



The European Agency for the Evaluation of Medicinal Products

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

1995

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Foreword
by

Strachan Heppell
Chairman
Management Board

The Management Board is required each year to adopt a report for the Member States, Commission, Council and European Parliament on the activities of the European Agency for the Evaluation of Medicinal Products.

I am pleased to be presenting this, the first General Report on the Activities of the Agency, which is at the heart of the new European system for the evaluation, authorisation and supervision of human and veterinary medicinal products.

The work of the Board

The Board had an important role to play in the early days of the Agency, including decisions on the initial budget, the nomination of Fernand Sauer as Executive Director and the selection of a site in London's Canary Wharf for the Agency's offices. Throughout, the members of the Board - representatives of the Member States and Community Institutions - worked together in a spirit of co-operation and partnership.

Meeting five times between December 1993 and January 1995, the Management Board was able to declare the Agency ready to receive applications as from 1 February 1995.

Role of the Agency

The Agency is responsible for co-ordinating and managing the new system. It has four principal elements. The Management Board, which is the governing body, is responsible for budgetary matters, for appointing the Executive Director and for monitoring the performance of the Agency. The two Scientific Committees, the Committee for Proprietary Medicinal Products and the Committee for Veterinary Medicinal Products, have to provide objective high level scientific advice and ensure proper co-ordination of work between the Agency and National Competent Authorities. The Permanent Secretariat, headed by the Executive Director, is responsible for the day-to-day operations of the Agency.

The role of the Agency is defined by the new system, which breaks new ground in two important respects.

First, it has to meet two different objectives - the protection of public and animal health and the strengthening of the European single market for human and veterinary pharmaceuticals.

Second, unlike other regulatory regimes for medicines, it is designed as a devolved structure. It is co-ordinated and managed at the centre by the Agency. But the assessment work is carried out by European experts designated by Member States drawing on the experience and expertise of national regulatory agencies.

Achieving the Agency's objectives

The Agency recognises very clearly the importance of the work it has to do both for public health and for the pharmaceutical industry in Europe. We recognise our direct responsibilities to the European Parliament, Member States and the European Commission - all of whom are represented on the Management Board. And we recognise our wider responsibilities to the public, patients, health professions and health care organisations.

To ensure that the Agency lives up to these responsibilities, the Management Board is developing performance goals and indicators which will measure whether these goals have been achieved. The Agency will consult widely before finally deciding on these goals and indicators. Once they have been established, the Agency will regularly publish details of its performance. This will enable all concerned to judge whether the Agency is doing its job properly and whether the new system is working well.

Looking to the future

I believe that on the record set out in this Report the new system for regulating medicinal products in Europe has got off to a good start. For this, the hard work and expertise of the European Institutions, national authorities, experts and the Agency's staff deserve much credit. The positive and continuing support from the pharmaceutical industry and consumer organisations has also made a most welcome contribution.

The challenges facing the Agency are only beginning. Our aim now must be to build successfully on the experience of the first year's operations so that we can achieve in full the objectives of the new system. It is important for everyone in the European Union that we succeed.

Introduction

by

Fernand Sauer
Executive Director
European Agency for the Evaluation of Medicinal Products

The new European system for the authorisation and supervision of medicinal products for human and veterinary use has four key objectives which concern the European Agency for the Evaluation of Medicinal Products (EMA) as well as all European national competent authorities dealing with human and veterinary medicinal products:

- to protect public health by mobilising the best scientific resources existing within the European Union
- to promote health care through the effective regulation of new pharmaceuticals and better information for users and health professionals
- to facilitate quicker access and the free circulation of pharmaceuticals within the European single market
- to support the European pharmaceutical research and development industry by developing efficient, effective and responsive operating procedures

Openness and transparency

The EMA feels strongly that it has to provide health professionals with the relevant basic scientific information and patients with package leaflets in all EU official languages written in a clear and simple way. Better information for consumers is an absolute must for a more rational use of medicines, which will lead to improvements in public health and benefit health care budgets.

While consumers remain its primary concern, and indeed that of the whole of the European regulatory framework, the Agency also has an important role in supporting the European pharmaceutical research-based industry as part of the European Union industrial policy in this sector.

The experience of the Agency in 1995 has been that consumers and industry alike are supportive of our work. Industry has given the Agency a welcome vote of confidence which can be seen from the larger than expected number of voluntary applications made under the centralised procedure.

Relations have also been established with European consumers' representatives who have welcomed the transparency and openness of the Agency.

Representatives of consumers, industry and health professionals have been invited to meet members of the Scientific Committees at regular intervals.

Internal and international dimension

With the establishment of the Agency, free movement of medicines will become a reality. The diversity in regulatory practices is a complex challenge and the EMEA benefits from the richness of the different traditions.

In the new system, the European Commission retains its role as legislator and interpreter of EU legislation, but also has the new responsibility of decision-taker. It is important, therefore, that the Agency, in particular its Scientific Committees, provides the European Institutions with high quality, unambiguous and detailed scientific information to allow them to fully enforce the EMEA's Opinions.

The work of the Agency is not purely turned inwards towards the European Union. The EU is the single biggest trading bloc in the world and its industry represents a major player in the world pharmaceutical trade. The EMEA has a technical contribution to make in relations with regulators and industry from outside of the Union in close cooperation with the Commission, which remains the chief negotiator in international affairs. The Agency has, therefore, an important role in making sure that countries outside of the Union understand and trust the new European authorisation procedures.

Within the context of current activities of the ICH process (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) between the EU, Japan and the US, the workload is shared between the Commission for general policy issues and the EMEA on technical aspects.

Future challenges for the Agency

During 1995 the level of revenues, from the EU budget and fees, was constantly reviewed and discussed and will continue to be the subject of close scrutiny in 1996. However, the questions concerning the Agency's revenues will be more fully addressed in 1998 when the European Parliament and Council of the European Union reconsider the Fee Regulation governing fees paid for services performed by the Agency.

All parties involved in the new European system, in particular the European Institutions, must be aware that the Agency needs adequate resources with which to carry out all of its main tasks.

Additionally, the need to tighten the regulatory, administrative and financial framework of the Agency was well recognised and this will be a major task in 1996.

Now that it has been operational for one year it can be seen that the EMEA has achieved concrete results. Nevertheless, it is still early and the EMEA will continue to strive to ensure it meets its objectives. The strong support of consumers and industry alike will continue to be needed, especially since we expect the workload of the Agency to rise dramatically over the next few years.

I. The First Steps of the European Medicines Evaluation Agency

I.1 Background to the Agency's Creation: Thirty Years of Pharmaceutical Harmonisation

The creation of the Community centralised and decentralised authorisation procedures for medicinal products for human and veterinary use, including the creation of the Agency, is the culmination of thirty years of Community regulatory co-operation in the field of pharmaceuticals.

The driving force behind this ever closer co-operation has been the desire to seek better protection of public and animal health and to ensure free circulation of medicinal products within the European Union.

Council Directive 65/65/EEC (OJ No L.147, 9.6.75, p.13) laid down the principle of granting pre-marketing authorisations for medicinal products in all Member States and that they should be granted on scientific grounds of quality, safety and efficacy, without regard to socio-economic considerations.

This first Directive still forms the basis of the regulatory framework today.

Ten years later, in 1975, Member States consolidated their experience and agreed on common principles for the granting of marketing authorisations and the testing of medicinal products for human use. The creation of the original Committee for Proprietary Medicinal Products and the start of a non-binding co-ordination procedure marked an important development in Member State co-operation.

In 1981, similar provisions were adopted to cover veterinary medicinal products, including the creation of the original Committee for Veterinary Medicinal Products.

Through these earlier Committees - which were composed of representatives of the Member States and the Commission - it was hoped that the increasing level of harmonisation would make the conversion of national marketing authorisations easier, first with the introduction of the multi-state procedure and later with direct presentation by research-based companies to the two Committees in the so-called 'concertation' procedure dealing with biotechnology products.

Member States recognised the importance of working together and accumulated experience much of which is relevant to the new European system. However these procedures were not binding from the outset and did not systematically result in similar marketing authorisations throughout the Community.

Pharmaceuticals were an integral part of the 1985 White Paper on the completion of the internal market and all the relevant legislation was successfully adopted before the final deadline. This drive towards the completion of the '1992' single European market added a number of important pieces of legislation to the growing regulatory framework, extending European legislation to cover all industrially manufactured medicines,

including vaccines, blood derivatives, radiopharmaceuticals and homeopathic medicines.

The European Commission is currently considering making proposals for the codification of the existing body of pharmaceutical legislation in 1996. A series of volumes containing all the rules governing medicinal products in the European Union is available from the European Commission. Details of these publications can be found in Annex 6 to this Activity Report.

1.2 From Legislation to Reality

The end of 1990 saw the publication of the most far-reaching set of proposals, relating to the creation of the Agency and the new Community system for the granting of marketing authorisations. After two and a half years of debate, the Council of Ministers finally adopted Council Regulation (EEC) No 2309/93 on 22 July 1993 (OJ No L.214, 24.8.93, p.1), along with three Directives introducing the necessary modifications to existing human and veterinary medicinal product legislation.

One of the major innovations in the new system was the transformation of the two pre-existing Committees into fully-fledged Scientific Committees and the introduction of binding decisions through the centralised procedure and binding arbitration through the decentralised procedure.

Another innovation was the creation of the European Agency for the Evaluation of Medicinal Products to manage and co-ordinate the new system.

The last outstanding matter concerned the seat of the Agency and at the meeting of Heads of State and Government of 29 October 1993 the decision was taken to fix the seat in London.

1.3 The First Steps: The Agency from 1993 to 1994

Although the Agency already existed on paper at the end of 1993, it only became operational some fourteen months later in February 1995. But it did not start from scratch. The Agency was able to build on the considerable base of previous co-operation and experience.

The former Committee for Proprietary Medicinal Products and Committee for Veterinary Medicinal Products could be seen as the precursors of the new Scientific Committees and although their mandates, roles and indeed the legal implications of their opinions have greatly changed, the experience gained has been of great importance. The work of these Committees continued right up until December 1994, with the new Committees established in January 1995.

The activities of the former Committees are recorded in Reports published by the European Commission. The most recent publications are 'Report on the Activities of the

Committee for Veterinary Medicinal Products during 1993 and 1994' (III/5055/95, May 1995) and 'Report on the Operation of the Committee for Proprietary Medicinal Products during 1993 and 1994'.

Early Decisions of the Management Board

Once the seat had been determined, planning was able to go ahead. The Agency owes much to the Commission, and in particular Directorate-General III, for its preparatory work and it was under the temporary chairmanship of the Commission that the Management Board met for the first time in Brussels on 13 December 1993.

Meeting for the second time on 13 April 1994, the Management Board elected Mr Strachan Heppell to be Chairman and appointed Mr Fernand Sauer as Executive Director of the Agency, who formally took up his new post on 1 September 1994.

The third important decision taken by the Management Board was the selection of 7 Westferry Circus as the Agency's headquarters at its meeting of 23 June 1994. A number of alternatives had been presented to the Board, but after discussion the final choice was made based on the considerable cost advantages and the possibility for expansion offered by location in Canary Wharf.

At the same meeting, members of the Board also elected Dr Romano Marabelli to be Vice-Chairman.

1994 Budget

The adoption by the Management Board of the 1994 budget was particularly urgent in order to allow the Commission to transfer the Agency's subsidy and to enable the Agency in turn to make financial commitments for staff and office premises. The 1994 budget and indeed the budgets during the first few years of operation provide the investment capital which will allow the Agency to properly meet its tasks in future.

Following the adoption of an initial budget in April 1994 of ECU 7,720,000, two subsequent adjustments became necessary in November and December. The first adjustment was made to meet specific needs of the Agency, whilst the second adjustment was made following the European Parliament's decision to cut the reserve of ECU 750,000. The final budget for 1994 of ECU 6,813,085 was adopted by the Management Board on 15 December 1994.

First Recruitment Wave

The first wave of recruitment, for Heads of Unit and Sector and other senior posts, was carried out during the second half of 1994. The posts and the profiles for these posts for this initial wave of recruitment had been agreed to by the Management Board at earlier meetings and once appointed, the Board mandated the Executive Director to implement the selection procedure.

With the aid of Commission DG XII (Science and Research), a selection jury was appointed composed of three representatives of the Management Board (a representative each of the Chairman and Vice-Chairman of the Management Board and of the European Parliament) and three representatives of staff from Community institutions, in addition to which Fernand Van Hoeck, former Director of the European Medical Research Programme, was appointed as chairman.

Following the announcement in the Official Journal of the EC and national press, some 2,500 applications were received for the fourteen key management posts. Starting work in September 1994, the Selection Committee was able to complete its tasks towards the end of January 1995.

1.4 Inauguration of the Agency: Open for Business

The inauguration of the Agency took place on 26 January 1995, attended by representatives of the European Parliament, French Presidency of the Council of Ministers, Commission, the UK Government, the newly-elected Chairmen of the Scientific Committees and Member State national competent authorities.

Representatives of the Japanese and US authorities were also present, as were the various European associations representing the human and veterinary pharmaceutical industries, consumers and other interests.

Earlier the same day, the Management Board had declared that the Agency would become operational as of 1 February 1995. The decision to make the Agency operational had been delayed pending a clear indication that the Council of Ministers would adopt the scale of fees payable to the Agency.

Council Regulation (EC) No 297/95 on fees payable to the Agency was adopted on 10 February 1995 after difficult discussions, putting into place the missing piece of the European licensing system - and the Agency was open for business.

Since January 1995, and without waiting for the Agency to be fully operational, the two new Scientific Committees have met in a systematic manner and each created their structures while the Secretariat was being established. Office space was available at the end of January 1995 and the conference services on Level 4, in particular the interpretation facilities, were ready in March 1995.

Throughout 1995 the Agency continued to attract attention. A delegation from the European Parliament Committee on the Environment, Public Health and Consumer Protection led by its Chairman, Mr Kenneth Collins, visited the Agency in September.

An open hearing to review the first nine months of the new European authorisation system was held in October in the presence of Dr Martin Bangemann, Member of the Commission with responsibility for industrial policy. Some 100 representatives from a

wide range of industry, consumer and other interests were invited to this fruitful exchange.

At this occasion it was clear that the input of the national competent authorities of the Member States into the new European authorisation system was of paramount importance. The success of the Agency and the European system in 1995 is recognition of the enormous contribution of the experts working for both the national and European systems.

In her capacity as Member of the Commission with responsibility for science, research and development, the Agency was also pleased to receive Mrs Edith Cresson when she visited the Agency in November.

The Agency has also attracted a great deal of interest from the pharmaceutical industry. A number of information days, jointly hosted by the Agency, were held in 1995 with industry representative bodies. Certain of these bodies have now established a permanent presence in Canary Wharf.

Interest from non-EU countries has also been strong. Countries from whom visitors were received in 1995 included the Czech Republic, Iceland, Japan, Korea, Norway, Poland, Slovakia, South Africa, Switzerland, Turkey and the United States.

II. Setting up the EMEA

II.1 Activities of the Management Board in 1995

The Management Board met four times in London in 1995 (26 January, 25 April, 20 September, 6 December). With the EMEA operational, the Board was able to concentrate on the immediate issues facing the Agency.

Budgetary Decisions

The adoption of the initial 1995 budget was delayed pending the decision of the Council of the European Union on the Regulation on the fees payable for the services of the Agency (OJ L.35, 15.2.95, p.1). The Board in January adopted provisional budgetary measures by written procedure to allow the Agency to continue its tasks.

Following adoption of the Fees Regulation, the Management Board had to consider a number of options for the 1995 budget in light of uncertainties regarding additional funding for enlargement of the European Union and release of the Reserve by the European Parliament.

As a consequence, the Board adopted an initial budget of ECU 18.47 million in February, which was later revised to ECU 14.4 million to take account of a shortfall in expected revenues.

At the request of the Executive Director, the Board also considered the conditions and criteria for the waiving or reduction of fees. At its December meeting, the Board decided that fee waivers and reductions should only be available for so-called orphan drugs in the human medicines sector and comparable products in the veterinary sector, including the determination of certain maximum residue limits of old products. It was decided that such waivers would be financed using the ECU 750,000 released from the Reserve by the European Parliament.

Relationship between the EMEA and National Competent Authorities

The new European system is rooted in co-operation between the Agency and the national competent authorities of the Member States. The Executive Director submitted proposals on the partnership between the EMEA and the national competent authorities when they provide expertise for European evaluation activities, to be complemented by standard contracts which would govern the individuals' tasks and duties.

At its December meeting the Management Board endorsed a general statement of principles governing the relationship between national competent authorities and the Agency, and consensus was reached that ad hoc contracts between the Agency and the national competent authorities of Rapporteurs would be established for the provision of evaluation services.

The Board was also called to address the matter of remuneration for evaluation activities undertaken by Rapporteurs and experts on behalf of the EMEA. Consensus was reached to exclude direct payment to individuals and that the financial relationship should instead be between institutions.

A temporary scale of fees to be paid by the EMEA to national competent authorities was adopted in June 1995 whereby half of the fee received by the Agency would be allocated to the remuneration of scientific evaluation services involved in a procedure. Pending a survey of actual costs incurred by different Rapporteurs and experts, the Management Board in October extended the temporary scale of fees until the end of 1996.

The Board adopted in April the basis for reimbursement of travel and accommodation expenses to delegates and experts attending EMEA meetings. On request of the Board, the Secretariat later agreed with each delegation, on a bilateral basis, the best way to implement the reimbursement provisions.

The Board also considered a proposal from the Executive Director concerning the possibility of national competent authorities seconding national experts to the Agency. Such national experts would serve various functions including helping to establish the relationship between national authorities and the Agency, and contributing to a better understanding of medical practices and terminology in the Member States.

Relations with Other Institutions and Interested Parties

Various European and international organisations, as well as non-EU countries, approached the Commission and the EMEA in 1995 expressing the wish to establish working relationships with the Scientific Committees as observers. On a proposal from the European Commission, the Management Board decided at its September meeting to invite the European Pharmacopoeia to certain EMEA working groups.

The Agency organised a number of contacts with representatives of industry, consumers, patients and the health professions in 1995. The Board has supported the policy of transparency and dialogue with interested parties and was regularly informed of such contacts with the Scientific Committees or Secretariat.

Working Groups on Performance Indicators and Public Health

The Management Board established two Working Groups in 1995, both of which met twice during the second half of the year.

The Working Group on performance indicators was set up to examine and develop indicators and goals to be applied to the EMEA, national competent authorities and other parties involved in the centralised and decentralised procedures. At its December

meeting the Board noted the first results of the Group's work which will be subject to consultation with the Agency's partners in the European system in 1996.

The Public Health Working Group was established to examine how best the Agency can contribute to the improvement of human and animal health and also to public health in general.

Other Business

A number of other important matters were dealt with by the Board in 1995, including the confirmation of the appointments of a number of staff members, including Ms Birgit Snoeren who was appointed as Financial Controller in April 1995. The Board also confirmed the nominations of the Accounting Officer and Assistant Accounting Officers.

The Board's attention was also drawn to the European experts list (1,200 in the human and 400 in the veterinary medicines sectors), which will be made available to the public in January 1996.

II.2 Personnel of the EMEA Secretariat

The Permanent 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 has no permanent staff yet and staff recruited through the competitions are offered contracts of five years. Recruitment to the Agency follows the normal rules and practices of the EU institutions. Once selected by an independent jury, candidates are placed on a reserve list from which they may be selected for a post. Whilst there is no quota system for nationality of staff, the Agency seeks to respect the multi-cultural nature of the European Union. Staff come from throughout the European Union and it is anticipated that the increased number of staff will allow a fair presence of all nationalities.

A second round of recruitment was launched in May 1995 for the remaining Heads of Unit and Sector, technical and administrative positions. The staff structure evolved rapidly during 1995, as can be seen from the table below. Starting with 16 people at the beginning of the year, the Agency grew to some 67 by the end of the year.

Recruitment is planned to reach 100 by mid-1996. This represents a relatively small number of staff compared to other regulatory authorities around the world which employ several thousands of staff in the pharmaceutical sector.

A Staff Committee was elected and in addition to its important role in the representation of staff in general policy matters, was able to take a number of initiatives during the year.

	1.10.94	1.01.95	1.04.95	1.07.95	1.10.95	31.12.95
A						
- temporary	1	2	4	11	12	15
- auxiliary	3	5	5	7	14	14
B	1	6	8	7	8	8
C	-	1	3	6	10	13
Interim	1	2	2	5	11	17
Total	6	16	22	36	55	67

II.3 EMEA Premises

Since no building had been provided or identified by the host country, an early priority for the EMEA was to determine its future headquarters in London. The fitting out costs, in addition to rent, had to come out of the Agency's own budget. More than 100 candidate locations were considered by the Agency and a selection of the most suitable premises were presented to the Management Board. After these premises had been visited by a task force of the Management Board, the Board decided on 23 June 1994 to locate in Canary Wharf.

A very favourable agreement was reached with the owners of 7 Westferry Circus and the framework lease was signed on 26 October 1994 for a period of fifteen years. A total of 5,500 m² was taken over the fifth, fourth and part of the third floors of the building, with an option for the remaining 1,000 m² of the third floor. Rent was fixed for five years at a level below that of other parts of London (and lower than equivalent rents in Brussels and Luxembourg) and a negotiating ceiling introduced for rent reviews thereafter.

Work started on the fitting out of the building in October 1994 and, with the co-operation of the landlords, was ready between January and the end of March 1995.

The facilities available at the Agency include a restaurant and archives on the third floor, with the reception and conference rooms on the fourth floor. There are three conference rooms, the largest of which can seat up to 100 delegates with nine interpretation cabins. The two smaller rooms can each hold 50 delegates, one with four and the other with five cabins for interpreters. Each of these rooms is equipped with modern audio-visual facilities. The fifth floor houses the administrative offices of the Agency, the library and a number of small meeting rooms.

In September 1995 the Management Board agreed that the option for the remaining space on the third floor should be exercised and the Agency's support services are currently supervising the new installation which should be finished in the second quarter of 1996.

II.4 EMEA 1995 Budget and Financial Control

1995 Budget

The revenues of the Agency consist of a contribution from the European Union's budget and the fees paid by the pharmaceutical industry for obtaining and maintaining central marketing authorisations as well as other services provided by the Agency.

As previously described, the initial budget for 1995 amounted to ECU 18.47 million, but was later modified by the Management Board in September 1995 to ECU 14.4 million. The Community subsidy element of the modified budget for 1995 amounted to ECU 9.4 million, including ECU 650,000 from the EU enlargement budget and ECU 750,000 which was released from the reserve by the European Parliament at the end of 1995.

Financial Control

In its financial operations, the Agency has during 1995 followed by analogy the Financial Regulation of the Commission, including the use of public tenders for all services. A Financial Regulation for the Agency was submitted to the Court of Auditors and the Commission for opinion and will be adopted by the Management Board in 1996.

Budgetary and control activities in 1995 emphasised the difficulty of finding a suitable computerised accounting system for the Agency. The existing system used by the Commission proved too complex for the Agency and other available systems were found to be unsuitable. It was therefore decided, in conjunction with the other decentralised Agencies of the European Union, that a tender procedure would be opened for the development of a dedicated system.

The accounting procedures and system currently employed by the Agency have, however, been confirmed by a visit of the Court of Auditors in February 1995. Until the appointment of the Agency's Financial Controller was confirmed by the Management Board in July 1995, the Agency's accounts had been under the supervision of the Commission Financial Control.

II.5 Structure and Administration of the EMEA Secretariat

An organigram showing the structure of the Agency is to be found in Annex 4 of this Report. Operating under the Executive Director, the Secretariat is divided into four main units - three scientific/technical and one administrative units. Three Units became operational between May and July 1995. The Technical Co-ordination Unit will become fully operational in 1996.

The activities of the scientific units detailed elsewhere in this Report are central for the success of the EMEA, but the role played by the Administrative Unit should not be

overlooked. The support services of the Administrative Unit have throughout 1995 contributed to the setting up of the Agency.

The biggest challenge faced by the Personnel Service in 1995 was the organisation and supervision of the second recruitment round which attracted some 1,890 applications. Interviews started in the second half of 1995 and appointments will be made early in 1996.

The Administrative Unit provides a range of services essential to the proper operation of the Agency. In addition to personnel management, an important part of the work was the putting in place of information technology resources and the organisation of delegates meetings.

Computing and information technology services

The last few months of 1994 and the beginning of 1995 were dedicated mainly to the preparation and execution of calls for tender for the necessary initial IT structure of the EMEA in accordance with EU procurement rules. During the second half of the year the Agency received and was able to install the hardware and software, while at the same time facing an increasing demand for support as a result of the steady increase in staff and their workload.

Local and Wide Area Network (LAN and WAN) Communications have been installed at the Agency. A LAN-based service for outgoing faxes was introduced in June, with network distribution of faxes made available in August 1995. External E-mail connections were gradually installed from July 1995, one of the primary uses of which is the electronic exchange of documents with the European Commission DG III and the Translation Centre in Luxembourg.

In addition, each of the national and European Institution delegation offices, the three conference rooms and conference support staff were similarly equipped.

The centre piece of the Agency's aim to fully integrate information technology into its daily working and decision-making activities will be the Application Tracking System (ATS) for the centralised procedure. A pilot ATS was developed during 1995 and is currently undergoing testing with input of live information.

- ETOMEPE and EudraNet

The European Commission's Joint Research Centre at Ispra has signed an agreement with the EMEA to establish a technical office on the premises of the EMEA. This office (ETOMEPE) is 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) is an inter-networking service provided by ETOMEPE to EU medicinal regulatory authorities in collaboration with Commission Directorate-General III.

EudraNet can be found on Internet, the international public information network, at the following location reference <http://www.eudra.org>. It provides information and various services, including basic generic functions such as electronic mail, file transfer and specific network-based applications for market authorisation.

III. Medicinal Products for Human Use

III.1 Preface by Prof. Jean-Michel Alexandre Chairman of the Committee for Proprietary Medicinal Products

The main purpose of the Agency is the protection and promotion of public health in the fields of medicines. The role of the CPMP within the Agency is to give scientific opinions to support these aims. In addition to the evaluation of medicinal products for marketing authorisation, the CPMP also has a role in pharmacovigilance issues, the drawing up of guidelines, the giving of specific scientific advice to companies in the development of innovatory medicinal products, and the provision of quality information to both health professionals and patients.

In performing its tasks the CPMP has worked in a spirit of consensus. There is a strong desire on the part of all members of the CPMP to arrive at a common position by working together and sharing the workload to ensure a solid scientific basis for the European drug authorisation system. An important step forward is the possibility for the CPMP to have recourse to external expertise from the Agency's European experts list. These experts may accompany members during meetings or participate in the work of both the permanent working parties and ad hoc groups.

In its first year the CPMP succeeded in arriving at eight positive consensus opinions in the centralised procedure, tackled a number of pharmacovigilance matters and gave scientific advice in response to requests from companies. These achievements are proof of the CPMP's contribution to public health and to ensuring that innovatory medicinal products reach the market and patients under the best possible conditions.

III.2 Unit for the Evaluation of Medicinal Products for Human Use

The increasingly large volume of work faced by the CPMP in 1995 has been accompanied by a steady increase in the size of the Human Medicines Evaluation Unit. Starting from only one scientific administrator to serve the CPMP in January, the scientific staff of the Unit was made up of one senior administrator, three administrators and four junior administrators working under its Head of Unit at the end of December 1995, supported by two technical assistants and five secretaries.

Pharmacovigilance activities are provided by a scientific administrator and one junior scientific administrator, assisted by a secretary. Officers in Charge of centralised procedures and decentralised procedures are expected to be appointed in early 1996.

III.3 Committee for Proprietary Medicinal Products

The new CPMP met for the first time on 16 and 17 January 1995 in Brussels with the cooperation of the Commission because the facilities of the Agency had not at that time been finished. Prof. Jean-Michel Alexandre was elected as Chairman of the Committee for a period of three years, with Dr Henning Hovgaard as Vice-Chairman. The first CPMP meeting at the Agency's premises was held on 26 and 27 April.

The Committee met a total of 12 times in 1995, meeting every month except August and twice in October. With meetings now lasting almost a week, the involvement of CPMP members and the commitment of Member States has been considerable.

The increasing confidence of industry in the centralised procedure as shown by the number of expected submissions in 1996 will mean that this commitment will be increasingly called upon in the future.

'Converted' Procedures and First European Marketing Authorisations

With the coming into force of the new system in January 1995 a total of 18 applications were outstanding under the old concertation procedure; 9 falling under Part A and 9 under Part B of the Annex to Council Regulation (EEC) No 2309/93. These were 'converted' to the new system. By the end of 1995 eight positive Opinions had been given by the CPMP and transmitted to the European Commission and Member States.

Details of the procedure for these converted applications may be found in Annex 7.

On 20 October 1995 the first Community Marketing Authorisation was approved by the European Commission for Gonal-F (follitropin-alpha) produced by the Italian-Swiss company Ares-Serono.

For the Agency and the European system, this marks an important milestone. For the first time a single authorisation permitting the marketing of a medicinal product in all Member States, without further national formalities, and giving patients access to these products throughout the whole of the Union.

Equally as important as the Community Marketing Authorisation is the European Public Assessment Report (EPAR). Allowing public access for the first time to the scientific assessment report for a medicinal product, this is a major step forward in giving both health professionals and consumers full information about the medicines that are available. The EPAR is a condensed version of a more detailed scientific assessment report presented and adopted by the Scientific Committees, together with their Opinions. Commercially sensitive information is removed before publication.

In addition to Gonal-F, Community Marketing Authorisations were also approved by the Commission on 27 November 1995 for Taxotere (docetaxel) by Rhône-Poulenc Rorer of France and on 30 November 1995 for Betaferon (interferon beta-1b) by Schering of Germany.

It is expected that the Committee will issue opinions on the remaining 'converted' concertation applications by mid-1996.

New Applications under the Centralised Procedure

The number of applications under the centralised procedure have exceeded expectations. At the end of 1995 a total of 30 new applications had been received or announced (9 in List A and 21 from List B), representing 26 new active substances. Rapporteurs and Co-Rapporteurs were appointed for the new applications, 20 of which started their evaluation process in 1995.

For the Agency it has been a measure of industry's confidence in the centralised procedure that approximately two-thirds of these applications are for products in Part B of the Annex to Council Regulation (EEC) No 2309/93, and therefore that applicants have voluntarily elected to use the procedure.

Various difficulties were encountered with applications, posing problems with the validation of applications, relating particularly to translation of the summary of product characteristics (SPC), package leaflets and labels. Other difficulties which were encountered included the late recognition of the need for pre-approval inspections and also potential problems relating to a single brand name.

In order to resolve some of these external difficulties, the Secretariat took the initiative to develop standards and templates for the preparation of assessment reports (including the EPAR) as well as the phrasing of key aspects of the opinion and Annexes, especially the SPC and package leaflet. These difficulties did not unduly delay the process at Agency level.

However, it should be noted that although the clock was artificially started on 1 January 1995 for the 'converted' ex-concertation applications, the dossiers did not in reality reach the Agency until a later stage when the EMEA became operational in February 1995. The slight additional delay in three instances (see Annex 7) can be accounted for this reason. The 210 day limit was respected for the other Opinions despite initial start-up problems.

Rapporteurships in the Centralised Procedure

The CPMP confirmed the status of the previously nominated Rapporteurs and Co-Rapporteurs for all 18 'converted' ex-concertation applications. For 10 of the applications the Rapporteur had been chosen from the UK, from France in 3 cases, Belgium and Italy had been appointed in 2 cases each and The Netherlands was Rapporteur for one of the applications.

Co-Rapporteurs had not been systematically appointed under the old procedure. Germany and the UK were Co-Rapporteur for 2 applications, with Belgium and France acting as Co-Rapporteur in one application each.

For the new centralised procedures Rapporteur and Co-Rapporteur have been assigned systematically. The sharing of the workload between Members of the new Scientific Committees takes into account the special expertise offered by Members and current

workload. The CPMP was able in 1995 to take into account the applicant's proposal for Rapporteur and Co-Rapporteur in each case.

The CPMP members from the United Kingdom were involved as Rapporteur or Co-Rapporteur in 9 cases, with the members from France and Germany involved in 8 and 7 instances respectively. Delegates from Denmark, Ireland and Sweden acted as Rapporteur or Co-Rapporteur in 5 cases each, with members from The Netherlands and Austria involved in 4 cases. Members from Finland were appointed in 3 cases, with delegates from Belgium, Spain, Italy, Luxembourg and Portugal acting in 2 instances each. The Greek delegates were not appointed in any case 1995, although are willing to do so in 1996.

Scientific Advice

With the creation of the Agency, European research-based companies have for the first time the possibility to seek scientific advice long before they submit their application. This new possibility attracted a great deal of interest during 1995, although the procedural details have yet to be fully determined.

During 1995 the CPMP received numerous requests for scientific advice, although not all were fully justified given the current state of understanding. The Committee agreed to examine 14 requests for scientific advice and determined its final advice in 7 instances in 1995.

Pharmacovigilance

During the course of 1995, three referrals were made to the CPMP under Article 12 of Council Directive 75/319/EEC, as modified. Even though these procedures concerned nationally-authorized products, the CPMP was asked to define a common position on the restrictions which each Member State concerned should apply.

Two of these referrals led to opinions in 1995.

The first of these concerned injectable preparations of naftidrofuryl, a vasodilator with local anaesthetic properties. Concerns over toxicity and lack of efficacy in the treatment in a number of indications, led to a referral to the Committee and the establishment of an ad hoc Pharmacovigilance Working Group. Based on the Group's Report the CPMP recommended on 8 June 1995 that marketing authorisations for injectable products containing naftidrofuryl should be withdrawn. Following notification of the CPMP Opinion, appeals were lodged by marketing authorisation holders. After appeal the Committee decided on 19 October 1995 to maintain its first Opinion that marketing authorisation should be withdrawn.

The second opinion related to the phototoxicity and cardiotoxicity of an anti-bacterial product containing sparfloxacin. At its meeting of 19 December the CPMP came to the opinion that the marketing authorisation for the 100 mg strength of the product should

be withdrawn, with the authorisation for the 200 mg strength being maintained under restricted conditions.

During 1995 the CPMP and the Pharmacovigilance Working Party held several meetings and hearings on an entire class of slimming agents called anorectics and the possible risk of primary pulmonary hypertension. The Committee reviewed 14 different substances marketed by some 80 companies. It is expected that the CPMP could come to an opinion on the matter early in 1996.

The CPMP adopted a Position Statement on so-called 'third generation' combination oral contraceptives containing gestodene or desogestrel, at a special meeting held on 27 October 1995. This Statement was made public. At this occasion it became clear that the provisions of Article 12 were not entirely appropriate for dealing with large numbers of substances in a short period of time. The attention of the Commission has been drawn to the need to consider a more flexible procedure to deal with such complex cases.

CPMP Working Parties

In formulating the opinion of the Agency on any question concerning human medicinal products, the CPMP is assisted by working parties which provide additional advice on specific matters related to the quality, efficacy and safety of medicinal products.

To support its activities the CPMP can rely on a pool of 1250 experts put at the disposal by the EU Member States. These experts may also participate in any of the following CPMP working parties as well as in the activities of the International Conference on Harmonisation (ICH).

In addition to the permanent Working Parties listed below, ad hoc groups are formed to address important issues as they arise. There are presently four CPMP Working Parties and one joint CPMP/CVMP Working Party:

- The Biotechnology Working Party, chaired by Prof. Vicari, advises the CPMP on any matter concerning biotechnology derived products and biologicals. It deals both with centralised procedure applications and scientific questions of general interest.
- The Efficacy Working Party is responsible for drawing up and updating methodological guidelines in established therapeutic areas and elaborating position papers on efficacy issues of developing clinical areas. It is chaired by Prof. Hildebrandt.
- The Safety Working Party, chaired by Prof. Sjöberg, provides a forum for dialogue and understanding on pre-clinical safety issues and methodological guidelines.
- The Pharmacovigilance Working Party, chaired by Dr Wood, provides a forum for dialogue and understanding between National Authorities and the EMEA on pharmacovigilance matters (i.e. harmonisation of terminology, development of IT communication facilities, setting up of pharmacovigilance procedures in Member States) and examines questions relating to drug safety or changes in risk-benefit.

- A Joint CVMP/CPMP Quality Working Party, chaired by Dr Robert, has been set up to provide, at the request of the CVMP/CPMP, a forum for dialogue and understanding between pharmaceutical experts to maintain a harmonised approach to quality issues and to avoid national divergence in assessing quality problems.

Guidelines

Over the years the EU has already adopted a series of Guidelines on many aspects of quality, safety, efficacy and testing of medicinal products. These have been published by the European Commission and details can be found in Annex 6 of this Report. The CPMP therefore decided in 1995 to concentrate attention on updating existing Guidelines where necessary.

The Committee is also involved in the development of Guidelines within the trilateral ICH process between EU, Japan and US. These international harmonisation aspects have mobilised not only the Chairman of the CPMP, who represents the Agency on the ICH Steering Committee, but also many CPMP Members and European experts appointed as rapporteurs or topic leaders in the preparatory work of the ICH and in particular in ICH working groups on quality, safety, efficacy and biotechnology.

During the third major conference held in Yokohama 28 November to 1 December ('ICH3') considerable progress was made, with 19 trilateral Guidelines already finalised and 19 other topics to be completed within the next 2 years.

Beside the ICH Guidelines, which have been a priority for CPMP Working Parties, additional Guidelines were reviewed or started by the CPMP in 1995. Details of all ICH and CPMP Guidelines which have been considered by the CPMP in 1995 may be found in Annex 7.

Contacts with Interested Parties

Following the model of the CVMP, the CPMP has attempted to define its contacts with interested third parties. After preliminary contacts between the EMEA and representatives of European consumer organisations, co-ordinated by BEUC, as well as various trade and professional organisations (Association Européenne des Spécialités Pharmaceutiques Grand Public, Groupement des Pharmaciens Europeens, European Federation of Pharmaceutical Industries' Associations and Standing Committee of European Doctors) a first meeting took place after the October CPMP meeting. It was agreed that such 'debriefing' meetings would take place on a quarterly basis.

These meetings will usually be attended by the CPMP Chairman, Vice-Chairman and any other Members of the Committee who wish to attend. Representatives of the EMEA Secretariat and European Commission also attend. These meetings are held without interpretation and at no additional cost to the Agency.

Decentralised Procedure

Under Directive 93/39/EEC on medicinal products (OJ No L.214, 24.8.93, p.22) all biotechnology and other high technology products which had been the subject of opinions of the old CPMP before 1 January 1995 automatically fall under the decentralised procedure. This means that divergent opinions of Member States on these products would become subject to arbitration by the Agency.

Details of these products may be found in the reports published by the Commission on the operations of the former Committee for Proprietary Medicinal Products.

There was a relatively low occurrence of new decentralised procedures in 1995. By the end of 1995, 30 new decentralised procedures, subject to mutual recognition, had been notified to the EMEA Secretariat by the companies concerned.

The need for enforcing the principle of mutual recognition in both cases (for both old and newly authorised products) has been largely recognised by all competent authorities. An ad hoc Mutual Recognition Facilitating Group was formed to deal with these matters in an attempt to facilitate the application of this principle, especially during the transitional period until January 1998.

In co-operation with the Member States authorities, through the Mutual Recognition Facilitating Group, the EMEA Secretariat has indicated that it is ready to support, if required, the mutual recognition procedure.

No requests were received from Member States in 1995 for binding arbitration either in the case of new applications under the decentralised procedure or variations to existing authorisations.

Multi-State Procedures

In addition to the ex-concertation applications, 64 Multi-State applications were also inherited by the CPMP, of which 4 were subsequently abandoned by the companies concerned. These applications are subject to the rules which applied prior to the entry in force of Council Regulation (EEC) No 2309/93 and the opinions of the CPMP are therefore non-binding.

A total of 44 positive non-binding Multi-State opinions were adopted in 1995 and one negative opinion, with the remaining procedures expected to be completed early in 1996.

IV Medicinal Products for Veterinary Use

IV.1 Preface by Prof. Reinhard Kroker Chairman of the Committee for Veterinary Medicinal Products

The animal health industry had expressed concern that there would be disadvantages in creating an Agency which considers both human and veterinary medicines together. Given that the total market for veterinary products approximates to only 4 percent of the total pharmaceutical market of the European Union, there are obvious advantages of scale in being located in the same Agency together with human medicinal products. The sharing of major resources such as administration support, information technology and financial services offer real benefits in terms of cost savings.

Other benefits have come from being able to address logistical and procedural problems common to both Scientific Committees.

Another key concern at the outset had been the workload which had been difficult to predict; no industry survey had yet addressed this issue at the time the Agency opened its doors. Discussions were held by the Veterinary Medicines Evaluation Unit in 1995 with FEDESA (European Federation of Animal Health) to initiate a survey of companies on their intentions to file applications through the new system, the results of which should become available in the first quarter of 1996.

The attitude of the animal health industry to the Agency and the new procedures had appeared to be somewhat mixed at the outset. Whilst some companies appear reluctant to use the centralised procedure, others had adopted a very positive attitude. FEDESA has stated that it can see a "growing climate of confidence from its membership". This is certainly borne out from the meetings with companies, progress made in CVMP meetings and discussions with interested parties - and the increasing numbers of letters of intention to submit applications received by the Unit in the last quarter of 1995.

IV.2 Unit for the Evaluation of Medicinal Products for Veterinary Use

At the end of 1995, the Unit was staffed by 6 people: three scientific officers, one administrative assistant and two secretaries. Although this structure proved able to deal with the workload in 1995, resources were rapidly becoming stretched. Towards the end of 1995 it became clear that the volume of work was increasing significantly, not least with rising numbers of applications for determination of maximum residue limits (MRLs) for new substances or extensions to existing substances.

IV.3 Committee for Veterinary Medicinal Products

The new CVMP met for the first time on 24 and 25 January 1995 in Brussels with the co-operation of the Commission because the facilities of the Agency had not at that time been finished. Prof. Reinhard Kroker was elected as Chairman for a period of three

years, with Mr Cyril O'Sullivan as Vice-Chairman. The first CVMP meeting at the Agency's premises was held on 11 and 12 May 1995.

The Committee met a total of 8 times in 1995 at regular intervals, with meetings lasting two days. Along with the large number of Working Group meetings, especially relating to the establishment of maximum residue limits, the involvement of CVMP Members and the commitment of Member States has been considerable.

'Converted' Procedures and First Positive Opinion

By the time Council Regulation (EEC) No 2309/93 came into force on 1 January 1995, only one outstanding application, for a biotechnological vaccine, remained from the old concertation procedure. This was 'converted' into the new procedure and in July 1995 the new CVMP gave its first positive opinion recommending the granting of a marketing authorisation. Given the objections raised by certain Member States in the Standing Committee for Veterinary Medicinal Products, a Commission Decision was not reached in 1995.

New Applications under the Centralised Procedure

The CVMP is currently examining two new centralised applications

- a biotechnology-derived vaccine for cats (List A)
- a new anti-microbial for food-producing animals (List B)

With regard to the scope of application of List B, the CVMP accepted the advice given by the European Commission that all criteria applicable to veterinary medicines in Part B of the Annex to Council Regulation (EEC) No 2309/93 for authorisation through the centralised procedure should apply to products for non-food producing animals. This extends to new substances as well, providing that the non-food animal species indicated is one of a number of species on a multi-species label of which at least one is a food-producing animal.

Old and New Maximum Residue Limit Applications

In accordance with Council Regulation (EEC) No 2377/90 (OJ No L.224, 18.8.90, p.1), an application for the determination of MRL must be made for all new veterinary substances for use with food-producing animals. For existing substances, a definitive MRL must be established by 31 December 1996, failing which they will no longer be able to be marketed within the Community.

- Existing veterinary substances

At the explicit request of the Commission, the new CVMP inherited some 450 applications, without fees, for the determination of maximum residue limits (MRLs) for existing veterinary substances.

The CVMP Safety of Residues Working Party met eight times in 1995 and made considerable progress. However, it would appear impossible to complete the required work by the deadline of 31 December 1996 and other options will have to be considered.

Since the time when the Agency took over administrative responsibility for the establishment of MRLs the Veterinary Medicines Evaluation Unit has liaised closely with FEDESA and the Federation of Veterinarians in Europe to keep these parties informed of the progress being made in the assessment of MRLs for old substances. A list of substances which were defended or an application received in 1995 was distributed to all interested parties.

- New MRL applications

Ten new applications were received by the Agency for the establishment of MRLs under the new system under Article 6 of Council Regulation (EEC) No 2377/90. The time frame laid down in the legislative framework for the assessment to be completed by the CVMP was respected in each case.

- CVMP recommendations on MRLs

Recommendations of the CVMP have been transmitted to the European Commission and most of them have already been adopted, after consultation with the Standing Committee on Veterinary Medicinal Products, and published in the Official Journal of the European Union:

- Commission Regulation (EC) No 1441/95, OJ No L.143, 27.6.95, p.22
- Commission Regulation (EC) No 1442/95, OJ No L.143, 27.6.95, p.26
- Commission Regulation (EC) No 2796/95, OJ No L.290, 5.12.95, p.1
- Commission Regulation (EC) No 2804/95, OJ No L.291, 6.12.95, p.8

At the end of 1995, the Committee had made the following recommendations:

- definitive MRLs were determined for 12 substances to be placed in Annex I of Council Regulation (EEC) No 2377/90
- the list of substances not subject to an MRL (Annex II) was extended by 139 substances
- additives with an E number were also included in Annex II where they have been approved for foodstuffs for human consumption, with the exception of preservatives listed in Part C of Annex III of Directive 95/2/EC
- homeopathic substances whose concentrations do not exceed one part per ten thousand were also included in Annex II

- provisional MRLs were fixed for 17 substances (Annex III) pending additional data from applicant and the expiry times for provisional MRLs for 12 substances were extended
- two substances (furazolidone and colchicine) were added to Annex IV which lists those substances whose use in the EU is prohibited in food-producing animals
- a further 42 substances were determined to fall outwith the scope of Council Regulation (EEC) No 2377/90

Scientific and Administrative Advice

Within the general principles set out in the draft Notice to Applicants for Veterinary Products, the CVMP decided that it would offer scientific advice to companies on the conduct of various tests and trials only where new fields of scientific investigation were being considered and when no guidelines existed or when existing guidelines did not provide sufficient information.

The Committee agreed to consider one request for scientific advice in 1995 concerning minimum data requirements for documenting genetic stability prior to the development of a new recombinant vaccine. The matter is currently being considered by experts in the Immunological Veterinary Medicinal Products Working Party.

On procedural issues, companies are encouraged to meet with the Veterinary Medicines Evaluation Unit to discuss the various aspects of potential applications prior to application, provided that a written request is submitted in advance stating clearly the issues to be addressed.

Mutual Recognition

Decentralised procedures arise both from the old concertation procedures finalised before 31 December 1994, and for new applications which are submitted to national competent authorities. Although there was a very low occurrence of new decentralised procedures in 1995, it has to be expected that the use of this procedure will increase dramatically from 1996 onwards, and will play an important role in the overall European veterinary medicines market.

A total of 22 old concertation procedures for which a non-binding opinion had been adopted before the end of 1994 were inherited by the CVMP at the beginning of 1995. By the end of 1995 3 new decentralised procedures, subject to mutual recognition, had been notified to the EMEA Secretariat by the companies concerned. No requests were received from Member States in 1995 for binding arbitration either in the case of new applications under the decentralised procedure or variations to existing authorisations.

In addition, two non-binding but positive opinions were reached by CVMP in July and September 1995 for applications introduced before 1995 under the old multi-state pro-

cedure for an anthelmintic intra-ruminal device for cattle and an anti-parasiticide for cats.

Guidelines

In addition to the pre-existing Guidelines adopted by the EU in the veterinary medicines sector, the CVMP agreed in 1995 that Guidelines should be prepared for advice to industry in three major areas:

- Environmental safety guidelines

Two drafts were already in preparation when the CVMP took over responsibility from the Commission in this area: Phase I and Phase II of Guidelines on the Environmental Risk Assessment for the Use of Veterinary Medicinal Products. The Phase I Guideline seeks to identify products which can be exempted from further testing because they are unlikely to have any harmful effect, whilst the Phase II Guideline provides guidance for further assessment of products not exempted in Phase I. These Guidelines are still under consideration and are likely to be released for consultation to interested parties in early 1996.

A draft environmental risk assessment Guideline on immunological veterinary medicinal products was also released for consultation in July 1995 by the CVMP.

- Quality guidelines

Guidelines on quality requirements for products intended for incorporation into animal feedingstuffs (medicated premixes) and guidelines on the manufacture of finished dosage forms were released for a six-month consultation period in December.

- Withdrawal period guideline

A Guidelines on the harmonisation of withdrawal periods was also released for consultation in May. The CVMP will consider the Guideline again in early 1996.

CVMP Working Parties

Three Working Parties have been established by the CVMP

- Safety of Residues
- Immunological Veterinary Medicinal Products
- Veterinary Pharmacovigilance

- Safety of Residues Working Group

The Working Party, chaired by Dr Kevin Woodward, met frequently throughout 1995 working in a determined manner to meet the objective of completing, within the deadline, the review of old substances for which an MRL has to be established by the end of 1996.

Thanks to the efforts of the Working Party a significant breakthrough in the backlog of substances still to be assessed at the beginning of the year was made. From an approximate figure of 450 received from the European Commission on 1 March 1995, the number of pending applications decreased to 260 at the end of 1995.

- Immunological Veterinary Medicinal Products Working Group
Chaired by Prof. Paul-Pierre Pastoret of Belgium, the Working Party on Immunological Veterinary Products (IVMP) met only once in 1995. The Group offers advice on biological products when called upon to do so by the CVMP.

In addition, the Working Party has been working on a list of items which it should address in the near future. Among these, it was agreed that guidelines on potency tests and on the expression units would be given first priority.

- Veterinary Pharmacovigilance Working Party
This Working Party was established under the chairmanship of Dr Agostino Macri. Although it did not meet in 1995, a number of issues will be addressed in 1996, including safe administration of intra-ruminal boluses in cattle and redrafting of the pharmacovigilance guidelines in the Notice to Applicants.

Whilst several Member States have established pharmacovigilance systems for veterinary medicinal products, others are still in the process of putting their systems into place. The Pharmacovigilance Working Party will also look at what support could be given to those Member States who have yet to complete the establishment of a pharmacovigilance monitoring system.

Contacts with Interested Parties

The CVMP has attempted to define its contacts with interested third parties. Various European representative organisations held observer status within the old CVMP, but it is clear that the legal status of the new CVMP and the decisions it takes prohibits the participation of non-authorised persons.

Recognising the useful contribution which observers bring to its work, the CVMP decided in September 1995 that consultation sessions would be held at the end of most Committee meetings at the Agency's premises. These meetings are usually attended by the CVMP Chairman, Vice-Chairman and any other members of the Committee who wish to attend. Representatives of the EMEA Secretariat and European Commission also attend. These meetings are held without interpretation and at no cost to the Agency.

V Activities of Common Interest to Human and Veterinary Medicinal Products

V.1 Technical Co-ordination

Whilst most scientific activities of the Agency are divided between medicinal products for human and for veterinary use, certain activities common to both are dealt with together in the Technical Co-ordination Unit. These include inspection and quality activities. The Scientific Committees have established a Joint Working Party to which quality questions are referred, made up of human and veterinary medicine experts.

Inspections

The Agency is responsible for co-ordinating any inspections that are requested by the Scientific Committees in connection with the assessment of applications made under the new centralised procedure. These inspections may be necessary to verify specific aspects of the manufacture and control of the product and also, in the case of manufacturers in non-European Union countries, to ensure compliance with Good Manufacturing Practice (GMP) and quality assurance systems.

Inspections are carried out on behalf of the EU by one or more Member States' Inspection Services. Where inspections have to be carried out at facilities outside of the EU, inspections are performed by a European team, composed of representatives of the "Supervisory" Member State and of the Rapporteurs. In 1995, third country inspections were carried out in Switzerland and the US.

The Agency made proposals to the Scientific Committees at the end of 1995 for regular meetings of a new group of experts to provide advice on GMP and inspection issues both to the Agency's expert Scientific Committees and to its Secretariat.

The table below gives figures for inspections carried out for both 'converted' ex-concertation and new centralised procedure applications:

Inspection Status	Number of applications
Inspections completed	
- new inspections carried out	8
- no special inspection necessary on basis of existing information	11
Planned	9
Waiting for decision on need to inspect	3

European Pharmacopoeia

The Agency, given its areas of responsibility within the European system, now participates directly in the work of the European Pharmacopoeia Commission as a technical member of the European Commission delegation. The European Pharmacopoeia, which operates under the aegis of the Council of Europe of which all EU Member States are members, seeks to harmonise and set standards for the quality of ingredients and excipients.

The EMEA values the efforts of the Pharmacopoeia Commission Secretariat in setting up a network, on behalf of the European Commission, to co-ordinate the activities of the official control laboratories of EU Member States (OMCL Network). The Agency is also closely following the development of biological standards and batch release arrangements for biological products.

V.2 Documentation and Archiving

In 1995 the Agency's incoming mail and faxes rose dramatically from about 450 in January to about 2500 items of correspondence a month by December 1995. Given the confidential and sensitive nature of some of the documentation a secure system of archiving is in place, along with security grading to protect public and commercial interests. Copies of all outgoing and incoming correspondence are stored in the Agency's central archives.

Documents are graded as follows:

- *confidential* where unauthorised disclosure might have consequences prejudicial to the interests of the Agency, the Commission or one or more Member States
- *restricted* where disclosure or, in particular, premature disclosure would be prejudicial to the smooth functioning of the Agency, including relations with the Commission or the Member States
- *ordinary internal or public*

Such classification measures are in addition to the duty of confidence which all members of the Management Board, Scientific Committees and EMEA staff have to abide by.

The documentation services were also occupied in 1995 in setting up the Agency's library and the acquisition of selected publications to help staff in their work. These include a number of scientific monographs, reference works and periodicals. At the end of 1995 the library contained some 300 works and collections of periodicals. Other information resources include access to all Commission databases (e.g. CELEX, Rapid, etc).

V.3 Conference and Language Services

The Agency houses three conference rooms, complete with interpretation facilities and audio-visual material. In 1995 some 80 different meetings took place over a total of 180 days. Interpretation for these meetings in 1995 were provided by the EU Joint Interpreting and Conference Service and represented approximately 400 interpreting days.

Although a Translation Centre for the Bodies of the European Union was created by Regulation in 1994, the Centre has yet to become operational. The translation of key documents - some 2,500 pages of text in 1995 - into all eleven official Community languages proved a major difficulty for the emerging Translation Centre to cope with in 1995. Pending the Centre's coming into operation in 1996, the translation requirements of the Agency were handled by the Commission's own Translation Services in Luxembourg.

The highly technical nature of certain scientific texts creates additional difficulties (e.g. scientific assessment reports, opinions of Scientific Committees, package labelling and leaflets), which nevertheless did not significantly delay the decision-making at Agency level. A provisional solution was found thanks to the co-operation of members of the Scientific Committees, Secretariat staff and the assistance of applicant companies.

In the meantime, out of all the newly-created EU Agencies, the EMEA has become the biggest user of the Translation Centre's services and also the biggest investor in the new Centre, having paid some ECU 500,000 in 1995 for its setting-up.

ANNEXES

- Annex 1 Membership of the Management Board
- Annex 2 Membership of the Committee for Proprietary Medicinal Products
- Annex 3 Membership of the Committee for Veterinary Medicinal Products
- Annex 4 Organigram of the EMEA Permanent Secretariat
- Annex 5 EMEA Budget for 1994 and 1995
- Annex 6 Rules Governing Medicinal Products in the European Community
- Annex 7 CPMP Opinions in 1995 on Centralised Human Medicinal Product Applications
- Annex 8 CPMP/ICH Guidelines Considered in 1995

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 MICOSI

Fernando MANSITO CABALLERO

Belgique/België

Eliane MESMAEKER

Jean-Antoine DE MUYLDER

Danmark

Ib VALSBORG

Knud KRISTENSEN

Deutschland

Karl FEIDEN

Hermann PABEL

ELLADA/Greece

Stavros KAZAZIS

Nikolaos KOKOLIS

España

Pilar GONZALEZ GANCEDO

Cleto SANCHEZ VELLISCO

France

Didier TABUTEAU

Jacques BOISSEAU

Ireland

Seamus HEALY

Tom MOONEY

Italia

Luigi FRATI

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 ARANDA DA SILVA

Graça TEIXEIRA QUEIROS

Suomi/Finland

Mauno LINDROOS

Hannes WAHLROOS

Sverige

Birgitta BRATTHALL

Anders BROSTRÖM

United Kingdom

Keith JONES

Alistair CRUICKSHANK

Annex 2

**MEMBERSHIP OF THE
COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS**

Chairman

Prof. Jean-Michel ALEXANDRE

Belgique/België

Mr Noël WATHION
Dr Luk BLONDEEL

Danmark

Mr Henning HOVGAARD
(Vice-Chairman)
Dr Gorm JENSEN

Deutschland

Prof. Alfred HILDEBRANDT
Prof. Reinhard KURTH

ELLADA/Greece

Prof. Marios MARSELOS
Mrs Julia YOTAKI

España

Ms Carmen COLLADO ALVAREZ
Prof. Fernando de ANDRES-TRELLES

France

Dr Patrick LECOURTOIS
Prof. Jean-Hughes TROUVIN

Ireland

Dr Mary TEELING
Dr David LYONS

Italia

Prof. Giuseppe VICARI
Mr Bruno SCIOTTI (*)

Grand-Duché du Luxembourg

Prof. Jean-Louis ROBERT
Ms Jacqueline GENOUX-HAMES

Nederland

Dr Hans van BRONSWIJK
Mr Willem van der GIESEN

Österreich

Dr Heribert PITTNER
Dr Walter FUCHS

Portugal

Prof. José GUIMARES MORAIS
Dr Henrique LUZ-RODRIGUES

Suomi/Finland

Dr Christer STROMBERG
Dr Eeva ALHAVA

Sverige

Prof. Kjell STRANDBERG
Prof. Per SJOBERG

United Kingdom

Dr David JEFFERYS
Dr Susan WOOD

(*) Mr Bruno Sciotti was replaced in December 1995 by Prof. Vittorio Silano

Annex 3

MEMBERSHIP OF THE COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

Chairman

Prof. Reinhard KROKER

Belgique/België

Prof. Paul-Pierre PASTORET
Mrs Françoise FALIZE

Danmark

Ms Birgitte KRISTENSEN
† Dr Nils GYRD-HANSEN (*)

Deutschland

Dr Sabine EGLIT
Mr Manfred MOOS

ELLADA/Greece

Dr Vassilios ELEZOGLOU
Mr Dimistrios MIGOS

España

Dr Luis Fernando CORBALAN
Dr Odon SOBRINO

France

Dr Jacques BOISSEAU
Dr Dominique MOUROT

Ireland

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

Italia

Dr Agostino MACRI
Ms Gabriella CONTI

Grand-Duché du Luxembourg

Mr Marc WIRTOR
Mr Albert HUBERTY

Nederland

Dr Herman LENSING
Dr Peter HEKMAN

Österreich

Dr Eugen OBERMAYR
Dr Johannes DICHTL

Portugal

Ms Margaride PRATAS
Mr José PIRES DUARTE BELO

Suomi/Finland

Dr Liisa KAARTINEN
Ms Elina KOSKINEN

Sverige

Dr Annika WENNBERG
Dr Jan LUTHMAN

United Kingdom

Dr Michael RUTTER
Dr Kevin WOODWARD

(*) Dr Nils Gyrd-Hansen was replaced by Dr Claus Willadsen in December 1995.

Annex 4

ORGANIGRAM OF THE EMEA PERMANENT SECRETARIAT

DIRECTORATE

Executive Director Fernand Sauer

- Financial control Birgit Snoeren

Administration and Support Services

Head of Unit Marino Riva

- Personnel and administration Frances Nuttall
- Accounting Gerard O'Malley
- Computing and conference Riccardo Ettore

Evaluation of Human Medicines

Head of Unit Rolf Bass

- Centralised procedures
- Decentralised procedures Josep Torrent Farnell

Technical Co-ordination

Acting Head of Unit Rolf Bass

- Pharmacovigilance Annekarin Bertelsmann (acting)
- Inspection Stephen Fairchild
- Documentation and archiving Beatrice Fayl

Evaluation of Veterinary Medicines

Head of Unit Peter Jones

- Decentralised procedures
- Fixing of maximum residue limits for veterinary medicinal products

Annex 5

EMEA BUDGET FOR 1994 AND 1995

The summarised comparative budget statements for 1994 and 1995 are as follows:

	1994	1995
Revenues		
European Community subsidy	6 800 000	9 400 000
Evaluation fees		4 000 000
Miscellaneous revenue	13 085	262 000
Total revenue	6 813 085	14 412 000
Expenditure		
Staff costs		
- staff salaries and allowances	544 264	3 934 000
- other staff costs	69 149	1 469 000
Total staff costs	<u>613 413</u>	<u>5 403 000</u>
Building equipment & other internal costs		
- Fitting out, lease & other building related costs	4 811 000	2 420 000
- IT, data processing	1 197 918	600 000
- Other current administrative expenditure	110 754	1 091 000
Total internal costs	<u>6 119 672</u>	<u>4 304 000</u>
Operational and expertise related costs		
- Committee meetings	80 000	1 245 000
- Fees of rapporteurs and experts		2 200 000
Total operational and expertise costs	<u>80 000</u>	<u>3 445 000</u>
Translation costs		
- Luxembourg Translation Centre		<u>500 000</u>
Other expenditure		
- Publishing and information		10 000
Total expenditure	6 813 085	14 412 000

Annex 6

RULES GOVERNING MEDICINAL PRODUCTS IN THE EUROPEAN COMMUNITY

The Office for Official Publications of the European Communities produces in a series of eight volumes the legal texts and notices on human and veterinary medicinal products:

- Volume I The rules governing medicinal products for human use in the European Union
catalogue n° CO-86-94-319-EN-C, also available in ES, DA, DE, GR, FR, IT, NL, PT
- Volume II Notice to applicants for marketing authorisations for medicinal products for human use in the European Union
catalogue n° CO-55-89-239-EN-C, also available in ES, DE, FR, IT
- Volume III Guidelines on the quality, safety and efficacy of medicinal products for human use
catalogue n° CO-55-89-843-EN-C, also available in ES, DE, FR, IT
Addenda volumes published in July 1990 (*n° CB-59-90-936-EN-C, also in ES, DE, FR*) and May 1992 (*n° CO-75-92-558-EN-C, also in ES, DE, FR, IT*)
- Volume IV Good manufacturing practices for medicinal products
catalogue n° CO-71-91-760-EN-C, also available in ES, DA, DE, GR, FR, NL, PT
- Volume V/A The rules governing veterinary medicinal products in the European Community
catalogue n° CO-77-92-384-EN-C, also available in ES, DE, FR, IT
- Volume V/B Notice to applicants for marketing authorisations for veterinary medicinal products in the European Union
catalogue n° CO-78-93-443-EN-C, also available in ES, DE, FR, IT
- Volume VI Establishment in the EC of maximum residue limits for residues of veterinary products in foodstuffs of animal origin
catalogue n° CO-71-91-768-EN-C, also available in ES, DE, FR, IT
- Volume VII Guidelines for the testing of veterinary medicinal products
catalogue n° CO-86-94-383-EN-C

These volumes may be obtained from:

Office for Official Publications of the EC Tel: (+352) 29291

2, rue Mercier

L - 2985 Luxembourg

Fax: (+352) 48 85 73/48 68 17

Telex: PUBOF LU 1324 b

Annex 7

CPMP OPINIONS IN 1995 ON CENTRALISED HUMAN MEDICINAL PRODUCT APPLICATIONS

<i>Name of product</i> · <i>INN</i> · <i>Brandname</i> · <i>List A/B</i>	<i>Company</i> · <i>Name</i> · <i>Origin</i>	<i>Therapeutic area</i> · <i>ATC</i> · <i>Indication</i>	<i>Presentation</i> · <i>Form</i> · <i>Dosage</i> · <i>N° of Presentations</i>	<i>EMEA/CPMP</i> · <i>Validation</i> · <i>Opinion</i> · <i>Active time</i> · <i>Clock stop</i>	<i>Commission</i> · <i>Date of decision</i> · <i>Date of publication</i>
· follitropin-alpha · Gonal-F · List A	· Ares-Serono · IT/CH	· L02A X · treatment of infertility	· powder for injection · 75IU, 150 IU · 16	· 01.01.95 · 17.05.95 · 107 days · 30 days	· 23.10.95 · OJ No C.22 of 26.01.96
· interferon beta-1b · Betaferon · List A	· Schering · DE	· L03A A.... · immuno-stimulation · multiple sclerosis	· powder for injection · 025mg/ml · 1	· 01.01.95 · 12.07.95 · 138 days · 55 days	· 30.11.95 · OJ No C.22 of 26.01.96
· docetaxel · Taxotere · List B	· Rhône-Poulenc Rorer · FR	· L01X.... · cytostatic	· concentrate for infusion · 80mg/2ml · 20mg/0.5ml · 2	· 01.01.95 · 12.07.95 · 100 days · 93 days	· 27.11.95 · OJ No C.22 of 26.01.96
· mycophenolate mofetil · CellCept · List B	· Hoffmann-La Roche · CH	· L04AX · prevention of kidney transplant rejection	· capsules & tablets · 250 & 500mg · 2	· 01.01.95 · 17.10.95 · 243 days · 47 days	· 14.02.96 · OJ No C.54 of 23.02.96
· toremifene · Fareston · List B	· Orion · FIN	· L02BAA02 · treatment of certain breast cancer tumours	· tablets · 60mg · 2	· 01.01.95 · 17.10.95 · 240 days · 50 days	· 14.02.96 · OJ No C.54 of 23.02.96
· factor VIIa · NovoSeven · List A	· Novo-Nordisk · DK	· B02B D05 · coagulation factor	· powder for injection · 60, 120, 240 KIU · 3	· 01.01.95 · 12.09.95 · 210 days · 80 days	· 23.02.96 ·
· · · List A	· · USA	· to be fixed · treatment of diabetes mellitus	· solution for injection · 40IU/ml vials · 100IU/ml vials & cartridges · 3	· 01.01.95 · 22.11.95 · 250 days · 86 days	· ·
· · · List A	· · NL	· G03GA · infertility treatment	· powder for injection · 50, 75, 100 & 150IU · 16	· 01.01.95 · 20.12.95 · 203 days · 151 days	· ·

Names of products and companies remain confidential until the Commission implements the CPMP opinion in a Decision. Only at this time will this information be made available to the public.

Annex 8

CPMP/ICH GUIDELINES AND CPMP GUIDELINES CONSIDERED IN 1995

Efficacy Topics

Topic CPMP no.	Title	Status
CPMP/ICH/379/95 (ICH Topic E7)	Studies in support of special populations: geriatrics	Adopted September 93
CPMP/ICH/378/95 (ICH Topic E4)	Dose response information to support drug registration	Adopted May 94
CPMP/ICH/375/95 (ICH Topic E1A)	Population exposure: the extent of population exposure to assess clinical safety	Adopted November 94
CPMP/ICH/377/95 (ICH Topic E2A)	Clinical safety data management: definitions and standards for expedited reporting	Adopted November 94
CPMP/ICH/137/95 (ICH Topic E3)	Clinical study reports: format and content	Adopted December 95
CPMP/ICH/135/95 (ICH Topic E6)	Good clinical practices: consolidated guideline	Trilateral agreement expected May 96
CPMP/ICH/288/95 (ICH Topic E2C)	Clinical safety data management: periodic safety update reports for marketed drugs	Step 2 guideline released by CPMP in December 95
CPMP/ICH/289/95 (ICH Topic E5)	Ethnic factors in the acceptability of foreign clinical data	Step 2 expected in May 96
CPMP/ICH/287/95 (ICH Topic E2B)	Data elements for transmission of individual case safety reports	On-going
CPMP/ICH/291/95 (ICH Topic E8)	General considerations for clinical trials	On-going
CPMP/ICH/376/95 (ICH Topic E1B)	Population exposure: prospective and retrospective studies of databases on population exposure	On-going study by industry
CPMP/EWP/233/95	The clinical investigation of medicinal products in the treatment of chronic peripheral arterial occlusive disease	Adopted November 95
CPMP/EWP/235/95	The clinical investigation of medicinal products in the treatment of cardiac failure	Adopted November 95
CPMP/EWP/237/95	Antiarrhythmics	Adopted November 95
CPMP/EWP/239/95	The clinical requirements for locally applied, locally acting products containing known constituents	Adopted November 95
CPMP/EWP/240/95	Fixed combination medicinal products	On-going (revision)
CPMP/EWP/462/95	Development medicines for children	On-going (revision)
CPMP/EWP/205/95	Evaluation of anticancer medicinal products in man	On-going (revision)
CPMP/EWP/553/95	Antidementia medicinal products	On-going (new)
CPMP/EWP/234/95	Antianginal Medicinal Products	On-going (revision)
CPMP/EWP/555/95	Haematopoietic growth factor	On-going (new)
CPMP/EWP/238/95	Antihypertensive agents	On-going (revision)
CPMP/EWP/559/95	Schizophrenia	On-going (new)
CPMP/EWP/552/95	Osteoporosis	On-going (new)
CPMP/EWP/558/95	Antimicrobial agents	On-going (revision)
CPMP/EWP/563/95	Parkinson	On-going (new)
CPMP/EWP/556/95	Disease modifying compounds in arthritis	On-going (new)

Quality/Biotechnology Topics

Topic CPMP no.	Title	Status
CPMP/ICH/380/95 (ICH Topic Q1A)	Stability testing guidelines: stability testing of new drug substances and products	Adopted December 93
CPMP/ICH/381/95 (ICH Topic Q2A)	Validation of analytical methods: definitions and terminology	Adopted November 94
CPMP/ICH/142/95 (ICH Topic Q3A)	Impurities testing guideline: impurities in new drug products	Adopted May 95
CPMP/QWP/486/95	Manufacture of the finished dosage form	Adopted September 95
CPMP/ICH/139/95 (ICH Topic Q5B)	Analysis of the expression construct in cell lines used for production of r-DNA derived protein products	Adopted December 95
CPMP/ICH/138/95 (ICH Topic Q5C)	Stability testing of biotechnological/biological products	Adopted December 95
CPMP/ICH/279/95 (ICH Topic Q1B)	Guideline for the photostability testing of new drug substances and products	Step 2 guideline released by CPMP in December 95
CPMP/ICH/280/95 (ICH Topic Q1C)	Stability testing requirements for new dosage forms	Step 2 guideline released by CPMP in December 95
CPMP/ICH/281/95 (ICH Topic Q2B)	Validation of analytical procedures: methodology	Step 2 guideline released by CPMP in December 95
CPMP/ICH/282/95 (ICH Topic Q3B)	Impurities in new drug products	Step 2 guideline released by CPMP in December 95
CPMP/ICH/295/95 (ICH Topic Q5A)	Viral safety evaluation of biotechnological products derived from cell lines of human or animal origin	Step 2 guideline released by CPMP in December 95
CPMP/ICH/283/95 (ICH Topic Q3C)	Impurities: residual solvents	Step 2 expected in May 96
CPMP/ICH/294/95 (ICH Topic Q5D)	Derivation and characterisation of cell substrates used for production of biotechnological/ biological products	Step 2 expected May 96
CPMP/ICH/412/95 (ICH Topic Q4)	Harmonisation of pharmacopoeia	Convergence of monographs
CPMP/QWP/580/95	The stability of generics (incl. 'variations' and 'changes')	On-going
CPMP/QWP/567/95	The use of antioxidants and preservatives in medicinal products	On-going
CPMP/QWP/475/95	Development pharmaceuticals and process validation	On-going
CPMP/BWP/268/95	Virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses	On-going
CPMP/BWP/269/95	Medicinal products derived from human plasma	On-going
CPMP/BPWP/388/95	Guidelines to assess efficacy and safety of normal intravenous immunoglobulin products for marketing authorisations	On-going
CPMP/BPWP/198/95	Efficacy and safety of human plasma derived factor VIII and IX products in clinical trials before and after authorisation	On-going

Safety Topics

Topic CPMP no.	Title	Status
CPMP/ICH/386/95 (ICH Topic S5A)	Reproductive toxicology: detection of toxicity to reproduction for medicinal products	Adopted September 93
CPMP/ICH/384/95 (ICH Topic S3A)	Toxicokinetics: a guidance for assessing systemic exposure in toxicology studies	Adopted November 94
CPMP/ICH/385/95 (ICH Topic S3B)	Pharmacokinetics: guidance for repeated dose tissue distribution studies	Adopted November 94
CPMP/ICH/141/95 (ICH Topic S2A)	Genotoxicity: guidance on specific aspects of regulatory genotoxicity tests for pharmaceuticals	Adopted September 95
CPMP/ICH/140/95 (ICH Topic S1A)	Guideline on the need for carcinogenicity studies of pharmaceuticals	Adopted December 95
CPMP/ICH/136/95 (ICH Topic S5B)	Reproductive toxicology: toxicity to male fertility	Adopted December 95
CPMP/ICH/299/95 (ICH Topic S1B)	Carcinogenicity: Utility of two rodent species	Step 2 expected in May 96
CPMP/ICH/174/95 (ICH Topic S2B)	Genotoxicity: Definition of standard battery tests	Step 2 expected in May 96
CPMP/ICH/383/95 (ICH Topic S1C)	Carcinogenicity: dose selection for carcinogenicity studies of pharmaceuticals	On-going
CPMP/ICH/300/95 (ICH Topic S4B)	Repeat dose toxicity testing	On-going
CPMP/ICH/302/95 (ICH Topic S6)	Safety studies on biotechnology products	On-going
CPMP/SWP/465/95	Pre-clinical safety testing of vaccines	On-going

Multidisciplinary Topics

Topic CPMP no.	Title	Status
CPMP/ICH/284/95 (ICH Topic M1)	Standardisation of medical terminology for regulatory purposes	Pilot version 1.5 of MEDDRA
CPMP/ICH/285/95 (ICH Topic M2)	Electronic standards for the transfer of regulatory information	On-going (testing)
CPMP/ICH/286/95 (ICH Topic M3)	Guidelines for non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals	On-going

Pharmacovigilance Topics

Topic CPMP no.	Title	Status
CPMP/180/95	Guideline for post-authorisation safety studies for metered dose inhalers formulated with the new propellants	Adopted June 95
CPMP/175/95	Procedure for competent authorities on the undertaking of pharmacovigilance	Adopted June 95