EEC) No 2309/93 and 1 being recombinant vaccines under Part A of the Annex.

The Veterinary Unit has worked hard to establish a positive relationship with industry to build confidence in the centralised procedure and to maximise efficiency in processing those applications received. Meetings with interested parties, including industry representatives, have taken place on a quarterly basis and bilateral meetings with FEDESA, also on a quarterly basis, have provided an excellent forum for frank and in-depth discussions on the issues of the day.

Two successful joint EMEA/FEDESA Info-Days were held in February and September where members of the CVMP and industry representatives were able to review and debate critical matters of mutual interest, many of which related to optimising the performance of the centralised procedure.

Nevertheless, the number of applications in 1997 has been disappointing. The exclusion of new entries for small animals under Part B of the Annex to Council Regulation (EEC) No 2309/93 continues to restrict potential applicants

with products coming through development for small animals. Nonetheless, those companies which have submitted applications to the Agency appear to be satisfied with the performance of the system so far.

#### *Guidelines and updates on international harmonisation*

The CVMP continues to focus on regulatory issues associated with the authorisation of veterinary medicines and on which a need for guidance is considered appropriate. During the year a further group of CVMP guidelines have been adopted.

In addition the CVMP took into consideration Commission Decision 97/534/EEC on transmissible spongiform encephalopathies and revised its BSE guidelines accordingly to ensure that no specified risk material is used as a source of starting material in the manufacture of medicine. The Committee also took note of recent concerns expressed at the impact that the current guidelines on the establishment of MRLs for minor species including salmonidae and other fin fish was having on the availability of medicines for such species. It consequently reviewed these guidelines to allow for a more pragmatic approach to this critical issue and the new guidelines were released for consultation.

Reference number	Title of guideline	Status
EMEA/CVMP/055/96	Environmental risk assessment for veterinary medicinal products	Adopted in January 1997
EMEA/CVMP/014/96	Guidance for an assessor preparing variation assessment reports for veterinary biologicals	Adopted in March 1997
EMEA/CVMP/128/95	Investigation of chiral active substances	Adopted in June 1997
EMEA/CVMP/116/96	Harmonisation of requirements for equine influenza vaccine	Adopted in July 1997
CVMP/QWP/115/95	Inclusion of antioxidants and antimicrobial preservatives in veterinary medicines	Adopted in July 1997
EMEA/CVMP/183/96	Pharmacovigilance of veterinary medicinal products	Adopted in July 1997
EMEA/CVMP/153a/97	Establishment of MRLs for minor species	Adopted in November 1997
EMEA/CVMP/145/97 (see also CPMP/BWP/877/96)	Minimising the risk of transmitting agents causing spongiform encephalopathy via veterinary medicinal products	Adopted in November 1997

On the international front the EMEA has continued to co-ordinate the input of the CVMP and Commission, the regulatory parties at European level into the VICH initiative, where good progress has been made in the harmonisation process.

At the second meeting held in Paris in August 1997 the VICH Steering Committee reviewed the work completed to date by the Working Groups on Quality, Safety, Good Clinical Practice, Anthelmintic Efficacy Requirements and Environmental Risk Assessment on the basis of reports by the topic leaders and chairpersons.

The first two draft guidelines (validation of analytical procedures: definition and terminology, and validation of analytical procedures: methodology) elaborated on the basis of ICH guidelines were adopted for consultation.

### 4.3 Establishment of maximum residue limits (MRLs)

#### *Maximum residue limits for new substances*

As a result of an initial increase in new MRL applications under Article 6 of Council Regulation (EEC) No 2377/90 received during the second part of 1996, the actual number of MRL applications in 1997 was lower than estimated.

In total 19 applications for the establishment of MRLs were received by the EMEA in 1997, of which 6 were full applications and 13 were applications for modifications or extensions to new species.

The dossiers received were, on average validated by the Secretariat within 10 days of the 30 days formally allowed. The target period of 15 days set for 80 per cent of the applications laid down in the 1997 work plan was met with one exception (18 days), where a complex but deficient dossier required more review time and consultation with the rapporteurs, leading to an invalidation. The CVMP adopted opinions for 10 substances and recommended their inclusion into Annex I, II or III of Council Regulation (EEC) No 2377/90, whereas for a further 16 substances the assessments could not be concluded and a consolidated list of questions was sent to the applicants.

The average time the CVMP required to undertake the assessment, resulting in an opinion recommending an MRL or adopting a list of questions, was 108 days of the 120 day legislative time frame laid down in Council Regulation (EEC) No 2377/90. In those cases, where a list of questions was sent to the applicants, the CVMP finalised the assessment with one exception well within the time frame of 90 days provided for in the legislation.

#### *Maximum residue limits for old substances*

The original deadline, by which the establishment of MRLs for old substances had to be concluded, was extended to 1 January 2000 for all those substances which had been on the market on 1 January 1992 and for which documented dossiers had been submitted before 1 January 1996 (Council Regulation (EC) No 434/97 of 3 March 1997). The list of substances for which valid applications had been received by the Commission or EMEA by the aforementioned deadline and therefore considered as 'defended' was subsequently published by the EMEA (Communication of the EMEA, OJ C 335, 31.5.1997, p3).



This list contained a large number of herbal medicines and homeopathic substances which had not been originally accounted for prior to the Agency taking over responsibility for the setting of MRLs. Their evaluation had not been foreseen in the overall plans. Indeed their inclusion in the work plan before the extended deadline has now added significantly to the tasks which must be undertaken by the MRL sector.

At the beginning of 1997 recommendations for inclusion of 253 of these substances into Annex I, II, III or IV of Council Regulation (EEC) No 2377/90 had already been adopted. For 49 others, lists of questions requesting additional data/information or clarification of that already provided had been sent to the applicants. In total, at the beginning of 1997 the assessment

of about 300 substances still remained for the CVMP and its Safety of Residues Working Party (SRWP), chaired by Mr Gabriel Beechinor.

The Working Party has established a revised and detailed work plan for the assessment of the outstanding substances to ensure the establishment of MRLs for all remaining defended old substances by the new deadline. Priority was given to those substances for which the dossiers provided were considered inadequate and where additional data needed to be provided by the applicants. For these the target was set to prepare the lists of questions to the applicants by the end of 1997 to allow them sufficient time to prepare the responses and conduct, where necessary, additional studies and to complete the assessment by the Working Party and CVMP well before the deadline of 1 January 2000.

The SRWP has continued to meet 8 times per year with 3 days for each meeting in order to maximise work output. Additional measures to improve procedures, for example streamlining written comments and their consideration, have been agreed on. The average review time for documents was 2 meetings for Annex I or III proposals and 1 meeting for Annex II proposals and proposals for status reports with lists of questions. For the assessment of the about 50 substances of vegetable origin contained in herbal remedies, a separate sub-group was formed by the CVMP in order to streamline their assessment, which is making good progress in these particular evaluations.

The commitments previously given in the 1997 Work Programme, that is to complete the assessment of MRL applications for old products for at least 100 substances, were completed satisfactorily.

As Council Regulation (EC) No 434/97 exempted certain specified substances from the extended transition date in the year 2000, and fixed for them an earlier deadline of 1 January 1998, immediate action after adoption of the Regulation was taken to finalise the assessment of the 5 substances concerned in the time allowed.

The Committee agreed recommendations on 3 topics concerning the elaboration of MRLs and release for consultation position papers on:

- requirements for Limit of Quantification (LOQ)/MRL ratio;
- selection of target tissues for the establishment of MRLs;
- definition of substances capable of pharmacological action in the context of Council Directive 81/851/EEC with particular reference to excipients.

The CVMP has been unable to establish MRLs for some rather important medicinal products because applicants have not provided sufficient data and information in response to questions posed by the Committee. This has arisen where a substance had been accorded a provisional MRL in Annex III of the Regulation and which has expired thereby resulting in the product being withdrawn from the market; in other cases deficiencies were evident in the responses by applicants following the initial assessment by rapporteurs.

In addition, the CVMP prepared a scientific position regarding issues for discussion at Codex Alimentarius, as well as specific scientific aspects related to the draft amendment of Council Regulation (EEC) No 2377/90, for example establishment of MRLs for clinical trials.

## 4.4 CVMP Working Parties

As well as the established working parties on Safety of Residues (see 4.3), Pharmacovigilance, Immunological and Quality (joint CVMP/CPMP), the Efficacy Working Party was reconvened in 1997 as a result of the Committee's decision to review existing guidelines where justified, and to consider new topics where further guidance is required.

### *Efficacy Working Party*

This working party (EWP) was reconvened during the year in order to review the existing efficacy guidelines and also to draw up new guidelines that were considered necessary. The working party met once with Dr L. Kaartinen as chairperson. A work plan has been agreed for the work involved with the priority list of guidelines drawn up by the CVMP.

It is recognised that there is a need for close collaboration with the VICH activities and in particular with the Working Parties on Anthelmintic Efficacy and Good Clinical Practice which are priority topics.

### *Immunologicals Working Party*

The Immunologicals Working Party (IWP) met 4 times in 1997 under the chairmanship of Professor Paul-Pierre Pastoret. Much has been achieved and good progress made in meeting the targets set for the working party at the beginning of the year. Guidelines have been elaborated and adopted by CVMP on the following topics:

- variation assessment reports for immunologicals;
- harmonisation of requirements for authorisation of equine influenza vaccines.

In addition, the Working Party has provided guidance on

- potency testing of biologicals;
- interpretation of "protection" against diseases and "reduction" of clinical symptoms in the context of efficacy claims for vaccines;
- the definition of a new active substance, with regard to biologicals ; and
- the need for compliance with monographs of the European Pharmacopoeia.

Furthermore the IWP is preparing guidance on DNA vaccines and the use of adjuvants in veterinary biologicals.

### *Pharmacovigilance Working Party*

This working party (PhVWP) met twice under the chairmanship of Professor A. Macri. No serious adverse reactions on centrally approved products were brought to the attention of the Committee.

By the end of the consultation period, many comments from various parties had been received on the draft CVMP pharmacovigilance guidelines released by the Committee in October 1996. The Working Party redrafted the guidelines and they were adopted by CVMP at their meeting in July 1997.

An ad hoc working group under the chairmanship of Professor Keck from France met on 3 occasions in the course of the year to elaborate a dictionary of defined terms for veterinary pharmacovigilance, to include system organ classification, clinical terminology and species identity.

The Working Party considered several adverse reaction reports from the competent authorities of some Member States on the use of diazinon solution in dogs, the use of fipronil in dogs resulting in human reactions, and the use of florfenicol concurrently with flunixin in young calves. The limited incidence of such reactions did not in the opinion of the Working Party merit any further action at Community level.

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

Due to the relevance to veterinary interests of numerous topics on the agenda of the Quality Working Party, it was agreed in 1997 that veterinary experts should attend each meeting. Whilst a section on the agenda is still focused on specific veterinary items, more and more of the work is of a similar nature.

During 1997, the Working Party followed the developments of the VICH process with great interest and provided guidance when requested. With regard to general CVMP veterinary guidelines, the Working Party produced a number of concept papers, required before new guidelines can be developed or existing ones revised; these included papers on development pharmaceuticals, process validation and maximum shelf-life for sterile veterinary medicinal products after first opening. The Working Party also finalised the guideline on excipients used in veterinary medicinal products.

## **4.5 Mutual recognition for veterinary medicinal products**

The establishment and first meeting of the Veterinary Mutual Recognition Facilitation Group in April 1997 held at the EMEA has provided a forum for the Member States to discuss applications and has been well received by all participants. The Group is currently chaired by the United Kingdom. As well as issues relating to the assessment of the applications, regulatory points are also discussed by the Group in order to provide a consistent and high quality assessment of submitted dossiers. A Best Practice Guide has been adopted and a list of ideal submission dates has been endorsed for applications to ensure adherence to the strict timetables.

The number of mutual recognition procedures in 1997 was 26 new applications finalised with 1 in progress and 9 pending. With regard to variations, a total of 12 type I variations have been finalised (of which 4 related to ex-‘concertation’ procedures) and 1 type II has been finalised with a further type II in progress. These figures show a steady increase on last year and it must be expected that 1998 will see a sharper increase in the number of applications.



# 5. TECHNICAL CO-ORDINATION ACTIVITIES

## 5.1 Development of the Technical Co-ordination Unit

For Technical Co-ordination 1997 was an important year for preparation of future work developments. Competitions initiated in 1996 came to fruition and new staff have taken up tasks in each of the four sectors, most notably in IT and inspections. The position of Head of Conference Services was filled by Sylvie Bénéfice in August 1997.

The Unit provides technical support to the Agency, mainly to the two Units in charge of medicinal products for human and veterinary use, and to the joint CPMP/CVMP Quality Working Party. Contacts with national agencies were expanding and productive, in particular the Inspectors Meeting as well as regular meetings of the ad hoc Group on Quality of Documents.

Technical Co-ordination co-operates directly with the European Technical Office for Medicinal Products (ETOMEP) from the Commission Joint Research Centre at Ispra and with the European Pharmacopoeia based in Strasbourg (Council of Europe).

## 5.2 Co-ordination of inspections and quality of human and veterinary medicines

### *Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP)*

During 1997 a total of 62 inspections were requested by the CPMP and CVMP in connection with the assessment of 68 applications. 29 inspections were carried out in response to these requests of which 4 inspections were in the EU and 25 in third countries (mainly in the USA). The average time for completion from request to report was 4.1 months.

These inspections were carried out by the Good Manufacturing Practice (GMP) Inspectorates of Belgium, Denmark, Germany, Spain, France, Ireland, Italy, the Netherlands, Portugal, Sweden, and the United Kingdom. They were accompanied by experts from the assessment teams responsible for the application on 13 occasions.

Four ad hoc meetings of EU inspectors were held at which progress with GMP inspections for centralised applications were monitored and harmonisation initiatives progressed. At the end of 1997 agreement has been reached on procedures for co-ordinating inspections and dealing with inspection findings

5.1 Development of the Technical Co-ordination Unit

5.2 Co-ordination of inspections and quality of medicines

5.3 Document management and publishing

5.4 Conference and linguistic support

5.5 Information technology

5.6 ETOMEP

on a guideline for preparing inspection reports and a community format for inspection reports.

The development of a strategy on Good Clinical Practice (GCP) inspections has started, together with the development of harmonised Community procedures of GCPs.

#### *Certification of medicinal products*

The system for issuing certificates which confirm the status of medicinal products authorised under the centralised system and GMP compliance of the sites where they are manufactured has been operating since July 1996. These certificates are in compliance with the World Health Organisation recommendations.

The demand for these certificates increased during 1997 to a total of 3 364 individual certificates being issued in 1 087 sets. These were requested by 15 marketing authorisation holders for 115 countries. The average response time to issue certificates was 4.5 days.

Improvements were made to streamline the process by which certificates are produced and in their detailed content following suggestions by user companies.

During October the EMEA collaborated with EFPIA and other interested parties in a workshop to review the performance of the certification system and identify areas for improvements. This will be followed up by regular reviews with interested parties of the performance of the system.

Certificates issued by the EMEA have to be legalised to make them acceptable in the destination country. Since the start of the system this has been carried out by notaries and institutions in EU Member States. Following a decision by the European Commission in July arrangements have been made for the Commission's delegation in London to legalise certificates.

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

The Joint CPMP/CVMP Quality Working Party met on three occasions during the year under the Chairmanship of Dr Jean-Louis Robert. The meetings cover a wide range of quality topics for veterinary and human medicinal products. The attendance of veterinary experts has now been extended to all meetings of the Committee.

The working party continued the development and revision of CPMP guidelines and also provided support for the EU topic leaders in both ICH and VICH expert working groups and for the provision of scientific advice by the CPMP and CVMP.

Work continues on a number of guidelines including those on prolonged release products, development pharmaceuticals and process validation.

Reference number	Title of guideline	Status
CPMP/CVMP/QWP/115/95	The use of antioxidants and preservatives in medicinal products	Adopted in July 1997
CPMP/ICH/283/95 (Q3C)	Impurities: residual solvents	Adopted in September 1997
CPMP/ICH/367/96 (Q6A)	Specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances	Released for consultation in September 1997
CPMP/QWP/556/96	Stability testing of existing active substances and related finished products	Released for consultation in March 1997
CPMP/QWP/576/96	Stability testing for variation to a marketing authorisation type II	Released for consultation in March 1997
CPMP/QWP/130/96	Chemistry of the new active substance	Released for consultation in April 1997
CPMP/QWP/297/97	Summary of requirements to active substances in part II of the dossier	Released for consultation in April 1997
CPMP/QWP/159/96	Maximum shelf-life for sterile products for human use after first opening or following reconstitution	Re-released for consultation in June 1997
CPMP/QWP/609/96	Declaration of storage conditions for medicinal products	Released for consultation in June 1997
CPMP/QWP/157/96	Reduced stability testing - bracketing and matrixing	Adopted in November 1997
CPMP/QWP/158/96	Note for guidance on dry powder inhalers	Released for consultation in October 1997

### 5.3 Document management and publishing

During 1997 the focus of interest for the sector for documentation and archiving moved towards document management and publishing.

The main activities of the sector are to ensure the continuation of the co-ordination of quality management of routine operations in support of the Agency's functioning in the areas of product information quality, translations, coherence of regulatory documents (templates and opinions), document management, document dissemination (production and distribution), library services, mail services and archiving.

#### *Product information quality*

In its third year of co-operation with the Translation Centre in Luxembourg, the EMEA had 5 770 pages translated for a total of 220 documents. The progress in standardisation at the EMEA allowed the use of templates for most scientific opinion documents. The timeliness and quality of the translations was closely monitored in order to provide feedback to the Translation Centre in a common effort to satisfy user demands.

In 1997, the EMEA participated in 3 working groups organised by the Translation Centre and attended by representatives of all agencies. The purpose was to agree a billing system of payment for performed work. Common quality

problems were also discussed. A software package for terminological databases was introduced at the Translation Centre and tested at the EMEA.

The Working Group on the Quality Review of Documents finalised and adopted 26 document templates and linguistically reviewed 29 CPMP/CVMP opinions during the 7 meetings the Group held during 1997.

#### *Document management*

As part of the migration from Apple MacIntosh to IBM-compatible personal computers, the organisation of data on shared working areas according to the work processes in the Agency began. Furthermore, work was done to improve version control and minimise duplication of documents.

The improvement of the use of IT tools made it possible to manage business data and electronic documents, to use provided IT tools better, for example calendar, e-mail, to organise work flow and forward documents. The core and key support processes of the Agency were identified and mapped.

With the subscription service, the EMEA aims to provide a reliable and professional service, supplying subscribers with documents, and their updates, in a timely and automatic manner. Users are able to obtain documents systematically either through the Internet (immediate access) or in paper format (monthly mailings). An administrative charge is made to cover handling, mailing and maintenance costs. Many documents are in fact free of charge and this practice will continue. However, a reasonable charge is requested for documents of 30 pages or more in accordance with Commission policy.

Recognising the multicultural nature of the EU, efforts are made to make documents available in different EU official languages, including on the Internet. The subscription service offers a second language version of documents free of charge where they are available.

#### *EMEA Website and Mail services*

The number of documents contained on the EMEA Website increased to over 550 in 1997. Over 4 million 'hits' (requests for information) were recorded and some 120 000 documents were downloaded in total, of which EPARs and guidelines were the most frequently demanded.

	1995	1996	1997
<b>Mail in</b>	7,350	27,218	36,419
<b>Mail out</b>	n/a	13,323	36,330

The mail services continued to increase strongly over the previous year.

#### *Library*

The library acts as a reference library for EMEA staff and delegates and increased its collection by 60 per cent compared with the previous year. The collection consists mainly of technical and scientific publications (monographs, journals, magazines and newspapers) and official publications of the EU. An effort is made to access more and more information electronically either via the Internet or via specialised databases.

## 5.4 Conference services and linguistic support

The Sector for Conference services provides for an interface between EMEA and delegates participating in meetings.

### *Meeting activity*

Conferences activity at the EMEA expanded in 1997 to reach a total of 173 statutory meetings carried out over 292 days. Numerous external organisations and delegations were invited to take part in a further 32 meetings over 37 days, bringing the total to 205 meetings and 329 meeting days. Together with an experienced pool of external conference support staff, the Sector managed to provide all necessary services to these meetings, as well as assuring the travel arrangements for the majority of delegates attending the meetings.

Interpretation needs were reviewed critically in order to tailor its provision to the real needs and expectations of delegates. As a consequence, the provision of interpretation now takes into account better the specific needs of each meeting.

### *Reimbursement, travel and hotel services*

The calculation of travel reimbursements for 2 024 delegate visits was processed within the target time of two weeks. Improved co-operation with national authorities allowed closer monitoring of expenses. A daily allowance cash payment introduced last year on arrival of delegates to the Agency was a real success in terms of reimbursement improvement while minimising the administrative overhead.

Almost 90 per cent of delegates were able to use the EMEA travel and accommodation services and assistance consistently throughout the year. At the request of the delegates, the choice of hotels with agreed EMEA rates was expanded into central London. A new issue of the delegates' manual provided updated information on travel, accommodation, the environment of the Agency and on useful services in London.

### *Reprographics*

Towards the end of the year the reprographics service was relocated but kept in the immediate vicinity of the main meetings.

The number of photocopies produced by Reprographics mainly in support of meetings reached 6 600 000 and made up for 73 per cent of the Agency's total. Division among Units was as follows:

•Human Medicines Unit	60.94%
•Veterinary Medicines Unit	12.63%
•Directorate and Administration	6.90%
•Conferences	5.06%
•Document Management	5.91%
•Inspections	3.50%

*Picture "Reprographics"*

The workload reflected the cyclical activity pattern of the EMEA: about 15 000 on routine days and 130 000 copies per day during CPMP meetings.



*Picture "VideoConference"*

#### *Video-conferencing*

Video-conferencing was increasingly introduced for routine consultations with the European Commission and for small meetings with industry and other partners of the EMEA. It proved to be a successful tool in securing external participation at large meetings taking place in the main conference rooms.

## **5.5 Information technology**

The mission of the Sector for Information technology is to ensure effective IT support to the daily operation and anticipate future business needs of the EMEA.

An IT strategy was adopted and introduced the concept of structured development of projects, requiring strong user involvement as well as a systematic and documented development and implementation cycle. The development plan included the following projects:

- new IT architecture;
- office system;
- development environment;
- corporate database;
- document management and work flow;
- application tracking system (ATS).

#### *Production support*

The production system could be kept up to support most operational needs. As anticipated, the limits of the system were reached in 1997. From July onwards, new Windows NT4 workstations were gradually introduced. Following the implementation of a new approach to resolving user problems, the number of monthly help desk calls was drastically reduced, illustrating the effect of standardisation and training provided to users.



*Picture "Computer Room"*

#### *New IT architecture*

Preparation for and implementation of a new Windows NT4-based IT architecture together with a range of supporting systems such as Microsoft Office 97, e-mail and Web access with high-level security was the heaviest task for the year. After specifications were completed and solutions for the many technical issues found, careful project management allowed installation without disruption of any production task of the EMEA. Three pilot phases were defined, each with formal acceptance criteria before the new set-up was phased in throughout the organisation as a whole. At the same time together with a large group of users a new business driven data storage structure was developed to which all

relevant data were migrated, ensuring secure access for all staff involved in the many functions that the EMEA performs.

In preparation for the new environment much attention was given to training in order to allow staff to prepare for the new environment, rapidly change to the new system and be able to operate it. To facilitate joint learning a training room was set up with 17 workstations. This same facility was also successfully used to train multi-user operation of distributed applications like EudraTrack and EudraWatch in training sessions for EMEA and Member State agencies. An internal forum for progressing user issues, the EMEA IT User Group, was set up.

### *New applications*

- ATS –the application tracking system – was further developed together with the ATS development team, composed of staff from ETOMEP and EMEA. Version 1 was available throughout the year and was successfully used by a small group of project managers. Their experience and additional requests lead to the development of version 2 for which all project managers were trained.
- ‘ActiTrak’ is designed to track time spent per task. Several sectors in different units used the application to determine the default task patterns to be loaded to the system.
- SI2 – the budget management system developed by the European Commission (DG XIX) – was provisionally installed and operational procedures were reviewed. Interaction with other European Agencies, especially the European Training Foundation in Turin, was intensified in support of the implementation of a production version of the system.
- ‘EudraWatch’ (pharmacovigilance database) was installed during the year and thoroughly tested. Acceptance testing together with Member States was completed. At the end of the year, the system was handed over from the Commission to the EMEA for operation.
- Active participation to the ‘EudraNet’ working party, especially in the definition and preparation of the network between all national agencies, contributed to the setting of time targets for this critically important project to be fully operational in 1998.



## **5.6 European Technical Office for Medicinal Products - ETOMEP**

The European Commission Joint Research Centre at Ispra has established a technical office at the Agency in charge of setting up a telecommunications network and other computer technologies to facilitate the dissemination of information on medicinal products – EudraNet (European Union Drug Regulatory Authorities Network) – which is an inter-networking service provided to EU Medicinal Regulatory Authorities in collaboration with the European Commission Directorate-General III. It will be opened to industry and the general public.

### *Network support: EudraNet*

During the first half of 1997, the existing ISDN-based network was completely installed in all EU regulatory authorities dealing with human and veterinary medicines. The link between the EudraNet London node and the JRC Ispra node is now based on "Frame Relay" (with an ISDN backup), as well as the link between London and the European Commission (DG III) in Brussels.

Performance system acceptance tests have been performed both on the backbone and on a number of end-user sites, giving good results. Firewall systems have been installed both in London and Ispra to protect the backbone services and are operated by the ETOMEPE team.

The help desk became fully operational in May 1997 and is accessible via phone, fax, e-mail and through a Web-based form. Software for the management of the Help Desk has been developed in-house and is regularly updated. Reporting is available to EudraNet users on the Intranet Web pages.

During the second half of 1997, discussions started between EudraNet users about the improvement of the communication layer from ISDN to Frame Relay services provided by a single character (GlobalOne) within the framework of the TESTA (Trans-European Services for Telematics between Administrations) initiative, managed by DG III/IDA. In the meantime, the implementation of Phase II of EudraNet (connection of local authority IT infrastructure with EudraNet) is progressing.

### *Support to EMEA activities*

Support to the European Agency for the Evaluation of Medicinal Products is mainly focused on the provision of the Web services publicly accessible through the Internet.

A major revision of the existing services is going on and the new site is expected to be available in 1998 to give more and better services to end-users.

A subscription service has been developed and put into operation to allow automatic distribution of EMEA documents as soon as they are released.

Network services (domain name management and Internet access) are operated by ETOMEPE as well as electronic mail services (X.400 and SMTP). Integration of these services with the new IT architecture (based on WinNT) is going on and will be fully available by the completion of the migration period.

# 6. ADMINISTRATION AND BUDGET

## 6.1 Personnel and support services

## 6.2 Budgetary control

### 6.1 Personnel and support services

#### *Personnel of the EMEA Secretariat*

The Secretariat of the Agency is primarily responsible for providing administrative and technical support to the Management Board, Scientific Committees and their Working Parties.

The Agency does not have permanent officials. Staff are recruited through open competitions and are offered five-year renewable contracts as Temporary Agents. Recruitment to the Agency follows the rules and practices of the EU institutions. Once selected by an independent selection board, candidates are placed on a reserve list from which they may be selected for a post in line with the staffing needs of the Agency.

The Agency's staff has substantially increased having grown from the 67 persons serving at the end of 1995 to a total of 143 at the end of 1997, in addition to 2 national experts on secondment and 9 external staff.

<b>EMEA Staff</b>	<b>31.12.1995</b>	<b>31.12.1996</b>	<b>31.12.1997</b>
A			
- temporary agents	15	45	70
- auxiliary staff	14	1	2
B	8	17	21
C and D	13	37	50
Total EMEA staff	50	100	143

National experts on secondment	0	3	2
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External interim staff	17	10	9
------------------------	----	----	---

The new Head of Sector for CVMP and Veterinary Procedures and Head of Sector for Conferences took up their duties in the course of the year. Twelve recruitment procedures were also initiated to recruit staff for positions as scientific administrators as well as a number of technical positions.

There is no quota system for the nationals of each Member State, but the Agency seeks to respect the balance of nationalities of the European Union. Staff come from throughout the European Union and all nationalities are represented, including 1 external interim staff from Luxembourg.

<b>Nationalities</b>	<b>B</b>	<b>DK</b>	<b>D</b>	<b>EL</b>	<b>E</b>	<b>F</b>	<b>IRL</b>
A	6	2	7	3	6	11	6
B	5	1	2	2	1	2	0
C	4	1	5	3	2	9	1
D	0	0	0	0	0	0	1
Total temporary and auxiliary agents	15	4	14	8	9	22	8
National experts	0	1	0	0	0	1	0
Interims	0	0	1	0	1	0	0
<b>TOTAL</b>	<b>15</b>	<b>5</b>	<b>15</b>	<b>8</b>	<b>10</b>	<b>23</b>	<b>8</b>
<b>Nationalities</b>	<b>I</b>	<b>NL</b>	<b>A</b>	<b>P</b>	<b>FIN</b>	<b>S</b>	<b>UK</b>
A	8	2	2	2	1	2	13
B	1	1	0	0	0	0	6
C	3	1	0	1	3	1	12
D	0	0	0	1	0	0	2
Total temporary and auxiliary agents	12	4	2	4	4	3	33
National experts	2	0	0	0	1	0	0
Interims	0	0	0	0	1	1	13
<b>TOTAL</b>	<b>14</b>	<b>4</b>	<b>2</b>	<b>4</b>	<b>6</b>	<b>4</b>	<b>46</b>

The first national experts on secondment came to the EMEA in 1996. During 1997 experts from Denmark, Italy and Finland returned to their national authorities. The French authorities extended the secondment of one expert, who was joined in the second half of 1997 by 1 new national expert from the Italian authorities.

New staff on arrival receive an extensive, individual briefing about their employment conditions. The Administration Unit holds periodic general information sessions for staff about employment rules. Representatives from Commission Directorate-General IX (Personnel and Administration) have addressed EMEA staff on medical insurance and pensions. These two services are carried out centrally by DG IX on behalf of all EU decentralised agencies.

### *Personnel initiatives*

The Welcome Partner Programme, begun in March 1996, is part of a range of personnel initiatives to support new staff whereby a colleague is nominated to assist the newcomer during the initial period at the Agency.

At the beginning of 1997 Administration introduced a questionnaire about the services provided to new staff. The responses demonstrate that the nature and range of services for new staff meet their needs. The comments enabled Administration to fine-tune its operations to respond better to the requirements of these staff members at a difficult time when starting a new job, often having also moved country.

An introduction training programme, first begun in 1996, was made systematic in 1997. This programme aims at giving new members of staff an overview and appreciation of the activities of all Units and how they all fit together.

To complement this initiative and to enable staff to keep up to date on the activities in other areas, periodic information lectures were introduced in 1997 to allow each Unit to give a presentation of its work and recent developments.

As part of the EMEA commitment to Quality Management, training courses for a large number of senior management staff and project managers were held in 1997. This training has benefited staff in making clear the nature of the managerial role and responsibilities and how to deal with cultural differences. Since EMEA staff come from a wide range of backgrounds the training has contributed to the emergence of a common management approach.

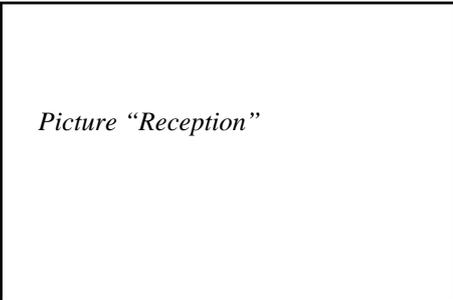
Some 23 staff members participated in language training courses held locally during 1997 and language training materials are now available in all eleven official EU languages.

### *EMEA facilities management*

The reprographics room on the fourth floor was relocated to provide extra space for additional computer equipment as a result of the changeover to the new information technology architecture. The new reprographics space remains close to the main meeting rooms and delegates' facilities.

Security of information and of the EMEA premises remains a high priority. As part of the modifications to the fourth floor a security office within the reception area was installed to provide better security coverage of visitors and for staff working on this floor.

As part of the development of a health and safety policy, a risk assessment was carried out during 1997. Details of the health and safety policy were circulated to all staff, in accordance with the legal provisions in force. In addition, changes in working practices were discussed and agreed with staff and relevant equipment provided where necessary.



*Picture "Reception"*

## 6.2 Budgetary control

The main EMEA accounting principles are as follows:

The accounts are kept in accordance with the requirements of the Financial Regulation (as last amended on 5 February 1997, EMEA/MB/011/97).

Accounts are kept in ECU, the revenue and expenditure account and the balance sheet are presented in ECU. Operations settled in currencies other than ECU are booked at the monthly accounting rates in force when they were transacted. The ECU exchange rates used for the preparation of the balance sheet are those applicable on 31 December.

The revenue of the financial year is the revenue collected in the year, with the exception of fees received, which are initially booked to a suspense account and subsequently accounted for as income when it is definitely established that the amount received is due.

The payments made in the financial year are those for which authorisation reaches the Financial Controller not later than 31 December and which are effected by the Accounting Officer not later than 15 January of the following year.

Certain appropriations may be carried over to the following financial year only, under strict conditions laid out in the Financial Regulations.

With a view to formulating an analytical approach to accounting, expenditure under each item of the EMEA budget was examined during 1997. This will assist the Agency to review its expenditure and to relate costs to its activities. An analysis has been developed for staff and operational expenses. These costs have been attributed to the two scientific units so that the overall costs for the human and veterinary activities can be determined and linked to the services provided.

The development of an analytical approach to accounting was begun in 1997. This is intended as a tool to assist the EMEA not only in reviewing its expenditure, but also to help relate the Agency's costs to its different activities. Costs under each item of the EMEA budget have been allocated to the Human and Veterinary Medicines Evaluation Units so that the overall costs for the activities can be determined and linked to the services provided.

Work continued in 1997 on the development of a computerised budgetary accounting system for the Agency, pending completion of which the current spreadsheet analysis will continue to be used. The system, initially developed and made available by the European Commission, requires considerable adjustment to make it suitable for the specificities of European financial and budgetary regulations.

On the operational side, a secure electronic banking link was established during the year through which information can be received and transactions executed. The introduction of a centralised, secure payee database resulted in a marked improvement in payments for all Units, including the payment of fees to national competent authorities.

# ANNEXES

1. Membership of the Management Board
2. Membership of the Committee for Proprietary Medicinal Products
3. Membership of the Committee for Veterinary Medicinal Products
4. National competent authority partners
5. Organigram of the EMEA Secretariat
6. EMEA budgets 1995 to 1997
7. CPMP opinions in 1997 on medicinal products for human use
8. CVMP opinions in 1997 on medicinal products for veterinary use
9. Reference documents



## Annex 1

### MEMBERSHIP OF THE MANAGEMENT BOARD

#### Chairman

Strachan HEPPELL

#### European Parliament

Gianmartino BENZI  
Dietrich HENSCHLER  
*Alternates*

Dame Roselinde HURLEY  
Jean-Pierre REYNIER

#### European Commission

Stefano MICOSSÌ  
.....<sup>(1)</sup>

#### Belgique/België

Jean-Pierre DEROUBAIX  
Michel CHOJNOWSKI

#### Danmark

Ib VALSBORG  
Mogens BJØRNBACK-HANSEN<sup>(2)</sup>

#### Deutschland

Hermann Josef PABEL  
Gerhard Josef KOTHMANN

#### /Greece

Stavros KAZAZIS<sup>(3)</sup>  
Nikolaos KOKOLIS

#### España

Ana María NAVEIRA NAVEIRA  
Valentín ALMANSA SAHAGÚN

#### France

Didier TABUTEAU<sup>(4)</sup>  
Jacques BOISSEAU

#### Ireland

Tom MOONEY  
Seamus HEALY<sup>(5)</sup>

#### Italia

Luigi FRATI<sup>(6)</sup>  
Romano MARABELLI (Vice-Chairman)

#### Grand-Duché du Luxembourg

Mariette BACKES-LIES

#### Nederland

André BROEKMANS  
Christian VAN DER MEIJS

#### Österreich

Alexander JENTZSCH  
Ernst LUSZCZAK

#### Portugal

José António ARANDA DA SILVA  
Maria Armanda MIRANDA

#### Suomi/Finland

Mauno LINDROOS<sup>(7)</sup>  
Hannes WAHLROOS

#### Sverige

Birgitta BRATTHALL  
Anders BROSTRÖM

#### United Kingdom

Keith JONES  
Michael RUTTER

<sup>(1)</sup> Awaiting nomination of new member.

<sup>(2)</sup> Mogens Bjørnback-Hansen was replaced by Ib Bo LUMHOLTZ as of the 4 July 1997 meeting.

<sup>(3)</sup> Stavros Kazazis was replaced by Gerasimos KAVVADIAS as of the 4 July 1997 meeting.

<sup>(4)</sup> Didier Tabuteau was replaced by Jean-René BRUNETIÈRE as of the 3 December 1997 meeting.

<sup>(5)</sup> Seamus Healy was replaced by John Albert COSTELLOE as of the 4 July 1997 meeting.

<sup>(6)</sup> Luigi Frati was replaced by Vittorio SILANO as of the 5 February 1997 meeting.

<sup>(7)</sup> Mauno Lindroos was replaced by Kimmo LEPPÖ as of the 1 October 1997 meeting.

## Annex 2

### MEMBERSHIP OF THE COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS

#### Chairman

Prof. Jean-Michel ALEXANDRE

#### Belgique/België

Mr Geert DE GREEF  
Dr Luk BLONDEEL <sup>(1)</sup>

#### Danmark

Mr Henning HOVGAARD (Vice-Chairman)  
Dr Gorm B. JENSEN

#### Deutschland

Prof. Alfred HILDEBRANDT  
Prof. Reinhard KURTH

#### /Greece

Prof. Marios MARSELOS  
Mrs Julia YOTAKI

#### España

Ms Carmen COLLADO ALVAREZ <sup>(2)</sup>  
Prof. Fernando de ANDRES-TRELLES

#### France

Dr Patrick LE COURTOIS <sup>(3)</sup>  
Prof. Jean-Hughes TROUVIN

#### Ireland

Dr Mary TEELING  
Dr David LYONS

#### Italia

Prof. Giuseppe VICARI  
Prof. Vittorio SILANO <sup>(4)</sup>

#### Grand-Duché du Luxembourg

Dr Jean-Louis ROBERT  
Ms Jacqueline GENOUX-HAMES

#### Nederland

Dr Hans van BRONSWIJK  
Mr Willem van der GIESEN

#### Österreich

Dr Heribert PITTNER <sup>(5)</sup>  
Dr Walter FUCHS <sup>(5)</sup>

#### Portugal

Prof. José GUIMARAES MORAIS  
Dr Henrique LUZ-RODRIGUES <sup>(6)</sup>

#### Suomi/Finland

Dr Christer STROMBERG <sup>(7)</sup>  
Dr Eeva ALHAVA

#### Sverige

Prof. Kjell STRANDBERG  
Dr Per SJOBERG

#### United Kingdom

Dr David JEFFERYS  
Dr Susan WOOD

- (1) Dr Luk Blondeel was replaced by Prof. Jean-Marie Boyenaems as of the 20 January 1997 meeting, who was in turn replaced by Dr Daniel BRASSEUR as of the 20 October 1997 meeting.
- (2) Ms Carmen Collado Alvarez was replaced by Mr José Félix OLLALA MARAÑÓN as of the 17 March 1997 meeting.
- (3) Dr Patrick Lecourtois was replaced by Dr Eric ABADIE as of the 22 September 1997 meeting.
- (4) Prof. Vittorio Silano was replaced by Prof. Silvio GARRATTINI as of the 17 March 1997 meeting.
- (5) Dr Heribert Pittner was replaced by Prof. Hans WINKLER as of the 22 September 1997 meeting and Dr Walter Fuchs was replaced by Dr Christa WIRTHUMER-HOCHE as of the 16 June 1997 meeting.
- (6) Dr Henrique Luz-Rodriguez was replaced by Prof. Miguel FORTE as of the 21 July 1997 meeting.
- (7) Dr Christer Stromberg was replaced by Dr Markku TOIVONEN as of the 16 June 1997 meeting.

## Annex 3

### MEMBERSHIP OF THE COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

#### Chairman

Prof. Dr Reinhard KROKER

#### Belgique/België

Prof. Paul-Pierre PASTORET  
Mrs Françoise FALIZE

#### Danmark

Ms Birgitte KRISTENSEN <sup>(1)</sup>  
Dr Claus WILLADSEN <sup>(1)</sup>

#### Deutschland

Dr Sabine EGLIT  
Prof. Manfred MOOS

#### /Greece

Prof. Vassilios ELEZOGLOU  
Mr Dimistrios MIGOS

#### España

Dr Luis Fernando CORBALAN  
Dr Odon SOBRINO

#### France

Dr Jacques BOISSEAU  
Dr Dominique MOUROT <sup>(2)</sup>

#### Ireland

Mr Cyril O'SULLIVAN  
(Vice-Chairman)  
Mr Gabriel BEECHINOR

#### Italia

Prof. Agostino MACRI  
Dr Gabriella CONTI

#### Grand-Duché du Luxembourg

Mr Marc WIRTOR  
Dr Albert HUBERTY

#### Nederland

Dr Herman H. LENSING  
Dr Peter HEKMAN

#### Österreich

Mgr Eugen OBERMAYR  
Dr Johannes DICHTL

#### Portugal

Dr Margarida PRATAS  
Dr José BELO

#### Suomi/Finland

Dr Liisa KAARTINEN  
Docent Satu PYÖRÄLÄ

#### Sverige

Dr Annika WENNBERG  
Prof. Jan LUTHMAN

#### United Kingdom

Dr Michael RUTTER  
Dr Kevin WOODWARD <sup>(3)</sup>

<sup>(1)</sup> Ms Birgitte Kristensen was replaced by Ms Anne PII as of the 14 January 1997 meeting, and Dr Claus Willadsen was replaced by Prof. Christian FRIIS as of the 15 July 1997 meeting.

<sup>(2)</sup> Dr Dominique Mourot was replaced by Mr Gérard MOULIN as of the 08 April 1997 meeting.

<sup>(3)</sup> Dr Kevin Woodward was replaced by Dr Jill Ashley-Smith as of the September 1996 meeting, who was in turn replaced by Mr John O'BRIEN as of the 15 July 1997 meeting.

## **Annex 4**

### **NATIONALCOMPETENTAUTHORITYPARTNERS**

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## Annex 5

### ORGANIGRAM OF THE EMEA SECRETARIAT

#### Directorate

Executive Director	Fernand Sauer
Financial control (a.i.)	Claus Christiansen

#### Administration Unit

Head of Unit	Marino Riva
Personnel and support services	Frances Nuttall
Accounting	Gerard O'Malley

#### Evaluation of Human Medicines Unit

Head of Unit	Rolf Bass
Regulatory affairs and pharmacovigilance	Noël Wathion
Biotechnology and biologicals	John Purves
New chemical substances	Josep Torrent Farnell

#### Evaluation of Veterinary Medicines Unit

Head of Unit	Peter Jones
CVMP and veterinary procedures	Jill Ashley-Smith
Safety of residues (MRLs)	Kornelia Grein

#### Technical Co-ordination Unit

Head of Unit	Karel de Neef
Inspections	Stephen Fairchild
Documentation and archiving	Beatrice Fayl
Conferences	Sylvie Bénédicte
Information technology	....

## Annex 6

### EMEABUDGETS1995TO1997

The summarised comparative budget statements for 1995 to 1997 are as follows:

	1995	1996	1997
<b>Revenues</b>			
European Community subsidy	10 150 000	13 750 000	14 000 000
Evaluation fees	4 000 000	8 600 000	14 000 000
Miscellaneous revenue	262 000	200 000	530 000
<b>Total revenue</b>	<b>14 412 000</b>	<b>22 550 000</b>	<b>28 530 000</b>
<b>Expenditure</b>			
1. Staff costs			
- staff salaries and allowances	2 902 000	7 495 000	11 284 000
- other staff costs	1 164 000	1 565 000	1 505 000
Total staff costs	<u>4 066 000</u>	<u>9 060 000</u>	<u>12 789 000</u>
2. Building equipment & other internal costs			
- Fitting out, lease & other building related costs	2 420 000	2 205 000	2 375 000
- IT, data processing	930 000	1 900 000	900 000
- Other current administrative expenditure	1 396 000	1 150 000	1 126 000
Total internal costs	<u>4 746 000</u>	<u>5 255 000</u>	<u>4 401 000</u>
3. Operational and expertise related costs			
- Committee meetings	1 540 000	2 210 000	2 010 000
- Fees of rapporteurs and experts	3 550 000	5 250 000	7 630 000
Total operational and expertise costs	<u>5 090 000</u>	<u>7 460 000</u>	<u>9 640 000</u>
4. Luxembourg Translation Centre	<u>500 000</u>	<u>735 000</u>	<u>1 400 000</u>
5. Publishing and information	<u>10 000</u>	<u>40 000</u>	<u>300 000</u>
<b>Total expenditure</b>	<b>14 412 000</b>	<b>22 550 000</b>	<b>28 530 000</b>

## Annex 7

### CPMPOPINIONSIN 1997 ON MEDICINAL PRODUCTS FOR HUMAN USE

<b>Product</b> a) Brand name b) INN c) Part A/B	<b>Company</b> a) Name b) Origin	<b>Therapeutic Area</b> a) ATC b) Indication	<b>Presentation</b> a) Form b) Dose c) Number of Presentations	<b>EMEA/CPMP</b> a) Validation b) Opinion c) Active Time d) Clock stop	<b>Commission</b> a) Opinion received on b) Date of decision c) Date of notification d) OJ No.
a) <b>NeoRecormon</b> b) epoetin beta c) Part A	a) Boehringer Mannheim b) DE	a) B03XA b) Antianaemic	a) Powder for injection b) 500, 1000, 2000, 5000, 10.000, 50.000, 100.000 IU c) 42 Presentations	a) 01.11.95 b) 16.10.96 c) 209 Days d) 140 Days	a) 08.01.97 b) 16.07.97 c) 17.07.97 d) OJ No.C 263/3 of 29.08.97
a) <b>Insuman</b> b) insulin human c) Part A	a) Hoechst AG b) DE	a) A10A b) Diabetes mellitus	a) Solution for Injection Suspension for Injection Solution for Infusion b) 40 IU/ml 100 IU/ml c) 27 Presentations	a) 06.12.95 b) 16.10.96 c) 158 Days d) 182 Days	a) 28.11.96 b) 21.02.97 c) 24.02.97 d) OJ No C 100/20 of 26.03.97
a) <b>Twinrix paediatric</b> b) comb. vaccine c) Part A	a) SmithKline Beecham b) BE	a) J07BC b) Immunisation against Hepatitis A/B in children	a) Suspension for injection b) c) 5 Presentations	a) 21.05.96 b) 16.10.96 c) 132 Days d) 35 Days	a) 29.11.96 b) 10.02.97 c) 11.02.97 d) OJ No. C 63 of 28.02.97
a) <b>Vitrasert implant</b> b) ganciclovir c) Part B	a) Chiron b) USA	a) J05AB06 b) Treatment of CMV reinitis in patient with AIDS	a) Tablet b) 4.5-6.4 mg c) 1 Presentation	a) 20.01.96 b) 20.11.96 c) 183 Days d) 119 Days	a) 07.01.97 b) 18.03.97 c) 19.03.97 d) OJ No C 129/4 of 25.04.97

<b>Product</b>	<b>Company</b>	<b>Therapeutic Area</b>	<b>Presentation</b>	<b>EMA/CPMP</b>	<b>Commission</b>
a) Brand name b) INN c) Part A/B	a) Name b) Origin	a) ATC b) Indication	a) Form b) Dose c) Number of Presentations	a) Validation b) Opinion c) Active Time d) Clock stop	a) Opinion received on b) Date of decision c) Date of notification d) OJ No.
a) <b>Avonex</b> b) interferon beta c) Part A	a) Biogen b) USA	a) LO3A A b) Immunostimulating agent	a) Powder for injection b) 30 mg/vial c) 1 Presentation	a) 01.06.95 b) 20.11.96 c) 216 Days d) 307 Days	a) 07.01.97 b) 13.03.97 c) 13.03.97 d) OJ No C 100/20 of 27.03.97
a) <b>Refludan</b> b) lepirudin c) Part A	a) Behringwerke AG b) DE	a) B01AX b) Anti-coagulation therapy for heparin-associated thrombocytopenia	a) Powder for injection or infusion b) 50 mg c) 1 Presentation	a) 15.01.96 b) 20.11.96 c) 200 Days d) 112 Days	a) 09.01.97 b) 13.03.97 c) 14.03.97 d) OJ No 100/20 of 27.03.97
a) <b>Vistide</b> b) cidofovir c) Part B	a) Gilead b) USA	a) J05 .... b) Treatment of CMV reinitis in patient with AIDS	a) Concentrate for infusion b) 375 mg c) 1 Presentation	a) 16.01.96 b) 18.12.96 c) 209 Days d) 112 Days	a) 22.01.97 b) 23.04.97 c) 12.05.97 d) OJ No 163/10 of 30.05.97
a) <b>Liprolog</b> b) insulin lispro c) Part A	a) Lilly Industries b) USA	a) A10AB04 b) Diabetes mellitus	a) Solution for injection b) 40 IU/ml vials 100 IU/ml vials + Cartridges c) 3 Presentations	a) 28.10.96 b) 18.12.96 c) 48 Days d) 0 days	a) 22.01.97 b) 07.05.97 c) 09.05.97... d) OJ No C 163/10 of 30.05.97
a) <b>Orlaam</b> b) levacetylmethadol c) Part B	a) BRI International b) BE	a) b) Substitution maintenance treatment of opiate addiction	a) Aqueous solution for oral use b) 10 mg/ml c) 1 Presentation	a) 01.01.95 b) 22.01.97 c) 201 Days d) 487 Days	a) 10.03.97 b) 01.07.97 c) 02.07.97 d) OJ No.C 226/6 of 25.07.97

<b>Product</b> a) Brand name b) INN c) Part A/B	<b>Company</b> a) Name b) Origin	<b>Therapeutic Area</b> a) ATC b) Indication	<b>Presentation</b> a) Form b) Dose c) Number of Presentations	<b>EMA/CPMP</b> a) Validation b) Opinion c) Active Time d) Clock stop	<b>Commission</b> a) Opinion received on b) Date of decision c) Date of notification d) OJ No.
a) <b>Cystagon</b> b) cysteamine c) Part B	a) Orphan Sarl b) FR	a) b) Nephropathic cystinosis	a) Capsule b) 50 mg, 150 mg c) 2 Presentations	a) 15.02.96 b) 19.02.97 c) 176 Days d) 181 Days	a) 25.03.97 b) 23.06.97 c) 24.06.97 d) OJ No.C 329/7 of 31.10.97
a) <b>Teslascan</b> b) mangafodipir c) Part B	a) Nycomed b) NO	a) V08CA05 b) Detection and characterisation of liver lesions	a) Solution of injection b) 0.01 mmol/ml c) 2 Presentations	a) 22.07.96 b) 19.02.97 c) 171 Days d) 27 Days	a) 25.03.97 b) 22.05.97 c) 25.05.97 d) OJ No C 197/4 of 27.06.97
a) <b>Revasc</b> b) desirudin c) Part A	a) Ciba-Geigy b) CH	a) B01AX b) Antithrombotic	a) Powder for injection b) 15 mg c) 1 Presentation	a) 10.07.95 b) 19.03.97 c) 181 Days d) 398 Days	a) 15.04.97 b) 09.07.97 c) 10.07.97 d) OJ No.C 226/6 of 25.07.97
a) <b>Tasmar</b> b) tolcapone c) Part B	a) Hoffmann-La Roche b) CH	a) N04BX01 b) Use in Parkinson disease	a) Tablets b) 100 mg, 200 mg c) 6 Presentations	a) 18.06.96 b) 19.03.97 c) 170 Days d) 90 Days	a) 23.04.97 b) 27.08.97 c) 27.08.97 d) OJ No.C 292/2 of 26.09.97
a) <b>Helicobacter Test INFAI</b> b) <sup>13</sup> C-urea c) Part B	a) INFAI b) DE	a) VO4CX b) Helicobacter pylori Test	a) Powder b) 75 mg/vial c) 1 Presentation	a) 23.09.96 b) 16.04.97 c) 162 Days d) 28 Days	a) 05.06.97 b) 14.08.97 c) 15.08.97 d) OJ No.C 263/3 of 29.08.97

<b>Product</b>	<b>Company</b>	<b>Therapeutic Area</b>	<b>Presentation</b>	<b>EMEA/CPMP</b>	<b>Commission</b>
a) Brand name b) INN c) Part A/B	a) Name b) Origin	a) ATC b) Indication	a) Form b) Dose c) Number of Presentations	a) Validation b) Opinion c) Active Time d) Clock stop	a) Opinion received on Transmission b) Date of decision c) Date of notification d) OJ No.
a) <b>Infanrix-HepB</b> b) DTPa-HB vaccine c) Part A	a) SmithKline Beecham Biologicals b) USA	a) b) active immunisation of infants	a) Suspension for injection b) c) 6 Presentations	a) 15.02.96 b) 16.04.97 c) 199 Days d) 217 Days	a) 26.05.97 b) 30.07.97 c) 01.08.97 d) OJ No.C 263/3 of 29.08.97
a) <b>Benefix</b> b) nonacog alpha c) Part A	a) Genetics Institute of Europe B.V. b) USA	a) BO2BD04 b) hemophilia B, factor IX deficiency	a) Powder for injection b) 250 IU, 500 IU, 1000 IU c) 3 Presentations	a) 23.09.96 b) 14.05.97 c) 162 Days d) 55 Days	a) 16.06.97 b) 27.08.97 c) 28.09.97 d) OJ No.C 292/2 of 26.09.97
a) <b>Karvea</b> b) irbesartan c) Part B	a) Bristol Myers Squibb EEIG b) FR	a) C02EX Treatment of Hypertension	a) Tablets b) 75 mg, 150 mg, 300 mg c) 9 Presentations	a) 21.10.96 b) 14.05.97 c) 163 Days d) 27 Days	a) 16.06.97 b) 27.08.97 c) 28.08.97 d) OJ No.C 292/2 of 26.09.97
a) <b>Aprovel</b> b) irbesartan c) Part B	a) Sanofi Pharma Bristol-Myers Squibb SNC b) BE	a) C02EX Treatment of Hypertension	a) Tablets b) 75 mg, 150 mg, 300 mg c) 9 Presentations	a) 21.10.96 b) 14.05.97 c) 163 Days d) 27 Days	a) 16.06.97 b) 27.08.97 c) 28.08.97 d) OJ No.C 292/2 of 26.09.97
a) <b>Sifrol</b> b) pramipexole c) Part B	a) Boehringer Ingelheim b) DE	a) N04BC b) Treatment of idiopathic Parkinson disease	a) Tablets b) 0.125 mg, 0.25 mg, 1.0 mg, 1.25 mg, 1.5 mg c) 10 Presentations	a) 18.06.96 b) 18.06.97 c) 208 Days d) 141 Days	a) 05.08.97 b) 14.10.97 c) 15.10.97 d) OJ No. C 329/7 of 31.10.97

<b>Product</b> a) Brand name b) INN c) Part A/B	<b>Company</b> a)Name b)Origin	<b>Therapeutic Area</b> a)ATC b)Indication	<b>Presentation</b> a)Form b)Dose c)Number of Presentations	<b>EMA/CPMP</b> a) Validation b)Opinion c)Active Time d)Clock stop	<b>Commission</b> a)Opinion received onTransmission b)Date of decision c)Date of notification d)OJ No.
a) <b>Mirapex</b> b) pramipexole c) Part B	a) Pharmacia & Upjohn b) SW	a) N04BC b) Treatment of idiopathic Parkinson disease	a) Tablets b) 0.125 mg, 0.25 mg, 1.0 mg, 1.25 mg, 1.5 mg c) 10 Presentations	a) 18.06.96 b) 18.06.97 c) 208 Days d) 141 Days	a) 05.08.97 b) ... c) ... d) ...
a) <b>Daquiran</b> b) pramipexole c) Part B	a) Dr. K. Thomae b) DE	a) N04BC b) Treatment of idiopathic Parkinson disease	a) Tablets b) 0.125 mg, 0.25 mg, 1.0 mg, 1.25 mg, 1.5 mg c) 10 Presentations	a) 18.06.96 b) 18.06.97 c) 208 Days d) 141 Days	a) 05.08.97 b) 27.10.97 c) 28.10.97 d) OJ No. C 362/2 of 28.11.97
a) <b>Cerezyme</b> b) imiglucerase c) Part A	a) Genzyme B.V b) NL	a) A16AB02 b) enzyme replacement therapy in patients with a type I Gaucher disease	a) Powder for infusion b) 200 IU c) 2 Presentations	a) 17.01.97 b) 23.07.97 c) 175 Days d) 30 Days	a) 22.08.97 b) 17.11.97 c) ... d) ...
a) <b>Viracept</b> b) nelfinavir c) Part B	a) Agouron Pharmaceuticals b) USA	a) J05 AX0 b) antiviral agent	a) Tablet, Oral powder b) 250 mg, 50 mg/g c) 3 Presentations	a) 18.02.97 b) 24.09.97 c) 180 Days d) 34 Days	a) 31.10.97 b) ... c) ... d) ....
a) Quadramed b) samarium [ <sup>153</sup> Sm] c) Part B	a) Cis Bio International b) FR	a) V10BX02 b) Therapeutic radiopharmaceutical for pain palliation	a) Solution for injection b) 1.5 ml, 2.3 ml, 3.1 ml c) 3 Presentations	a) 18.12.96 b) 22.10.97 c) 198 Days d) 95 Days	a) ... b) ... c) ... d) ...

<b>Product</b> a) Brand name b) INN c) Part A/B	<b>Company</b> a) Name b) Origin	<b>Therapeutic Area</b> a) ATC b) Indication	<b>Presentation</b> a) Form b) Dose c) Number of Presentations	<b>EMEA/CPMP</b> a) Validation b) Opinion c) Active Time d) Clock stop	<b>Commission</b> a) Opinion received on Transmission b) Date of decision c) Date of notification d) OJ No.
a) Primavax... b) combined vaccines c) Part A	a) Pasteur Merieux MSD b) FR	a) J07CA b) Bacterial and viral combined vaccines	a) Suspension for injection b) c) 2 Presentations	a) 21.01.97 b) 22.10.97 c) 201 Days d) 68 Days	a) ... b) ... c) ... d) ...
a) Turvel b) tovafloracin c) Part B	a) Roerig Farmaceutical b) IT	a) J01M A b) Antibacterial Agent	a) Tablets b) 100 mg, 200 mg c) 14 Presentations	a) 18.02.97 b) 22.10.97 c) 208 Days d) 34 Days	a) ... b) ... c) ... d) ...
a) Turvel iv b) alatrofloxaacin c) Part B	a) Roerig Farmaceutical b) IT	a) J01M A b) Antibacterial Agent	a) Concentrate for solution b) 100 mg, 200 mg, 300 mg c) 3 Presentations	a) 18.02.97 b) 22.10.97 c) 208 Days d) 34 Days	a) ... b) ... c) ... d) ...
a) Trovan b) tovafloracin c) Part B	a) Pfizer Ltd b) GB	a) J01M A b) Antibacterial Agent	a) Tablets b) 100 mg, 200 mg c) 14 Presentations	a) 18.02.97 b) 22.10.97 c) 208 Days d) 34 Days	a) ... b) ... c) ... d) ...
a) Trovan iv b) alatrofloxaacin c) Part B	a) Pfizer Ltd b) GB	a) J01M A b) Antibacterial Agent	a) Concentrate for solution b) 100 mg, 200 mg, 300 mg c) 3 Presentations	a) 18.02.97 b) 22.10.97 c) 208 Days d) 34 Days	a) ... b) ... c) ... d) ...

<b>Product</b>	<b>Company</b>	<b>Therapeutic Area</b>	<b>Presentation</b>	<b>EMA/CPMP</b>	<b>Commission</b>
a) Brandname b) INN c) Part A/B	a) Name b) Origin	a) ATC b) Indication	a) Form b) Dose c) Number of Presentations	a) Validation b) Opinion c) Active Time d) Clock stop	a) Opinion received on b) Date of decision c) Date of notification d) OJ No.

a) Viramune b) nevirapine c) Part B	a) Boehringer Ingelheim b) DE	a) J05AX04 b) Treatment of HIV-1 infected adults	a) Tablets b) 200 mg c) 2 Presentations	a) 20.06.97 b) 22.10.97 c) 125 Days d) 0 days	a) ... b) ... c) ... d) ...
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a) Pylobactell b) <sup>13</sup> C -urea c) Part B	a) B.S.I.A.	a) V04CX b) Helicobacter pylori Test	a) Tablet b) 100 mg c) 1 Presentation	a) 18.12.96 b) 19.11.97 c) 163 Days d) 158 Days	a) ... b) ... c) ... d) ...
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a) Combivir b) lamivudine/zidovudine c) Part B	a) Glaxo-Wellcome b) UK	a) J05AB20 b) treatment of HIV infected adults and children	a) film coated tablets b) 150 mg/300mg c) 2 Presentations	a) 25.07.97 b) 19.11.97 c) 119 Days d) 0 days	a) ... b) ... c) ... d) ...
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a) Rebif b) interferon beta-1a c) Part A	a) Serono b) CH	a) L03AA11 b) Treatment of multiple sclerosis	a) Solution for injection b) 6 MIU c) 3 Presentations	a) 22.07.96 b) 17.12.97 c) 181 Days d) 285 Days	a) ... b) ... c) ... d) ...
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## Annex 8

### CVMP OPINIONS IN 1997 ON MEDICINAL PRODUCTS FOR VETERINARY USE

#### Centralised Applications

<b>Product</b>	<b>Company</b>	<b>Therapeutic area</b>	<b>Presentation</b>	<b>EMEA/CVMP</b>	<b>Commission</b>
i) Brand name ii) INN iii) List A/B	a) Name b) Origin	a) Target species b) Indication	a) Form b) Dosage c) No. of presentations	a) Validation b) Opinion c) Active time d) Clockstop	a) Opinion received b) Decision c) Notification d) OJ No.
i) Nobivac-Porcoli ii) Inactivated vaccine iii) List A	a) Intervet International b) NL	a) Piglets b) Neonatal colibacillosis	a) Solution for injection b) Multidose c) 2	a) 01.01.95 b) 27.07.95 c) 107 days d) 94 days	a) 24.08.95 b) 29.02.96 c) 04.03.96 d) OJ No. C/96 of 29.03.96
i) Pentofel ii) Vaccine iii) List A	a) Fort Dodge Laboratories b) IRL	a) Cats b) Rhinotracheitis	a) Solution for injection b) Monodose c) 3	a) 16.06.95 b) 18.09.96 c) 208 days d) 235 days	a) 17.10.96 b) 05.02.97 c) 06.02.97 d) OJ No. C/63 of 28.02.97
i) Dicural ii) Difloxacin iii) List B	a) Fort Dodge Laboratories b) NL	a) Poultry b) Antibacterial for systematic use	a) Oral solution b) 100mg/ml c) 2	a) 06.12.95 b) 11.06.97 c) 218 days d) 337 days	a) 11.07.97 b) ... c) ...
i) Quadrisol ii) Vedaprophel iii) List B	a) Intervet International b) NL	a) Horses b) Control of inflammation	a) Gel for oral use b) 100 mg/ml c) 1	a) 07.05.96 b) 16.07.97 c) 209 days d) 235 days	a) 14.08.97 b) ... c) ...
i) Metacam ii) Meloxicam iii) List B	a) Boehringer Ingelheim b) DE	a) Cattle b) Adjunctive therapy	a) Solution for injection b) 5 mg/ml c) 1	a) 24.06.96 b) 16.07.97 c) 208 days d) 180 days	a) 14.08.97 b) ... c) ...
i) Nobilis B491 ii) Live vaccine iii) List B	a) Intervet International b) NL	a) Poultry/chicken b) Infectious bronchitis	a) Solution b) 30ml/1000 c) 5	a) 16.10.96 b) 12.11.97 c) 210 days d) 184 days	a) 12.12.97 b) ... c) ...
i) Clomicalm ii) Clomipramine iii) List B	a) Novartis b) FR	a) Dogs b) Treatment of anxieties	a) Tablets b) 5,20,80 mg c) 3	a) 13.11.96 b) 12.11.97 c) 210 days d) 156 days	a) 12.12.97 b) ... c) ...
i) Neocolipor ii) Inactivated vaccine iii) List A	a) Merial b) FR	a) Piglets b) Neonatal colibacillosis	a) Suspension for injection b) 2 ml c) 5	a) 02.10.96 b) 10.12.97 c) 191 days d) 245 days	a) ... b) ... c) ...

*Establishment of maximum residue limits for new substances*

<b>Substance (INN)</b>	<b>Target species</b>	<b>EMA/CVMP</b> a) Validation b) Opinion c) Active time d) Clockstop	<b>Commission</b> a) Sent to Commission b) Date of the regulation c) OJ No.
Difloxacin	Chicken & Turkeys	a) 16.05.95 b) 15.12.95 c) 134 days d) 49 days	a) 13.02.96 b) 08.07.96 c) OJ No. L 170 of 09.07.96
Ketoprofen (extension)	Porcine	a) 15.05.95 b) 22.03.96 c) 85 days d) 217 days	a) 25.04.96 b) 06.09.96 c) OJ No. L 226 of 07.09.96
Diclazuril	Ovine	a) 12.12.95 b) 24.04.96 c) 102 days d) 0	a) 24.05.96 b) 21.10.96 c) OJ No. L 269 of 22.10.96
Eprinomectin	Bovine	a) 22.02.96 b) 25.06.96 c) 108 days d) 0	a) 26.07.96 b) 08.01.97 c) OJ No. L 5 of 09.01.97
Doramectin (modification)	Bovine	a) 14.05.96 b) 24.07.96 c) 70 days d) 0	a) 23.08.96 b) 14.02.97 c) OJ No. L 45 of 15.02.97
Praziquantel	Ovine	a) 03.08.95 b) 18.09.96 c) 187 days d) 152 days	a) 16.10.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
Moxidectin (modification)	Bovine and Ovine	a) 12.06.96 b) 18.09.96 c) 97 days d) 0	a) 16.10.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
Difloxacin (modification)	Chicken, Turkeys	a) 10.07.96 b) 23.10.96 c) 104 days d) 0	a) 19.11.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
Ivermectin (extension)	Deer	a) 20.08.96 b) 11.12.96 c) 86 days d) 0	a) 09.01.97 b) 23.04.97 c) OJ No. L 106 of 24.04.97
Amitraz (extension)	Bees	a) 18.10.96 b) 22.02.97 c) 115 days d) 0	a) 12.03.97 b) 24.09.97 c) OJ No. L 263 of 25.09.97
Doramectin (extension)	Swine & Ovine	a) 10.06.96 b) 12.02.97 c) 118 days d) 127 days	a) 12.03.97 b) 24.09.97 c) OJ No. L 263 of 25.09.97

## Annex 9

### REFERENCEDOCUMENTS

#### a) *EU Official Publications*

Council Regulation (EEC) No 2309/93 of 22 July 1993  
(OJ L 214/1, 24.8.1993)

Council Regulation (EEC) No 2377/90 of 26 June 1990 as amended  
(OJ L 224/1, 18.8.1990)

Council Directive 75/319/EEC as amended  
(OJ L 147/13, 9.6.1975)

Council Directive 81/851/EEC as amended  
(OJ L 317/1, 6.11.1981)

The texts of these and other provisions may be also be found in the series *Rules governing medicinal products in the European Community*, volumes I to VII. These publications, along with copies of the Official Journal, are available from:

Office for Official Publications of the European Communities  
2, rue de Mercier  
L - 2985 Luxembourg

The texts will also be available in 1998 on the EudraLex Internet site at <http://www.eudra.org>

#### b) *EMEA documents*

- First General Report on the Activities of the European Agency for the Evaluation of Medicinal Products 1995 (ISBN 92-827-7491-0, Office for Official Publications of the European Communities)
- Second General Report on the Activities of the European Agency for the Evaluation of Medicinal Product 1996 (ISBN 92-9155-002-7, Office for Official Publications of the European Communities)
- Statement of principles governing the partnership between the national competent authorities and the EMEA (EMEA/MB/076/96)
- Financial Regulation applicable to the budget of the EMEA (EMEA/MB/011/97)
- Report on performance goals and indicators for the EMEA (EMEA/MB/062/96) \*
- EMEA contribution to the preparation of a Commission proposal for a definitive Council Regulation on fees payable to the EMEA (EMEA/MB/057/96) \*
- Interim report on the consultation exercise on transparency and access to documents of the EMEA (26 June 1997, Revision 1) \*

\* available in English only

These and other documents are available either on the Internet at <http://www.eudra.org/emea.html> or by writing to:

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