

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 and Article 152(4)(b) thereof,

Having regard to the proposal from the Commission¹,

Having regard to the Opinion of the Economic and Social Committee²,

Having regard to the Opinion of the Committee of the Regions³,

In accordance with the procedure referred to in Article 251 of the Treaty⁴,

Whereas:

- (1) Council Regulation No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products⁵ provides, in Article 71, that within six years of the entry into force of the Regulation the Commission is to publish a general report on the experience acquired as a result of the operation of the procedures laid down in the Regulation.
- (2) In the light of the Commission's report⁶ on the experience gained, it has proved necessary to improve the operation of the authorisation procedures for the placing of medicinal products on the market in the Community and to amend certain administrative aspects of the European Agency for the Evaluation of Medicinal Products.

¹ OJ L

² OJ L

³ OJ L

⁴ OJ L

⁵ OJ L 214, 24.8.1993, p. 1; Regulation as amended by Commission Regulation (EC) No 649/98 (OJ L 88, 24.3.1998, p. 7).

⁶ COM(2001) final.

- (3) It emerges from the conclusions of that report that the amendments to be made to the centralised procedure set up by Regulation (EEC) No 2309/93 consist of corrections to some of the operating procedures and adaptations to take account of the probable development of science and technology and the future enlargement of the European Union. It also emerges from the report that the general principles previously established which govern the centralised procedure should be maintained.
- (4) Moreover, since the European Parliament and the Council have adopted Directive 2001/83/EC of 23 October 2001 on the Community code relating to medicinal products for human use⁷ and Directive 2001/82/EC of 23 October 2001 on the Community code relating to veterinary medicinal products⁸, the updating of all the references contained in Regulation (EEC) No 2309/93 to the codified directives has to be undertaken.
- (5) For the sake of clarity, it is necessary to replace the said Regulation with a new regulation.
- (6) It is appropriate to preserve the Community mechanism, set up by the repealed Community legislation, for concertation prior to any national decision relating to a high-technology medicinal product.
- (7) Experience gained since the adoption of Council Directive 87/22/EEC⁹ of 22 December 1986 has shown that it is necessary to create a centralised authorisation procedure that is compulsory for high-technology medicinal products, particularly those resulting from biotechnical processes, in order to maintain the high level of scientific evaluation of these medicinal products in the European Union and thus to preserve the confidence of patients and the medical professions in the evaluation. This is particularly important in the context of the emergence of new therapies, such as gene therapy and associated cell therapies, and xenogenic somatic therapy. This approach should be maintained, particularly with a view to ensuring the effective operation of the internal market in the pharmaceutical sector.
- (8) With a view to harmonising the internal market for new medicinal products, this procedure should also be made compulsory for any medicinal product which is intended to be administered to humans or animals and contains an entirely new active substance, that is, one that has not yet been authorised in the Community.
- (9) As regards medicinal products for human use, optional access to the centralised procedure should also be provided for in cases where use of a single procedure produces added value for the patient. This procedure should remain optional for medicinal products which, although not belonging to the abovementioned categories, are nevertheless a therapeutic innovation. It is also appropriate to allow access to this procedure for medicinal product which, although not innovative, may be of benefit to society or to patients if they are authorised from the outset at Community level, such as certain medicinal products which cannot be supplied without a medical prescription. This option may be extended to generic medicinal products authorised by the Community, provided that this in no way undermines either the harmonisation

⁷ OJ L

⁸ OJ L

⁹ OJ L 15, 17.1.1987, p. 38; Directive repealed by Directive 93/41/EEC (OJ L 214, 24.8.1993, p. 40).

achieved when the reference medicinal products was evaluated or the results of that evaluation.

- (10) In the field of veterinary medicinal products, administrative measures should be provided for in order to take account of the specific features of this field, particularly those due to the regional distribution of certain diseases. The field of application of the centralised procedure should also include medicinal products used within the framework of Community provisions regarding prophylactic measures for epizootic diseases.
- (11) In the interest of public health, it is necessary that authorisation decisions under the centralised procedure be taken on the basis of the objective scientific criteria of quality, safety and efficacy of the medicinal product concerned, to the exclusion of economic and other considerations. However, Member States should be able exceptionally to prohibit the use on their territory of medicinal products for human use which infringe objectively defined concepts of public policy and public morality. Moreover, a veterinary medicinal product may not be authorised by the Community if its use would contravene the rules laid down by the Community within the framework of the Common Agricultural Policy.
- (12) Provision should be made whereby the quality, safety and efficacy criteria provided for by Directives 2001/83/EC and 2001/82/EC apply to medicinal products authorised by the Community.
- (13) The Community should have the means to carry out a scientific assessment of the medicinal products presented in accordance with the centralised Community authorisation procedures. Moreover, with a view to ensuring the effective harmonisation of administrative decisions taken by Member States with regard to medicinal products presented in accordance with centralised authorisation procedures, it is necessary to endow the Community with the means to resolve disagreements between Member States concerning the quality, safety and efficacy of medicinal products.
- (14) It is thus appropriate to establish a European Agency for the Evaluation of Medicinal Products (hereinafter referred to as the "Agency").
- (15) The structure and operation of the set of bodies making up the Agency should be designed in such a way as to take into account the need constantly to renew scientific expertise, the need for cooperation between Community and national institutions, the need for adequate representation of civil society, and the future enlargement of the European Union.
- (16) The chief task of the Agency should be to provide Community institutions and Member States with the best possible scientific opinions so as to enable them to exercise the powers regarding the authorisation and supervision of medicinal products conferred on them by Community legislation in the field of medicinal products. Only after a single scientific evaluation procedure addressing the quality, safety and efficacy of high-technology medicinal products has been conducted by the Agency, applying the highest possible standards, should marketing authorisation be granted by the Community, by means of a rapid procedure ensuring close cooperation between the Commission and Member States.

- (17) In order to ensure close cooperation between the Agency and the scientists operating in Member States, provision should be made so that the Management Board is composed in such a way as to guarantee that the competent authorities of the Member States are closely involved in the overall management of the Community system for authorising medicinal products by creating an Advisory Board responsible to the Executive Director of the Agency.
- (18) Exclusive responsibility for preparing the Agency's opinions on all questions concerning medicinal products for human use should be vested in a Committee for Medicinal Products for Human Use. As far as veterinary medicinal products are concerned, such responsibility should be vested in a Committee for Veterinary Medicinal Products . As regards orphan medicinal products, the task should fall to the Committee on Orphan Medicinal Products set up under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 2000 on orphan medicinal products¹⁰. [Lastly, as regards herbal medicinal products, this responsibility should be vested in the Committee on Herbal Medicinal Products set up under Directive 2001/83/EC].
- (19) The creation of the Agency will make it possible to reinforce the scientific role and independence of the committees, particularly through the setting-up of a permanent technical and administrative secretariat.
- (20) The field of activity of the Scientific Committees should be enlarged and their operating methods and composition modernised. Scientific advice for future applicants seeking marketing authorisation should be provided more generally and in greater depth. Similarly, structures allowing the development of advice for companies should be put in place. The Committees should be able to delegate some of their evaluation duties to standing working parties open to experts from the scientific world appointed for this purpose, whilst retaining total responsibility for the scientific opinions issued. The appeal procedures should be amended to provide a better guarantee for applicants' rights.
- (21) The number of members of the Scientific Committees participating in the centralised procedure should be established with a view to ensuring that the Committees remain of efficient size after the enlargement of the Union.
- (22) It is also necessary to reinforce the role of the Scientific Committees in such a way as to enable the Agency to have an active presence in the context of the international scientific dialogue and to develop certain activities that will be necessary, in particular regarding international scientific harmonisation and technical cooperation with the World Health Organisation.

¹⁰ OJ L 18, 22.1.2000, p. 1.

- (23) Furthermore, in order to create greater legal certainty it is necessary to define the responsibilities regarding the transparency rules for the Agency's work, to set certain conditions for the marketing of medicinal products authorised by the Community, to confer on the Agency powers to monitor the distribution of medicinal products authorised by the Community and to specify the sanctions and the procedures for implementing them in the case of failure to observe the provisions of this Regulation and the conditions contained in the authorisations issued under the procedures it establishes.
- (24) It is also necessary to take measures for the supervision of medicinal products authorised by the Community, and in particular for the intensive supervision of undesirable effects of these medicinal products within the framework of Community pharmacovigilance activities, so as to ensure the rapid withdrawal from the market of any medicinal product presenting an unacceptable level of risk under normal conditions of use.
- (25) In order to enhance the efficiency of market surveillance, the Agency should be responsible for coordinating Member States' pharmacovigilance activities. A number of provisions need to be introduced to put in place stringent and efficient pharmacovigilance procedures, to allow the competent authority to take provisional emergency measures, including the introduction of amendments to the marketing authorisation and, finally, to permit a reassessment to be made at any time of the risk/benefit balance of a medicinal product.
- (26) It is also appropriate to entrust the Commission, in close cooperation with the Agency and after consultations with the Member States, with the task of coordinating the execution of the various supervisory responsibilities vested in the Member States, and in particular with the tasks of providing information on medicinal products, and of checking the observance of good manufacturing, laboratory and clinical practices.
- (27) It is necessary to provide for the coordinated implementation of Community procedures for the authorisation of medicinal products, and of the national procedures of Member States which have already been broadly harmonised by Directives 2001/83/EC and 2001/82/EC. It is appropriate that the operation of the procedures laid down by this Regulation be reexamined by the Commission every ten years on the basis of experience gained.
- (28) In order to meet, in particular, the legitimate expectations of patients and to take account of the increasingly rapid progress of science and therapies, accelerated assessment procedures should be set up, reserved for medicinal products of major therapeutic interest, and procedures for obtaining temporary authorisations subject to certain annually reviewable conditions. In the field of medicinal products for human use, a common approach should also be followed, whenever possible, regarding the criteria and conditions for the compassionate use of new medicinal products under Member States' legislation.
- (29) In line with the current provisions of Directives 2001/83/EC and 2001/82/EC, the term of validity of a Community marketing authorisation should be unlimited. Furthermore, any authorisation not used for two consecutive years, that is to say, one which has not led to the placing on the market of a medicinal product in the Community during that period, should be considered invalid, in order, in particular, to avoid the administrative burden linked to maintaining such authorisations.

- (30) Environmental risks may arise from medicinal products containing or consisting of genetically modified organisms. It is thus necessary to subject such products to an environmental risk-assessment procedure similar to the procedure under Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC¹¹, to be conducted in parallel with the evaluation, under a single Community procedures, of the quality, safety and efficacy of the product concerned.
- (31) Since most of the measures necessary for the implementation of this Regulation are measures of individual scope, they should be adopted by use of the advisory procedure provided for in Article 3 of Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission¹², or else by use of the management procedure provided for under Article 4 of that Decision. In respect of measures of general scope within the meaning of Article 2 of that Decision, they should be adopted by use of the regulatory procedure provided for in Article 5 of that Decision,

HAVE ADOPTED THIS REGULATION:

TITLE I

DEFINITIONS AND SCOPE

Article 1

The purpose of this Regulation is to lay down Community procedures for the authorisation, supervision and pharmacovigilance of medicinal products for human and veterinary use, and to establish a European Agency for the Evaluation of Medicinal Products (hereinafter referred to as "the Agency").

The provisions of this Regulation shall not affect the powers of the Member States' authorities as regards setting the prices of medicinal products or their inclusion in the scope of the national health system or social security schemes on the basis of health, economic and social conditions. In particular, Member States shall be free to choose from the particulars shown in the marketing authorisation those therapeutic indications and pack sizes which will be covered by their social security bodies.

Article 2

The definitions laid down in Article 1 of Directive 2001/83/EC and those laid down in Article 1 of Directive 2001/82/EC shall apply for the purposes of this Regulation.

The holder of a marketing authorisation for the medicinal products covered by this Regulation should be established in the Community. The holder shall be responsible for placing those medicinal products on the market.

¹¹ OJ L 106, 17.4.2001, p. 1; Directive last amended by Regulation (EC) No .../2002 of the European Parliament and of the Council [of ... concerning the traceability of genetically modified organisms and the traceability of food products intended for human consumption, etc.].

¹² OJ L 184, 17.7.1999, p. 23.

Article 3

1. No medicinal product appearing in Annex I may be placed on the market within the Community unless a marketing authorisation has been granted by the Community in accordance with the provisions of this Regulation.
2. Any medicinal product not appearing in Annex I may be granted a marketing authorisation by the Community in accordance with the provisions of this Regulation, provided that the applicant shows that the medicinal product is a significant therapeutic, scientific or technical innovation or that the granting of authorisation in accordance with this Regulation is of interest to patients or to animal health at Community level.

Immunological veterinary medicinal products for the treatment of animal diseases subject to Community prophylactic measures may also be granted such authorisation.

3. A generic form of a medicinal product authorised by the Community may be authorised by the competent authorities of the Member States in accordance with Directive 2001/83/EC and Directive 2001/82/EC under the following conditions:
 - (a) the application for authorisation is submitted in accordance with Article 10 of Directive 2001/83/EC or Article 13 of Directive 2001/82/EC;
 - (b) the summary of the characteristics of the product is in all respects consistent with that of the medicinal product authorised by the Community; and
 - (c) the generic medicinal product is authorised under the same name in all the Member States where the application has been made.
4. After consulting the competent committee of the Agency set up under Article 49, Annex I may be re-examined in the light of technical and scientific progress, with a view to making any necessary amendments. Such amendments shall be adopted according to the procedure referred to in Article 77(2).

Article 4

1. In order to obtain the marketing authorisation referred to in Article 3, an application shall be submitted to the Agency.
2. The Community shall issue and supervise marketing authorisations for medicinal products for human use in accordance with Title II.
3. The Community shall issue and supervise marketing authorisations for medicinal products for veterinary use in accordance with Title III.

TITLE II

**AUTHORISATION AND SUPERVISION OF MEDICINAL PRODUCTS FOR
HUMAN USE**

CHAPTER 1

SUBMISSION AND EXAMINATION OF APPLICATIONS – AUTHORISATIONS

Article 5

1. A Committee for Human Medicinal Products is hereby established. The Committee shall be part of the Agency.
2. Without prejudice to Article 50 or to other tasks which Community law may confer on it, the Committee for Human Medicinal Products shall be responsible for formulating the opinion of the Agency on any matter concerning the admissibility of the files submitted in accordance with the centralised procedure, the granting, variation, suspension or withdrawal of an authorisation to place a medicinal product for human use on the market in accordance with the provisions of this Title and pharmacovigilance.
3. At the request of the Executive Director of the Agency or the Commission representative, the Committee for Human Medicinal Products shall also draw up an opinion on any scientific matter concerning the evaluation of medicinal products for human use.

Article 6

1. Each application for authorisation for a medicinal product for human use shall specifically include all the information and documents referred to in Articles 8(3), 10a and 11 of Directive 2001/83/EC, and Annex I thereto. The information and documents are to take account of the unique, Community nature of the authorisation requested, and particularly of the use of a single name for the medicinal product.

The application shall be accompanied by the fee payable to the Agency for the examination of the application.

2. In the case of a medicinal product for human use containing or consisting of genetically modified organisms within the meaning of Article 2 of Directive 2001/18/EC, the application shall be accompanied by:
 - (a) a copy of the the competent authorities' written consent to the deliberate release into the environment of the genetically modified organisms for research and development purposes where provided for in Part B of Directive 2001/18/EC or in Part B of Directive 90/220/EEC¹³;
 - (b) the complete technical dossier supplying the information required by Annexes III and IV to Directive 2001/18/EC;

¹³ OJ L 117, 8.5.1990, p. 15.

- (c) the environmental risk assessment in accordance with the principles set out in Annex II to Directive 2001/18/EC; and
- (d) the results of any investigations performed for the purposes of research or development.

Articles 13 to 24 of Directive 2001/18/EC shall not apply to veterinary medicinal products containing or consisting of genetically modified organisms.

3. The Agency shall ensure that the opinion of the Committee for Human Medicinal Products is given within 210 days of the receipt of a valid application.

In the case of a medicinal product for human use containing or consisting of genetically modified organisms, the opinion of the Committee shall respect the environmental safety requirements laid down by Directive 2001/18/EC. During the process of evaluating applications for marketing authorisations for medicinal products for human use containing or consisting of genetically modified organisms, the necessary consultations shall be held by the rapporteur with the bodies set up by the Community or the Member States in accordance with Directive 2001/18/EC.

4. The Commission shall, in consultation with the Agency, the Member States and interested parties, draw up detailed guidance as to the form in which applications for authorisation are to be presented.

Article 7

In order to prepare its opinion, the Committee for Human Medicinal Products:

- (a) shall verify that the particulars and documents submitted in accordance with Article 6 comply with the requirements of Directive 2001/83/EC, and shall examine whether the conditions specified in this Regulation for issuing a marketing authorisation are satisfied;
- (b) may ask for a State laboratory or a laboratory designated for this purpose to test the medicinal product for human use, its starting materials and, if need be, its intermediate products or other constituent materials in order to ensure that the control methods employed by the manufacturer and described in the application documents are satisfactory;
- (c) may, where appropriate, request the applicant to supplement the particulars accompanying the application within a specific timeperiod.

Where the Committee avails itself of the option under point (c) of the first paragraph, the time-limit laid down in the first subparagraph of Article 6 (3) shall be suspended until such time as the supplementary information requested has been provided. Likewise, this time-limit shall be suspended for the time allowed to the applicant to prepare oral or written explanations.

Article 8

1. Upon receipt of a written request from the Committee for Human Medicinal Products, a Member State shall forward the information showing that the manufacturer of a medicinal product or the importer from a non-member country is able to manufacture the medicinal product concerned and/or carry out the necessary control tests in accordance with the particulars and documents supplied pursuant to Article 6.
2. Where it considers it necessary in order to complete its examination of an application, the Committee for Human Medicinal Products may require the applicant to submit to a specific inspection of the manufacturing site of the medicinal product concerned.

The inspection shall be carried out within the time-limit laid down in the first subparagraph of Article 6(3), by inspectors from the Member State holding the appropriate qualifications, who may be accompanied by a rapporteur or an expert appointed by the Committee.

Article 9

1. The Agency shall forthwith inform the applicant when the opinion of the Committee for Human Medicinal Products is that:
 - (a) the application does not satisfy the criteria for authorisation set out in this Regulation;
 - (b) the summary of the product characteristics proposed by the applicant needs to be amended;
 - (c) the labelling or package leaflet of the product is not in compliance with Title V of Directive 2001/83/EC;
 - (d) the authorisation needs to be granted subject to the conditions provided for in Article 13(4) and (5).
2. Within 15 days of receipt of the opinion referred to in paragraph 1, the applicant may give written notice to the Agency that he/she wishes to appeal. In that case, the applicant shall forward the detailed grounds for his/her appeal to the Agency within 60 days of receipt of the opinion.

Within 60 days of receipt of the grounds for appeal, the Committee for Human Medicinal Products shall re-examine its opinion in accordance with the conditions laid down in the second subparagraph of Article 55(1). The reasons for the conclusion reached on the appeal shall be annexed to the final opinion.

3. Within 30 days of its adoption, the Agency shall send the final opinion of the Committee for Human Medicinal Products to the Commission, to the Member States and to the applicant, together with a report describing the assessment of the medicinal product by the Committee and stating the reasons for its conclusions.

4. If an opinion is favourable to the grant of the relevant authorisation to place the medicinal product concerned on the market, the following documents shall be annexed to the opinion:
 - (a) a draft summary of the product characteristics, as referred to in Article 11 of Directive 2001/83/EC;
 - (b) details of any conditions or restrictions which should be imposed on the supply or use of the medicinal product concerned, including the conditions under which the medicinal product may be made available to patients, having regard to the criteria laid down in Title VI of Directive 2001/83/EC;
 - (c) the draft text of the labelling and package leaflet proposed by the applicant, presented in accordance with Title V of Directive 2001/83/EC;
 - (d) the assessment report.

Article 10

1. Within 30 days of receipt of the opinion referred to in Article 5(2), the Commission shall prepare a draft of the decision to be taken in respect of the application.

In the event of a draft decision granting marketing authorisation, the draft shall include or make reference to the documents mentioned in points (a), (b) and (c) of the first subparagraph of Article 9(4).

Where the draft decision is not in accordance with the opinion of the Agency, the Commission shall annex a detailed explanation of the reasons for the differences.

The draft decision shall be forwarded to the Member States and the applicant.

2. The Commission shall take a final decision in accordance with the procedure referred to in Article 77(3) if the draft decision accords with the Agency's opinion.

The Commission shall take a final decision in accordance with the procedure referred to in Article 77(4) if the draft decision does not accord with the Agency's opinion,

3. The Standing Committee on Medicinal Products for Human Use referred to in Article 77(1) shall adjust its rules of procedure so as to take account of the tasks incumbent upon it under this Regulation.

These adjustments shall provide that:

- (a) the opinion of the Standing Committee is to be given in writing;
- (b) each Member State is to be allowed 15 days to forward written observations on the draft decision to the Commission. However, if a decision has to be taken urgently, a shorter time-limit may be set by the Chairman according to the degree of urgency involved;
- (c) each Member State is to be permitted to require in writing that the draft decision referred to in paragraph 1 be discussed by a plenary meeting of the Standing Committee, giving its reasons in detail.

4. Where, in the opinion of the Commission, the written observations of a Member State raise important new questions of a scientific or technical nature which have not been addressed in the opinion of the Agency, the Chairman shall suspend the procedure and refer the application back to the Agency for further consideration.
5. The Commission shall adopt the provisions necessary for the implementation of paragraph 3 in accordance with the procedure referred to in Article 77(2).
6. The Agency shall disseminate the documents referred to in points (a), (b) and (c) of Article 9(4).

Article 11

1. The marketing authorisation shall be refused if, after verification of the information and particulars submitted in accordance with Article 6, it appears that the quality, the safety or the efficacy of the medicinal product have not been properly or sufficiently demonstrated by the applicant.

Authorisation shall likewise be refused if the particulars and documents provided by the applicant in accordance with Article 6 are incorrect or if the labelling and package leaflets proposed by the applicant are not in accordance with Title V of Directive 2001/83/EC.

2. The refusal of a Community marketing authorisation shall constitute a prohibition on the placing on the market of the medicinal product concerned throughout the Community.

Article 12

1. Without prejudice to Article 4(4) of Directive 2001/83/EC, a marketing authorisation which has been granted in accordance with the procedure laid down in this Regulation shall be valid throughout the Community. It shall confer the same rights and obligations in each of the Member States as a marketing authorisation granted by that Member State in accordance with Article 6 of Directive 2001/83/EC.

The authorised medicinal products for human use shall be entered in the Community Register of Medicinal Products and shall be given a number which shall appear on the packaging.

2. Notification of marketing authorisation shall be published in the *Official Journal of the European Communities*, quoting in particular the date of authorisation and the registration number in the Community Register.
3. The Agency shall publish the assessment report on the medicinal product for human use drawn up by the Committee for Human Medicinal Products and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.
4. After marketing authorisation has been granted, the holder of the authorisation shall inform the Agency of the dates of actual marketing of the medicinal product for human use in the Member States, taking into account the various presentations authorised.

The holder shall also inform the Agency if the product ceases to be marketed.

Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the Agency with all data relating to the volume of sales of or prescriptions for the medical product concerned at Community level.

Article 13

1. Without prejudice to paragraphs 2 and 3, authorisation shall be valid for an unlimited period.
2. Any authorisation which is not followed by the actual placing of the medicinal product for human use authorised on the Community market within two years of authorisation shall cease to be valid.
3. When an authorised medicinal product previously placed on the market is no longer actually present on the market for two consecutive years, the authorisation shall cease to be valid.
4. Following consultation with the applicant, an authorisation may be granted subject to certain specific obligations, to be reviewed annually by the Agency.

By way of derogation from paragraph 1, the authorisation shall be valid for one year, on a renewable basis.

The arrangements for granting such authorisation shall be determined by a Commission regulation adopted according to the procedure referred to in Article 77(2).

5. In exceptional circumstances, when one of the grounds referred to in Annex I to Directive 2001/83/EC applies to an application, and following consultation with the applicant, authorisation may be granted only under specific conditions. Continuation of the authorisation shall be linked to the annual reassessment of these conditions.
6. When an application is lodged for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. Due reasons are to be given for the request.

If the Committee for Human Medicinal Products accepts the application, the time-limit laid down in the first subparagraph of Article 6(3) shall be reduced to 150 days.

7. When adopting its opinion, the Committee for Human Medicinal Products shall include a proposal concerning the criteria for the prescription or use of the medicinal products in accordance with Article 70 of Directive 2001/83/EC .
8. Medicinal products for human use which have been authorised in accordance with the provisions of this Regulation shall benefit from the ten-year period of protection referred to in Article 10(1) of Directive 2001/83/EC.

Article 14

The granting of authorisation shall not affect the civil and criminal liability borne by the manufacturer or the holder of the marketing authorisation by virtue of the prevailing national law of the Member States.

CHAPTER 2

SUPERVISION AND SANCTIONS

Article 15

1. After an authorisation has been issued in accordance with this Regulation, the holder of the marketing authorisation for a medicinal product for human use shall, in respect of the methods of manufacture and control provided for in points (d) and (h) of Article 8(3) of Directive 2001/83/EC, take account of technical and scientific progress and make any amendments that may be required to enable the medicinal products to be manufactured and checked by means of generally accepted scientific methods. He/she shall apply for approval for these amendments in accordance with this Regulation.
2. The holder of the marketing authorisation shall forthwith supply to the Agency, to the Commission and to the Member States any new information which might entail the amendment of the particulars and documents referred to in Articles 8(3), 10a and 11 of Directive 2001/83/EC , or in Annex I thereto, or Article 9(4) of this Regulation.

In particular, he/she shall forthwith inform the Agency, the Commission and the Member States of any prohibition or restriction imposed by the competent authorities of any country in which the veterinary medicinal product is marketed and of any other new information which might influence the evaluation of the benefits and risks of the veterinary medicinal product concerned.

3. If the holder of the authorisation for placing the medicinal product for human use on the market proposes to make any alteration to the information and particulars referred to in paragraph 2, he/she shall submit the relevant application to the Agency.
4. The Commission shall, after consulting the Agency, make appropriate arrangements for the examination of variations to the terms of a marketing authorisation.

The Commission shall adopt these arrangements in the form of a regulation in accordance with the procedure referred to in Article 77(2).

Article 16

1. In the case of medicinal products for human use manufactured within the Community, the supervisory authorities shall be the competent authorities of the Member State or Member States which have granted the authorisation provided for in Article 40 of Directive 2001/83/EC in respect of the medicinal product concerned

2. In the case of medicinal products imported from non-member countries, the supervisory authorities shall be the competent authorities of the Member States in which the controls referred to in Article 51(1)(b) of Directive 2001/83/EC are carried out, unless appropriate arrangements have been made between the Community and the exporting country to ensure that those controls are carried out in the exporting country and that the manufacturer applies standards of good manufacturing practice at least equivalent to those laid down by the Community.

A Member State may request assistance from another Member State or from the Agency.

Article 17

1. The supervisory authorities shall have responsibility for verifying on behalf of the Community that the holder of the marketing authorisation for the medicinal product for human use or the manufacturer or importer from a non-member country satisfies the requirements laid down in Titles IV and XI of Directive 2001/83/EC.
2. Where, in accordance Article 122 of Directive 2001/83/EC, the Commission is informed of serious differences of opinion between Member States as to whether the holder of the marketing authorisation for the medicinal product for human use, or a manufacturer or importer established within the Community satisfies the requirements referred to in paragraph 1, the Commission may, after consultation with the Member States concerned, request an inspector from the supervisory authority to undertake a new inspection of the marketing authorisation holder, the manufacturer or the importer; the inspector in question shall be accompanied by two inspectors from Member States which are not party to the dispute and/or by two experts nominated by the Committee for Human Medicinal Products.
3. Subject to any arrangements which may have been concluded between the Community and non-member countries in accordance with Article 16(2), the Commission may, following a reasoned request from a Member State, or from the Committee for Human Medicinal Products, or on its own initiative, require a manufacturer established in a non-member country to submit to an inspection.

The inspection shall be undertaken by inspectors from the Member State who possess the appropriate qualifications and who may be accompanied by a rapporteur or expert appointed by the Committee for Human Medicinal Products. The report of the inspectors shall be made available to the Commission, the Member States and the Committee for Human Medicinal Products.

Article 18

1. Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established on Community territory is no longer fulfilling the obligations laid down in Title IV of Directive 2001/83/EC, they shall forthwith inform the Committee and the Commission, stating their reasons in detail and indicating the course of action proposed.

The same shall apply where a Member State or the Commission considers that one of the measures envisaged in Titles IX and XI of Directive 2001/83/EC should be applied in respect of the medicinal product concerned or where the Committee for Human Medicinal Products has delivered an opinion to that effect in accordance with Article 5 of this Regulation.

2. The Commission shall request the opinion of the Agency within a time-limit which it shall determine in the light of the urgency of the matter, in order to examine the reasons advanced. Whenever practicable, the holder of the authorisation for placing the medicinal product for human use on the market shall be invited to provide oral or written explanations.
3. Following an opinion by the Agency, the Commission shall adopt the necessary provisional measures, which shall be applied immediately.

A final decision shall be adopted within six months, in accordance with the procedures referred to in Article 10(2).

4. Where urgent action is essential to protect human or animal health or the environment, a Member State may, on its own initiative or at the Commission's request, suspend the use on its territory of a medicinal product for human use which has been authorised in accordance with this Regulation.

When it does so on its own initiative, it shall inform the Commission and the Agency of the reasons for its action at the latest on the next working day following the suspension. The Agency shall inform the other Member States without delay. The Commission shall immediately initiate the procedure provided for in paragraphs 2 and 3.

5. The suspensive measures referred to in paragraph 4 may be maintained in force until such time as a definitive decision has been reached in accordance with the procedures referred to in Article 10(2).
6. The Agency shall, upon request, inform any person concerned of the final decision.

CHAPTER 3

PHARMACOVIGILANCE

Article 19

For the purpose of this Chapter, Article 106(2) of Directive 2001/83/EEC shall apply.

Article 20

The Agency, acting in close cooperation with the national pharmacovigilance systems established in accordance with Article 102 of Directive 2001/83/EC, shall receive all relevant information about suspected adverse reactions to medicinal products for human use which have been authorised by the Community in accordance with this Regulation. If necessary, the Committee for Human Medicinal Products may, in accordance with Article 5 of this Regulation, formulate opinions on the measures necessary.

These measures may include amendments to the marketing authorisation granted in accordance with Article 10. They shall be adopted in accordance with the procedures referred to in Article 10(2).

The holder of the marketing authorisation and the competent authorities of the Member States shall ensure that all relevant information about suspected adverse reactions to the medicinal products authorised under this Regulation are brought to the attention of the Agency in accordance with the provisions of this Regulation.

Article 21

The holder of an authorisation to place a medicinal product for human use on the market granted by the Community in accordance with the provisions of this Regulation shall have permanently and continuously at his/her disposal an appropriately qualified person responsible for pharmacovigilance.

That qualified person shall be resident in the Community and shall be responsible for the following:

- (a) the establishment and maintenance of a system which ensures that information about all suspected adverse reactions which are reported to the personnel of the company and to medical representatives, is collected, evaluated and collated so that it may be accessed at a single point within the Community;
- (b) the preparation of the reports referred to in Article 22(3) for the competent authorities of the Member States and the Agency in accordance with the requirements of this Regulation;
- (c) ensuring that any request from the competent authorities for the provision of additional information necessary for the evaluation of the benefits and risks of a medicinal product is answered fully and promptly, including the provision of information about the volume of sales or prescriptions for the medicinal product concerned;
- (d) providing the competent authorities with any other information relevant to the evaluation of the risks and benefits of a medicinal product, particularly information concerning post-authorisation safety studies.

Article 22

1. The holder of an authorisation to place a medicinal product for human use on the market shall ensure that all suspected serious adverse reactions occurring within the Community to a medicinal product authorised in accordance with the provisions of this Regulation which are brought to his/her attention by a health-care professional, are recorded and reported immediately to the Member States in whose territory the incident occurred, and in no case later than 15 days following the receipt of the information.

The holder of an authorisation to place a medicinal product on the market shall be obliged to record any other suspected serious adverse reactions which meet the notification criteria, in accordance with the guidelines referred to in Article 24, of which he/she may reasonably be expected to be aware, and to notify immediately the competent authority of the Member State on whose territory the incident occurred, no later than 15 days following receipt of the information.

2. The holder of the authorisation to place the medical product for human use on the market shall ensure that all suspected serious unexpected adverse reactions occurring in the territory of a non-member country are reported immediately to Member States and the Agency and in no case later than 15 days following the receipt of the information. The arrangements for the reporting of suspected unexpected adverse reactions which are not serious, whether in the Community or in a non-member country, shall be adopted in accordance with the procedure set out in Article 77(2).

Save in exceptional circumstances, these reactions shall be communicated in the form of a report transmitted electronically and in accordance with the guidelines referred to in Article 24.

3. The holder of the authorisation to place the medicinal product for human use on the market shall be required to maintain detailed records of all suspected adverse reactions within or outside the Community which are reported to him/her by a health-care professional.

Unless other requirements have been laid down as a condition of the granting of the marketing authorisation by the Community, these records shall be submitted, in the form of a updated periodical report on safety, to the Agency and Member States immediately upon request or at least every six months during the first two years following authorisation and once a year for the following two years. Thereafter, the records shall be submitted at three-yearly intervals, or immediately upon request.

These records shall be accompanied by a scientific evaluation.

Article 23

Each Member State shall ensure that all suspected serious adverse reactions occurring within their territory to a medicinal product for human use authorised in accordance with the provisions of this Regulation which are brought to their attention are recorded and reported immediately to the Agency and the marketing authorisation holder, and in no case later than 15 days following receipt of the information.

The Agency shall inform the national pharmacovigilance systems in accordance with Article 102 of Directive 2001/83/EC.

Article 24

The Commission in consultation with the Agency, Member States, and interested parties, shall draw up guidance on the collection, verification and presentation of adverse reaction reports.

In accordance with this guidance, holders of marketing authorisation shall use the medical terminology accepted at international level for the transmission of adverse reaction reports.

The Agency, in consultation with the Member States and the Commission, shall set up a data-processing network for the rapid transmission of data between the competent Community authorities in the event of an alert relating to faulty manufacture, serious adverse reactions and other pharmacovigilance data regarding medicinal products authorised in accordance with Article 6 of Directive 2001/83/EC.

Article 25

The Agency shall collaborate with the World Health Organisation in matters of international pharmacovigilance and shall take the necessary steps to submit to it, promptly, appropriate and adequate information regarding the measures taken in the Community which may have a bearing on public health protection in non-member countries; it shall send a copy thereof to the Commission and the Member States.

Article 26

Any amendment which may be necessary to update the provisions of this Chapter to take account of scientific and technical progress shall be adopted in accordance with the procedure referred to in Article 77 (2).

TITLE III

**AUTHORISATION AND SUPERVISION OF VETERINARY
MEDICINAL PRODUCTS**

CHAPTER 1 SUBMISSION AND EXAMINATION OF APPLICATIONS – AUTHORISATIONS

Article 27

1. A Committee for Veterinary Medicinal Products is hereby established. The Committee shall be part of the Agency.
2. Without prejudice to Article 50 and other tasks which Community law may confer on it, in particular under Council Regulation (EEC) No 2377/90¹⁴, the Committee for Veterinary Medicinal Products shall be responsible for formulating the opinion of the Agency on any question concerning the admissibility of the files submitted in accordance with the centralised procedure, the granting, variation, suspension or withdrawal of an authorisation to place a veterinary medicinal product on the market arising in accordance with the provisions of this Title and pharmacovigilance.
3. At the request of the Executive Director of the Agency or the Commission representative, the Committee for Veterinary Medicinal Products shall also draw up any opinions on scientific matters concerning the evaluation of medicinal products for veterinary use.

¹⁴ OJ L 224, 18.8.1990, p. 1.

Article 28

1. Each application for authorisation for a medicinal product for veterinary use shall specifically include all the information and documents referred to in Articles 12(3), 13a and 14 of Directive 2001/82/EC, and Annex I thereto. The information and documents are to take account of the unique, Community nature of the authorisation requested, and particularly of the use of a single name for the medicinal product.

The application shall be accompanied by the fee payable to the Agency for the examination of the application.

2. In the case of a veterinary medicinal product containing or consisting of genetically modified organisms within the meaning of Article 2 of Directive 2001/18/EC, the application shall also be accompanied by:
 - (a) a copy of any written consent or consents of the competent authorities to the deliberate release into the environment of the genetically modified organisms for research and development purposes, where provided for in Part B of Directive 2001/18/EC or in Part B of Directive 90/220/EEC;
 - (b) the complete technical file supplying the information requested in Annexes III and IV to Directive 2001/18/EC;
 - (c) the environmental risk assessment in accordance with the principles set out in Annex II to Directive 2001/18/EC; and
 - (d) the results of any investigations performed for the purposes of research or development.

Articles 13 to 24 of Directive 2001/18/EC shall not apply to veterinary medicinal products containing or consisting of genetically modified organisms.

3. The Agency shall ensure that the opinion of the Committee for Veterinary Medicinal Products is given within 210 days of the receipt of a valid application.

In the case of a veterinary medicinal product containing or consisting of genetically modified organisms, the opinion of the Committee shall respect the environmental safety requirements laid down by Directive 2001/18/EC. During the process of evaluating applications for marketing authorisations for veterinary medicinal products containing or consisting of genetically modified organisms, necessary consultations shall be held by the rapporteur with the bodies set up by the Community or the Member States in accordance with Directive 2001/18/EC.

4. The Commission shall, in consultation with the Agency, the Member States and interested parties, draw up detailed guidance on the form in which applications for authorisation are to be presented.

Article 29

1. In order to prepare its opinion, the Committee for Veterinary Medicinal Products:
 - (a) shall verify that the particulars and documents submitted in accordance with Article 28 comply with the requirements of Directive 2001/82/EC and examine whether the conditions specified in this Regulation for issuing a marketing authorisation are satisfied;
 - (b) may ask for a State laboratory or a laboratory designated for this purpose to test the veterinary medicinal product, its starting materials and, if need be, its intermediate products or other constituent materials in order to ensure that the control methods employed by the manufacturer and described in the application are satisfactory;
 - (c) may request a Community reference laboratory, State laboratory or laboratory designated for this purpose to verify, using samples provided by the applicant, that the analytical detection method proposed by the applicant in accordance with point j, second indent of Article 12(3) of Directive 2001/82/EC is satisfactory and is suitable for use to reveal the presence of residue levels, particularly those above the maximum residue level accepted by the Community in accordance with the provisions of Regulation (EEC) No 2377/90;
 - (d) may request the applicant to supplement the particulars accompanying the application within a specific time-limit.

Where the Committee avails itself of the option contained in point (d) of the first subparagraph, the time-limit laid down in the first subparagraph of Article 28(3) shall be suspended until such time as the supplementary information requested has been provided. Likewise, the time-limit shall be suspended for the time allowed to the applicant to prepare oral or written explanations.

2. In those cases where the analytical method has not been subject to verification by one of the abovementioned laboratories in the framework of the procedures established by Regulation (EEC) No 2377/90, the verification shall be carried out within the framework of this Article.

Article 30

1. Upon receipt of a written request from the Committee for Veterinary Medicinal Products, a Member State shall forward the information establishing that the manufacturer of a veterinary medicinal product or the importer from a non-member country is able to manufacture the veterinary medicinal product concerned and/or carry out the necessary control tests in accordance with the particulars and documents supplied pursuant to Article 28.
2. Where it considers it necessary in order to complete its examination of the application, the Committee for Veterinary Medicinal Products may require the applicant to submit to a specific inspection of the manufacturing site of the veterinary medicinal product concerned.

The inspection, which shall be completed within the time-limit referred to in the first subparagraph of Article 28(3), shall be undertaken by inspectors from the Member State who possess the appropriate qualifications and who may be accompanied by a rapporteur or expert appointed by the Committee.

Article 31

1. The Agency shall forthwith inform the applicant if the opinion of the Committee for Veterinary Medicinal Products is that:
 - (a) the application does not satisfy the criteria for authorisation set out in this Regulation;
 - (b) the summary of the product characteristics should be amended;
 - (c) the labelling or package leaflet of the product is not in compliance with Title V of Directive 2001/82/EC;
 - (d) the authorisation should be granted subject to the conditions provided for in Article 35(4).

2. Within 15 days of receipt of the opinion referred to in paragraph 1, the applicant may provide written notice to the Agency that he/she wishes to appeal. In that case the applicant shall forward the detailed grounds for his/her appeal to the Agency within 60 days of receipt of the opinion.

Within 60 days of receipt of the grounds for appeal, the Committee for Veterinary Medicinal Products shall re-examine its opinion in accordance with the conditions laid down in the second subparagraph of Article 55(1). The conclusions reached on the appeal shall be annexed to the final opinion.

3. Within 30 days of its adoption, the Agency shall forward the final opinion of the Committee for Veterinary Medicinal Products to the Commission, to the Member States and to the applicant, together with a report describing the assessment of the veterinary medicinal product by the Committee and stating the reasons for its conclusions.

4. In the event of an opinion in favour of granting the relevant authorisation to place the relevant veterinary medicinal product on the market, the following documents shall be annexed to the opinion:
 - (a) a draft summary of the product characteristics, as referred to in Article 14 of Directive 2001/82/EC; where necessary, this draft shall reflect differences in the veterinary conditions pertaining in the Member States;
 - (b) the case of a veterinary medicinal product intended for administration to food-producing animals, a statement of the maximum residue level which may be accepted by the Community in accordance with Regulation (EEC) No 2377/90;
 - (c) details of any conditions or restrictions which should be imposed on the supply or use of the veterinary medicinal product concerned, including the conditions under which the veterinary medicinal product may be made available to users, in conformity with the criteria laid down in Directive 2001/82/EC;

- (d) the draft text of the labelling and package leaflet proposed by the applicant, presented in accordance with Title V of Directive 2001/82/EC;
- (e) the assessment report.

Article 32

1. Within 30 days of receipt of the opinion referred to in Article 27(2), the Commission shall prepare a draft of the decision to be taken in respect of the application.

In the event of a draft decision which envisages the granting of marketing authorisation, the draft shall include the documents mentioned in points (a) to (d) of Article 31(4), or shall make reference to them.

Where the draft decision is not in accordance with the opinion of the Agency, the Commission shall annex a detailed explanation of the reasons for the differences.

The draft decision shall be forwarded to the Member States and the applicant.

2. The Commission shall take a final decision in accordance with the procedure referred to in Article 77(3) if the draft decision accords with the Agency's opinion.

The Commission shall take a final decision in accordance with the procedure referred to in Article 77(4) if the draft decision does not accord with the Agency's opinion.

3. The Standing Committee for Veterinary Medicinal Products referred to in Article 77(1) shall adjust its rules of procedure so as to take account of the tasks assigned to it by this Regulation.

These adjustments shall provide that:

- (a) the opinion of the Standing Committee is to be given in writing;
- (b) each Member State is allowed 15 days to forward written observations on the draft decision to the Commission; however, if a decision has to be taken urgently, a shorter time-limit may be set by the Chairman according to the degree of urgency involved;
- (c) each Member State shall be permitted to request in writing that the draft decision referred to in paragraph 1 be discussed at a plenary meeting of the Standing Committee; that request shall give reasons in detail.

4. Where, in the opinion of the Commission, the written observations of a Member State raise important new questions of a scientific or technical nature which have not been addressed in the opinion of the Agency, the Chairman shall suspend the procedure and refer the application back to the Agency for further consideration.
5. The provisions necessary for the implementation of paragraph 3 shall be adopted by the Commission in accordance with the procedure referred to in Article 77(2).
6. The Agency shall disseminate the documents referred to in points (a) to (d) of Article 31(4).

Article 33

1. The marketing authorisation shall be refused if, after verification of the information and particulars submitted in accordance with Article 28, it appears that:
 - (a) the quality, the safety or the efficacy of the veterinary medicinal product have not been properly or sufficiently demonstrated by the applicant;
 - (b) in the case of zootechnical veterinary medicinal products and growth promoters, when the safety and welfare of the animals and/or consumer safety and benefits in terms of health have not been sufficiently taken into account;
 - (c) the waiting time recommended by the applicant is not long enough to ensure that foodstuffs obtained from treated animals do not contain residues which might constitute a health hazard for the consumer or is insufficiently substantiated;
 - (d) the veterinary medicinal product is presented for a use prohibited under other Community provisions.

Authorisation shall likewise be refused if the particulars and documents provided by the applicant in accordance with Article 28 are incorrect or if the labelling and package leaflets proposed by the applicant are not in accordance with Title V of Directive 2001/82/EC.

2. The refusal of a Community marketing authorisation shall constitute a prohibition on the placing on the market of the veterinary medicinal product concerned throughout the Community.

Article 34

1. Without prejudice to Article 71 of Directive 2001/82/EC, a marketing authorisation which has been issued in accordance with this Regulation shall be valid throughout the Community. It shall confer the same rights and obligations in each of the Member States as a marketing authorisation granted by that Member State in accordance with Article 5 of Directive 2001/82/EC.

The authorised veterinary medicinal products shall be entered in the Community Register of Medicinal Products and shall be given a number which shall appear on the packaging.

2. Notification of marketing authorisation shall be published in the *Official Journal of the European Communities*, quoting in particular the date of authorisation and the number in the Community Register.
3. The Agency shall publish the assessment report on the veterinary medicinal product drawn up by the Committee for Veterinary Medicinal Products and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

4. After marketing authorisation has been granted, the holder of the authorisation shall inform the Agency of the dates of actual marketing of the veterinary medicinal product in the Member States, taking into account the various presentations authorised.

The holder shall also inform the Agency if the product ceases to be marketed.

Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the Agency with all data relating to the volume of sales of or prescriptions for the medical product at Community level, broken down by Member State.

Article 35

1. Without prejudice to paragraphs 2 and 3, authorisation shall be valid for unlimited duration.
2. Any authorisation which is not followed by the actual placing of the veterinary medicinal product authorised on the Community market within two years of authorisation shall cease to be valid.
3. When an authorised veterinary medicinal product previously placed on the market is no longer actually present on the market for two consecutive years, the authorisation for the product shall cease to be valid.
4. In exceptional circumstances and following consultation with the applicant, authorisation may be granted only under specific conditions. Continuation of the authorisation shall be linked to the annual reassessment of these conditions. Such exceptional decisions may be adopted only for objective and verifiable reasons.
5. When an application is lodged for a marketing authorisation in respect of veterinary medicinal products of major interest, particularly from the point of view of animal health and from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. Due reasons are to be given for the request.

If the Committee for Veterinary Medicinal Products accepts the application, the time-limits laid down in the first subparagraph of Article 28(3) shall be reduced to 150 days.

6. When adopting its opinion, the Committee for Veterinary Medicinal Products shall include a proposal concerning the conditions for the prescription or use of the veterinary medicinal products.
7. Veterinary medicinal products which have been authorised in accordance with the provisions of this Regulation shall enjoy the periods of protection referred to in Articles 13 and 13a of Directive 2001/82/EC.

Article 36

The granting of authorisation shall not affect the civil and criminal liability borne by the manufacturer or the holder of the marketing authorisation by virtue of the prevailing national law of the Member States.

CHAPTER 2

SUPERVISION AND SANCTIONS

Article 37

1. After an authorisation has been issued in accordance with this Regulation, the holder of the marketing authorisation shall, in respect of the methods of production and control provided for in points (d) and (i) of Article 12(3) of Directive 2001/82/EC, take account of technical and scientific progress and make any amendments that may be required to enable the medicinal products to be manufactured and checked by means of generally accepted scientific methods. He/she shall apply for approval for these amendments in accordance with this Regulation.
2. The competent authority in a Member State or the Agency may require the marketing authorisation holder to provide substances in sufficient quantities for the performance of tests to detect the presence of residues of the veterinary medicinal products concerned in foodstuffs of animal origin.
3. At the request of the competent authority of a Member State or the Agency, the holder of the marketing authorisation shall provide his technical expertise to facilitate the implementation of the analytical method for detecting residues of veterinary medicinal products by the Community reference laboratory or, where appropriate, national reference laboratories appointed in accordance with Council Directive 96/23/EC¹⁵.
4. The holder of the marketing authorisation shall forthwith supply to the Agency, the Commission and the Member States any new information which might entail the amendment of the particulars and documents referred to in Articles 12(3), 13a and 14 of Directive 2001/82/EC, and in Annex I thereto, and in Article 31(4) of this Regulation.

He/she shall forthwith inform the Agency, the Commission and the Member States of any prohibition or restriction imposed by the competent authorities of any country in which the veterinary medicinal product is marketed and of any other new information which might influence the evaluation of the benefits and risks of the veterinary medicinal product concerned.

5. If the holder of the authorisation for placing the veterinary product on the market proposes to make any alteration to the information and documents referred to in paragraph 4, he/she shall submit the relevant application to the Agency.
6. The Commission shall, after consulting the Agency, make appropriate arrangements for the examination of variations to the terms of a marketing authorisation.

The Commission shall adopt these arrangements in the form of a regulation in accordance with the procedure laid down in Article 77(2).

¹⁵ OJ L 125, 23.5.1996, p. 10.

Article 38

1. In the case of veterinary medicinal products manufactured within the Community, the supervisory authorities shall be the competent authorities of the Member State or Member States which have granted the authorisation provided for in Article 44 of Directive 2001/82/EC in respect of the manufacture of the medicinal product concerned.
2. In the case of veterinary medicinal products imported from non-member countries, the supervisory authorities shall be the competent authorities of the Member States in which the controls referred to in Article 55(2) of Directive 2001/82/EC are carried out unless appropriate arrangements have been made between the Community and the exporting country to ensure that those controls are carried out in the exporting country and that the manufacturer applies standards of good manufacturing practice at least equivalent to those laid down by the Community.

A Member State may request assistance from another Member State or the Agency.

Article 39

1. The supervisory authorities shall have responsibility for verifying on behalf of the Community that the holder of the marketing authorisation for the veterinary medicinal product or the manufacturer or importer established on Community territory satisfies the requirements laid down in Titles IV and VIII of Directive 2001/82/EC .
2. Where, in accordance Article 90 of Directive 2001/82/EC, the Commission is informed of serious differences of opinion between Member States as to whether the holder of the marketing authorisation for the veterinary medicinal product or a manufacturer or importer established within the Community satisfies the requirements referred to in paragraph 1, the Commission may, after consultation with the Member States concerned, request an inspector from the supervisory authority to undertake a new inspection of the marketing authorisation holder, the manufacturer or the importer; the inspector in question shall be accompanied by two inspectors from Member States which are not party to the dispute and/or by two experts nominated by the Committee.
3. Subject to any arrangements which may have been concluded between the Community and non-member countries in accordance with Article 38(2), the Commission may, upon receipt of a reasoned request from a Member State, the Committee for Veterinary Medicinal Products, or on its own initiative, require a manufacturer established in a non-member country to submit to an inspection.

The inspection shall be undertaken by inspectors from the Member State who possess the appropriate qualifications and who may, if need be, be accompanied by a rapporteur or expert appointed by the Committee for Veterinary Medicinal Products. The report of the inspectors shall be made available to the Commission, the Member States and the Committee for Veterinary Medicinal Products.

Article 40

1. Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established on Community territory is no longer fulfilling the obligations laid down in Title VII of Directive 2001/82/EC, they shall forthwith inform the Committee and the Commission, stating their reasons in detail and indicating the course of action proposed.

The same shall apply where a Member State or the Commission considers that one of the measures envisaged in Title VIII of Directive 2001/82/EC should be applied in respect of the veterinary medicinal product concerned or where the Committee for Veterinary Medicinal Products has delivered an opinion to that effect in accordance with Article 27 of this Regulation.

2. The Commission shall request the opinion of the Agency within a time-limit which it shall determine in the light of the urgency of the matter, in order to examine the reasons advanced. Whenever practicable, the holder of the authorisation for placing the medicinal product on the market shall be invited to provide oral or written explanations.
3. Following an opinion by the Agency, the Commission shall adopt the necessary provisional measures, which shall be applied immediately.

A final decision shall be adopted within six months, in accordance with the procedures referred to in Article 32(2).

4. Where urgent action is essential to protect human or animal health or the environment, a Member State may, on its own initiative or at the Commission's request, suspend the use on its territory of a veterinary medicinal product which has been authorised in accordance with this Regulation.

When it does so on its own initiative, it shall inform the Commission and the Agency of the reasons for its action at the latest on the next working day following the suspension. The Agency shall inform the other Member States without delay. The Commission shall immediately initiate the procedure provided for in paragraphs 2 and 3.

5. The suspensive measures referred to in paragraph 4 may be maintained until such time as a definitive decision has been reached in accordance with the procedures referred to in Article 32(2).
6. The Agency shall, upon request, inform any person concerned of the final decision.

CHAPTER 3

PHARMACOVIGILANCE

Article 41

For the purpose of this Chapter, Article 77(2) of Directive 2001/82/EEC shall apply.

Article 42

The Agency, acting in close cooperation with the national pharmacovigilance systems established in accordance with Article 73 of Directive 2001/82/EC, shall receive all relevant information about suspected adverse reactions to veterinary medicinal products which have been authorised by the Community in accordance with this Regulation. If necessary the Committee for Veterinary Medicinal Products may, in accordance with Article 27 of this Regulation, formulate opinions on the measures necessary.

These measures may include amendments to the marketing authorisation. They shall be adopted in accordance with the procedures referred to in Article 32(2).

The holder of the marketing authorisation to place the medicinal product on the market and the competent authorities of the Member States shall ensure that all relevant information about suspected adverse reactions to the veterinary medicinal products authorised under this Regulation are brought to the attention of the Agency in accordance with the provisions of this Regulation.

Article 43

The holder of an authorisation to place a veterinary medicinal product on the market granted in accordance with the provisions of this Regulation shall have permanently and continuously at his disposal an appropriately qualified person responsible for pharmacovigilance.

That qualified person shall be resident in the Community and shall be responsible for the following:

- (a) the establishment and maintenance of a system which ensures that information about all suspected adverse reactions which are reported to the personnel of the company and to medical representatives is collected, evaluated and collated so that it may be accessed at a single point within the Community;
- (b) the preparation of the reports referred to in Article 44(3) for the competent authorities of the Member States and the Agency in accordance with the requirements of this Regulation;
- (c) ensuring that any request from the competent authorities for the provision of additional information necessary for the evaluation of the benefits and risks of a veterinary medicinal product is answered fully and promptly, including the provision of information about the volume of sales or prescriptions for the veterinary medicinal product concerned;
- (d) providing the competent authorities with any other information relevant to the evaluation of the risks and benefits of a veterinary medicinal product, particularly information concerning post-marketing safety studies.

Article 44

1. The holder of the authorisation for placing a veterinary medicinal product on the market shall ensure that all suspected serious adverse reactions, and adverse human reactions, occurring within the Community to a veterinary medicinal product authorised in accordance with the provisions of this Regulation which are brought to his attention by a health-care professional are recorded and reported immediately to the Member States in whose territory the incident occurred, and in no case later than 15 days following the receipt of the information

The holder of the marketing authorisation shall be obliged to record any other suspected serious adverse reactions which meet the notification criteria, in accordance with the guidelines referred to in Article 46, of which he may reasonably be expected to be aware, and to notify immediately the Member States on whose territory the incident occurred and the Agency, no later than 15 days following receipt of the information.

2. The holder of the marketing authorisation for the veterinary medicinal product shall ensure that all suspected serious unexpected adverse reactions, and adverse human reactions, occurring in the territory of a non-member country, are reported immediately to the Member States and the Agency and in no case later than 15 days following the receipt of the information. The arrangements for the reporting of suspected unexpected adverse reactions which are not serious, whether arising in the Community or in a non-member country, shall be adopted in accordance with the procedure referred to in Article 77(2).

Save in exceptional circumstances, these reactions shall be communicated in the form of an electronically transmitted report and in accordance with the guidance referred to in Article 46.

3. In addition, the holder of the authorisation to place a veterinary medicinal product on the market shall be required to maintain detailed records of all suspected adverse reactions occurring within or outside the Community which are reported to him/her by a health-care professional.

Unless other requirements have been laid down as a condition of the granting of the marketing authorisation by the Community, these records shall be submitted, in the form of a updated periodical report on safety, to the Agency and Member States immediately upon request or at least every six months during the first two years following authorisation and once a year for the following two years. Thereafter, the records shall be submitted at three-yearly intervals, or immediately upon request.

These records shall be accompanied by a scientific evaluation.

Article 45

Each Member State shall ensure that all suspected serious adverse reactions, and adverse human reactions, occurring within its territory to a veterinary medicinal product authorised in accordance with the provisions of this Regulation which are brought to its attention are recorded and reported immediately to the Agency and the holder of the authorisation for placing the veterinary medicinal product on the market, and in no case later than 15 days following the receipt of the information.

The Agency shall forward the information to the national pharmacovigilance systems set up in accordance with Article 73 of Directive 2001/82/EC.

Article 46

The Commission in consultation with the Agency, Member States, and interested parties, shall draw up guidance on the collection, verification and presentation of adverse reaction reports.

In accordance with this guidance, holders of marketing authorisation shall use the medical terminology accepted at international level for the transmission of adverse reaction reports.

The Agency, in consultation with the Member States and the Commission, shall set up a data-processing network for the rapid transmission of data between the competent Community authorities in the event of an alert relating to faulty manufacture, serious adverse reactions and other pharmacovigilance data regarding veterinary medicinal products authorised in accordance with Article 5 of Directive 2001/82/EC.

Article 47

The Agency shall cooperate with international organisations concerned with veterinary pharmacovigilance.

Article 48

Any amendment necessary to update the provisions of this Chapter to take account of scientific and technical progress shall be adopted in accordance with the procedure referred to in Article 77(2).

TITLE IV

THE EUROPEAN AGENCY FOR THE EVALUATION OF MEDICINAL PRODUCTS RESPONSIBILITIES AND ADMINISTRATIVE STRUCTURE

CHAPTER 1

TASKS OF THE AGENCY

Article 49

A European Agency for the Evaluation of Medicinal Products is hereby established.

The Agency shall be responsible for coordinating the existing scientific resources put at its disposal by the competent authorities of the Member States for the evaluation and supervision of medicinal products.

Article 50

1. The Agency shall comprise:
 - (a) the Committee for Human Medicinal Products, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for human use;

- (b) the Committee for Veterinary Medicinal Products, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for veterinary use;
 - (c) the Committee on Orphan Medicinal Products;
 - [(d) the Committee on Herbal Medicinal Products;]
 - (e) a Secretariat, which shall provide technical and administrative support for the Committees and ensure appropriate coordination between them;
 - (f) an Executive Director, who shall exercise the responsibilities set out in Article 57;
 - (g) a Management Board, which shall exercise the responsibilities set out in Articles 58, 59, and 60;
 - (h) an Advisory Board, the functions of which are laid down in Article 59.
2. The Committees referred to in points (a) to (d) of paragraph 1 may each establish working parties and expert groups. For this purpose they shall adopt, in accordance with their rules of procedure, precise arrangements for delegating certain tasks to these working parties and groups.
 3. The Executive Director, in close consultation with the Committee for Human Medicinal Products and the Committee for Veterinary Medicinal Products, shall set up the administrative structures and procedures allowing the development of advice for companies, as referred to in point (1) of Article 51, particularly regarding the development of new therapies.

Each committee shall establish a standing working party with the sole remit of providing scientific advice to companies.

4. The Committee for Human Medicinal Products and the Committee for Veterinary Medicinal Products may, if they consider it appropriate, seek guidance on important questions of a general scientific or ethical nature.

Article 51

1. The Agency shall provide the Member States and the institutions of the Community with the best possible scientific advice on any question relating to the evaluation of the quality, the safety, and the efficacy of medicinal products for human or veterinary use, which is referred to it in accordance with the provisions of Community legislation relating to medicinal products.

To this end, the Agency, acting particularly through its Committees, shall undertake the following tasks:

- (a) the coordination of the scientific evaluation of the quality, safety and efficacy of medicinal products which are subject to Community marketing authorisation procedures;

- (b) transmitting on request and making available assessment reports, summaries of product characteristics, labels and package leaflets or inserts for these medicinal products;
- (c) the coordination of the supervision, under practical conditions of use, of medicinal products which have been authorised within the Community and the provision of advice on the measures necessary to ensure the safe and effective use of these products, in particular by evaluation, coordination of the implementation of pharmacovigilance obligations and the monitoring of this implementation;
- (d) assuring the dissemination of information on adverse reactions to medicinal products authorised in the Community, by means of a database permanently accessible to all Member States;
- (e) distributing appropriate pharmacovigilance information to the general public;
- (f) advising on the maximum limits for residues of veterinary medicinal products which may be accepted in foodstuffs of animal origin in accordance with Regulation (EEC) No 2377/90;
- (g) coordinating the verification of compliance with the principles of good manufacturing practice, good laboratory practice and good clinical practice;
- (h) upon request, providing technical and scientific support for steps to improve cooperation between the Community, its Member States, international organisations and non-member countries on scientific and technical issues relating to the evaluation of medicinal products, in particular in the context of discussions organised in the framework of international conferences on harmonisation;
- (i) recording the status of marketing authorisations for medicinal products granted in accordance with Community procedures;
- (j) creating a database on medicinal products, to be accessible to the general public, and giving technical assistance for its maintenance;
- (k) assisting the Community and Member States in the provision of information to health care professionals and the general public about medicinal products evaluated by the Agency;
- (l) advising companies on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products and, in particular, on the observance of good manufacturing practices;
- (m) checking that the conditions laid down in Community legislation on medicinal products and in the marketing authorisations are observed in the case of parallel distribution of medicinal products authorised in accordance with this Regulation;
- (n) drawing up, at the Commission's request, any other scientific opinion concerning the evaluation of medicinal products or the starting materials used in the manufacture of medicinal products.

2. The database provided for in point (j) of paragraph 1 shall include the summaries of product characteristics, the patient or user package leaflet and the information shown on the labelling. The database shall be developed in stages, priority being given to medicinal products authorised under this Regulation and those authorised under Chapters IV (Title III) of Directive 2001/83/EC and Directive 2001/82/EC respectively. The database shall subsequently be extended to include other medicinal products.

Article 52

The Agency may give a scientific opinion, in the context of cooperation with the World Health Organisation, for the assessment of certain medicinal products for human use intended exclusively for the markets of non-member countries. For this purpose, on the recommendation of the World Health Organisation, a request shall be submitted to the Agency, in accordance with the provisions of Article 6. The Committee for Human Medicinal Products shall be responsible for drawing up the Agency's opinion, in accordance with the provisions of Articles 6 to 9. The provisions of Article 10 shall not apply.

Article 53

1. The Agency shall take care to ensure early identification of potential sources of conflict between its scientific opinions and those of other bodies established under Community law carrying out a similar task in relation to issues of common concern.
2. Where the Agency identifies a potential source of conflict, it shall contact the body concerned in order to ensure that any relevant scientific information is shared and to identify the scientific points which are potentially contentious.
3. Where there is a fundamental conflict over scientific points and the body concerned is a Community agency or a scientific committee, the Agency and the body concerned shall work together either to solve the conflict or to submit a joint document to the Commission clarifying the scientific points of conflict.
4. Save as otherwise provided for in this Regulation, in Directive 2001/83/EC or in Directive 2001/82/EC, where there is a fundamental conflict over scientific points and the body concerned is a body in a Member State, the agency and the national body concerned shall work together either to solve the conflict or to prepare a joint document clarifying the scientific points of conflict.

Article 54

1. Each Member State shall appoint, for a three-year term which shall be renewable, one member to the Committee for Human Medicinal Products and one member to the Committee for Veterinary Medicinal Products. Members shall be chosen for their role and experience in the evaluation of medicinal products for human and veterinary use as appropriate and shall maintain relevant contacts with the competent national authorities.

The committees may coopt a maximum of five additional members chosen on the basis of their specific scientific competence. These members shall be appointed for a term of three years which shall be renewable.

The members of each Committee may be accompanied by experts in specific scientific or technical fields.

The Executive Director of the Agency or his/her representative and representatives of the Commission shall be entitled to attend all the meetings of the Committees and working parties convened by the Agency or its committees.

2. In addition to their task of providing objective scientific opinions to the Community and Member States on the questions which are referred to them, the members of each Committee shall ensure that there is appropriate coordination between the tasks of the Agency and the work of competent national authorities, including the consultative bodies concerned with the marketing authorisation.
3. The members of the Committees and the experts responsible for evaluating medicinal products shall rely on the scientific assessment and resources available to the national marketing authorisation bodies. Each competent national authority shall monitor the scientific level and independence of the evaluation carried out and facilitate the activities of the Committee members and experts nominated. The Member States shall refrain from giving the Committee members and experts any instruction which is incompatible with their own individual tasks or with the tasks and responsibilities of the Agency.
4. When preparing the opinion, each Committee shall use its best endeavours to reach a scientific consensus. If such a consensus cannot be reached, the opinion shall consist of the position of the majority of members and the divergent positions, with their grounds.
5. Each Committee shall establish its own rules of procedure.

These rules shall in particular lay down the procedures for appointing and replacing the Chairman, the procedures for delegating certain tasks to working parties and the establishment of a procedure for the urgent adoption of opinions, particularly in relation to the provisions on market surveillance and pharmacovigilance laid down in this Regulation.

They shall enter into force after receiving a favourable opinion from the Commission and the Management Board.

Article 55

1. Where, in accordance with the provisions of this Regulation, the Committee for Human Medicinal Products or the Committee for Veterinary Medicinal Products is required to evaluate a medicinal product, it shall appoint one of its members to act as rapporteur for the coordination of the evaluation. The Committee concerned may appoint a second member to act as co-rapporteur.

If there is an appeal against one of its opinions, the Committee concerned shall appoint a different rapporteur and, where necessary, a different co-rapporteur from those appointed for the initial opinion. This appeal procedure may deal only with the points of the opinion initially identified by the applicant and may be based only on the scientific data available at the time the Committee adopted the initial opinion.

2. Member States shall transmit to the Agency the names of national experts with proven experience in the assessment of medicinal products who would be available to serve on working parties or expert groups of the Committee for Human Medicinal Products or the Committee for Veterinary Medicinal Products, together with an indication of their qualifications and specific areas of expertise.

The Agency shall keep an up-to-date list of accredited experts. The list shall include the experts referred to in the first subparagraph and other experts appointed directly by the Agency. The list shall be updated.

3. The provision of services by rapporteurs or experts shall be governed by a written contract between the Agency and the person concerned, or where appropriate between the Agency and his employer.

The person concerned, or his/her employer, shall be remunerated in accordance with a scale of fees to be included in the financial arrangements established by the Management Board.

4. The performance of scientific services for which there are several potential providers may result in a call for an expression of interest, if the scientific and technical context allows, and if it is compatible with the duties of the Agency, in particular the need to provide a high level of public health protection.

The Management Board shall adopt the appropriate procedures on a proposal from the Executive Director.

5. The Agency or any of the committees referred to in points (a) to (d) of Article 50(1) may use the services of experts for the discharge of other specific tasks for which they are responsible.

Article 56

1. The membership of the committees referred to in points (a) to (d) of Article 50(1) shall be made public. When each appointment is published, the professional qualifications of each member shall be specified.
2. Members of the Management Board, members of the Advisory Board, members of the Committees, rapporteurs and experts shall not have financial or other interests in the pharmaceutical industry which could affect their impartiality. They shall undertake to act in the public interest and in an independent manner. All indirect interests which could relate to this industry shall be entered in a register held by the Agency which the public may consult.

Members of the Management Board, members of the Advisory Board, members of the Committees, rapporteurs and experts who participate in meetings or working groups of the Agency shall declare, at each meeting, any specific interests which could be considered to be prejudicial to their independence with respect to the points on the agenda.

Article 57

1. The Executive Director shall be appointed by the Management Board, on a proposal from the Commission, for a period of five years, which shall be renewable.
2. The Executive Director shall be the legal representative of the Agency. He/she shall be responsible:
 - (a) for the day-to-day administration of the Agency;
 - (b) for managing all the Agency resources necessary for conducting the activities of the committees referred to in points (a) to (d) of Article 50(1), including making available appropriate scientific and technical support;
 - (c) for ensuring that the time-limits laid down in Community legislation for the adoption of opinions by the Agency are complied with;
 - (d) for ensuring appropriate coordination between the committees referred to in points (a) to (d) of Article 50(1);
 - (e) for the preparation of the statement of revenue and expenditure and the execution of the budget of the Agency;
 - (f) for all staff matters;
 - (g) for requesting the opinion of the Advisory Board on any point concerning the Agency's activities regarding the procedures for authorising medicinal products;
 - (h) for providing the secretariat for the Management Board and the Advisory Board.
3. Each year, the Executive Director shall submit the following to the Management Board for approval, while making a distinction between the Agency's activities concerning medicinal products for human use and those concerning veterinary medicinal products:
 - (a) a draft report covering the activities of the Agency in the previous year, including information about the number of applications evaluated within the Agency, the time taken for completion of the evaluation and the medicinal products authorised, rejected or withdrawn;
 - (b) a draft programme of work for the coming year;
 - (c) the draft annual accounts;
 - (d) the draft forecast budget for the coming year.
4. The Executive Director shall approve all financial expenditure of the Agency.

Article 58

1. The Management Board shall consist of four representatives of the Member States, four representatives of the European Parliament, four representatives of the Commission, and four representatives of patients and industry, appointed by the Commission.

The full members of the Management Board may arrange to be replaced by alternates.

2. The term of office of the representatives shall be three years. It shall be renewable.
3. The Management Board shall elect its Chairman for a term of three years and shall adopt its rules of procedure. Decisions of the Management Board shall be adopted by a majority of two-thirds of its members.
4. Before 31 January each year, the Management Board shall adopt the general report on the activities of the Agency for the previous year and its programme of work for the coming year and forward them to the Member States, the European Parliament, the Council, and the Commission.

Article 59

The Advisory Board shall consist of one representative from each of the national authorities competent in the authorisation of human and veterinary medicinal products. The Executive Director or his representative and the representatives of the Commission shall have the right to attend the meetings of the Advisory Board.

The Commission may submit any question concerning Community procedures for the authorisation of medicinal products to the Advisory Board.

The opinions of the Advisory Board shall not be binding in any way.

The Management Board, on the proposal of the Executive Director and following a favourable opinion from the Commission, shall draw up the provisions necessary for the implementation of this Article.

CHAPTER 2

FINANCIAL PROVISIONS

Article 60

1. The revenues of the Agency shall consist of a contribution from the Community and the fees paid by undertakings for obtaining and maintaining a marketing authorisation and for other services provided by the Agency.
2. The expenditure of the Agency shall include the staff, administrative, infrastructure and operational expenses and expenses resulting from contracts entered into with third parties.

3. By 15 February of each year at the latest, the Director shall draw up a preliminary draft budget covering the operational expenditure and the programme of work anticipated for the following financial year, and shall forward this preliminary draft to the Management Board together with an establishment plan.
4. Revenue and expenditure shall be in balance.
5. The Management Board shall adopt the draft budget and forward it to the Commission, which on that basis shall establish the relevant estimates in the preliminary draft general budget of the European Communities, which it shall lay before the Council pursuant to Article 272 of the Treaty.
6. The Management Board shall adopt the Agency's final budget before the beginning of the financial year, adjusting it where necessary to the Community subsidy and the Agency's other resources.
7. The Director shall implement the Agency's budget.
8. Monitoring of the commitment and payment of all the Agency's expenditure and of the establishment and recovery of all the Agency's revenue shall be carried out by the financial controller of the Commission.
9. By 31 March of each year at the latest, the Director shall forward to the Commission, the Management Board and the Court of Auditors the accounts for all the Agency's revenue and expenditure in respect of the preceding financial year. The Court of Auditors shall examine them in accordance with Article 248 of the Treaty.
10. The Management Board, on a recommendation by the European Parliament, shall give a discharge to the Director in respect of the implementation of the budget.
11. After the Court of Auditors has delivered its opinion, the Management Board shall adopt the internal financial provisions specifying, in particular, the detailed rules for establishing and implementing the Agency's budget.

Article 61

The structure and the amount of the fees referred to in Article 60(1) shall be established by the Council acting under the conditions provided for by the Treaty on a proposal from the Commission, following the latter's consultation of organisations representing the interests of the pharmaceutical industry at Community level.

CHAPTER 3

GENERAL PROVISIONS GOVERNING THE AGENCY

Article 62

The Agency shall have legal personality. In all Member States it shall benefit from the widest powers granted by law to legal persons. In particular it may acquire and dispose of real property and chattels and institute legal proceedings.

Article 63

1. The contractual liability of the Agency shall be governed by the law applicable to the contract in question. The Court of Justice of the European Communities shall have jurisdiction pursuant to any arbitration clause contained in a contract concluded by the Agency.
2. In the case of non-contractual liability, the Agency shall, in accordance with the general principles common to the laws of the Member States, make good any damage caused by it or its servants in the performance of their duties.

The Court of Justice shall have jurisdiction in any dispute relating to compensation for such damages.

3. The personal liability of its servants towards the Agency shall be governed by the relevant rules applying to the staff of the Agency.

Article 64

The Protocol on the Privileges and Immunities of the European Communities shall apply to the Agency.

Article 65

The staff of the Agency shall be subject to the rules and regulations applicable to officials and other staff of the European Communities. In respect of its staff, the Agency shall exercise the powers which have been devolved to the appointing authority.

The Management Board, in agreement with the Commission, shall adopt the necessary implementing provisions.

Article 66

Members of the Management Board, members of the Advisory Board, members of the Committees referred to in points (a) to (d) of Article 50(1), and experts and officials and other servants of the Agency, shall be required, even after their duties have ceased, not to disclose information of the kind covered by the duty of professional secrecy.

Article 67

The Commission may, in agreement with the Management Board and the relevant Committee, invite representatives of international organisations with interests in the harmonisation of regulations applicable to medicinal products to participate as observers in the work of the Agency. The conditions for participation shall be determined beforehand by the Commission.

Article 68

The Management Board shall, in agreement with the Commission, develop appropriate contacts between the Agency and the representatives of the industry, consumers and patients and the health professions. These contacts may include the participation of observers in certain aspects of the Agency's work, under conditions determined beforehand by the Management Board, in agreement with the Commission.

Article 69

The Management Board shall, in the case of veterinary medicinal products which have limited markets, or in the case of veterinary medicinal products intended for diseases with a regional distribution, adopt the necessary administrative measures to provide help to pharmaceutical companies at the time of submission of their applications. These administrative measures shall include, in particular, the taking over responsibility for some translations by the Agency.

Article 70

To ensure an appropriate level of transparency, the Management Board, on the basis of a proposal by the Executive Director, in agreement with the Commission, shall adopt rules to ensure the availability to the public of regulatory, scientific or technical information concerning the authorisation or supervision of medicinal products which is not of a confidential nature.

TITLE V

GENERAL AND FINAL PROVISIONS

Article 71

1. All decisions to grant, refuse, vary, suspend, withdraw or revoke a marketing authorisation which are taken in accordance with this Regulation shall state in detail the reasons on which they are based. Such decisions shall be notified to the party concerned.
2. An authorisation to place a medicinal product, governed by this Regulation, on the market shall not be granted, refused, varied, suspended or withdrawn except through the procedures and on the grounds set out in this Regulation.

Article 72

1. Only one authorisation may be granted to a particular applicant for a specific medicinal product.

However for objective verifiable reasons relating to public health or the availability of medicinal products to health professionals and/or patients, the Commission may authorise the same applicant to submit more than one application to the Agency for that medicinal product.
2. As regards medicinal products for human use, the provisions of Article 98(3) of Directive 2001/83/EC apply to medicinal products authorised under this Regulation.
3. Without prejudice to the unique, Community nature of the content of the documents referred to in points (a), (b) and (c) of Article 9(4) and in points (a) to (d) of Article 31(4), this Regulation shall not prohibit the use of two or more commercial designs for a given medicinal product covered by a single authorisation.

Article 73

1. By way of derogation from Article 6 of Directive 2001/83/EC, a medicinal product not authorised for human use belonging to the categories referred to in Article 3(1) and (2) of this Regulation, which is potentially of major interest from the point of view of public health, may be made available to certain patients for compassionate reasons.
2. Before any decision is taken concerning the compassionate use of the medicinal products falling within the categories referred to in Article 3(1) and (2), the manufacturer or the person applying for a marketing authorisation shall notify the Agency.
3. Where a compassionate use is envisaged, the Committee for Human Medicinal Products, after consulting the manufacturer or the applicant, may adopt recommendations on the conditions for use, the conditions for distribution and the patients targeted. The Member States shall take any appropriate measures to ensure that the recommendations may be implemented under the applicable national legislation.
4. The Agency shall keep an up-to-date list of the medicinal products referred to in paragraph 1 made available for compassionate use. Article 22(1) and Article 23 shall apply *mutatis mutandis*.
5. The recommendations referred to in paragraph 3 do not affect the civil or criminal liability of the manufacturer or the applicant for marketing authorisation.
6. No medicinal product administered for compassionate reasons may be the subject of a paid transaction, except in special cases determined beforehand in national legislation.
7. The actual placing on the market of a medicinal product previously administered for compassionate reasons, following the granting of a marketing authorisation or a negative opinion by the Committee for Human Medicinal Products within the meaning of Article 9(2), shall render paragraphs 3 and 6 of this Article invalid.
8. This Article shall be without prejudice to Directive 2001/20/EC of the European Parliament and of the Council¹⁶.

Article 74

1. Without prejudice to the Protocol on the Privileges and Immunities of the European Communities, each Member State shall determine the penalties to be applied for the infringement of the provisions of this Regulation or the regulations adopted pursuant to it and shall take every measure necessary for their implementation. The penalties shall be effective, proportionate and dissuasive.

¹⁶ OJ L 121, 1.5.2001, p. 34.

Member States shall inform the Commission of these provisions no later than 31 December 2004 of the penalties laid down in accordance with the above subparagraph. They shall send notification of any subsequent alterations as soon as possible.

2. Member States shall inform the Commission immediately of the institution of any litigation concerning the infringement of this Regulation.
3. At the Agency's request, the Commission may impose financial penalties on the holders of marketing authorisations granted under this Regulation if they fail to observe certain obligations laid down in connection with the authorisations. The maximum amounts as well as the conditions and methods for collection of these penalties shall be laid down by the Commission in accordance with the procedure foreseen in Article 77(2).

Article 75

This Regulation shall not affect the competences vested in the European Food Authority created by Regulation (EC) No ... of the Parliament and of the Council¹⁷.

Article 76

At least every ten years, the Commission shall publish a general report on the experience acquired as a result of the operation of the procedures laid down in this Regulation, in Chapter 4 of Title III of Directive 2001/83/EC [relating to medicinal products for human use] and in Chapter 4 of Title III of Directive 2001/82/EC [relating to medicinal products for veterinary use].

Article 77

1. The Commission shall be assisted by the Standing Committee on Medicinal Products for Human Use set up by Article 121 of Directive 2001/83/EC and by the Standing Committee on Veterinary Medicinal Products set up by Article 89 of Directive 2001/82/EC.
2. Where reference is made to this paragraph, the regulatory procedure laid down in Article 5 of Decision 1999/468/EC shall apply, in compliance with Article 7 and Article 8 thereof.

The period provided for in Article 5(6) of Decision 1999/468/EC shall be three months.
3. Where reference is made to this paragraph, the advisory procedure laid down in Article 3 of Decision 1999/468/EC shall apply, in compliance with Article 7 and Article 8 thereof.
4. Where reference is made to this paragraph, the management procedure laid down in Article 4 of Decision 1999/468/EC shall apply, in compliance with Article 7 and Article 8 thereof.

¹⁷ OJ L

The period provided for in Article 4(3) of Decision 1999/468/EC shall be one month.

Article 78

Regulation (EEC) No 2309/93/EC is hereby repealed.

References to the repealed Regulation shall be construed as references to this Regulation and shall be read in accordance with the correlation table in Annex II.

Article 79

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Communities*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels,

For the European Parliament

The President

For the Council

The President

ANNEX I

1. Medicinal products developed by means of one of the following biotechnological processes:
 - recombinant DNA technology;
 - controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells;
 - hybridoma and monoclonal antibody methods.
2. Veterinary medicinal products, including those not derived from biotechnology, intended primarily for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals.
3. Medicinal products intended for administration to human beings, containing a new active substance which was not included in the composition of any medicinal product for human use authorised in the Community prior to the date of entry into force of this Regulation.
4. Medicinal products intended for veterinary use, containing a new active substance which was not included in the composition of any medicinal product for veterinary use authorised in the Community prior to the date of entry into force of this Regulation.

ANNEX II

Correlation table

| Present Regulation | Regulation (EEC) No 2309/93 |
|--------------------|-----------------------------|
| Article 1 | Article 1 |
| Article 2 | Article 2 |
| Article 3 | Article 3 |
| Article 4 | Article 4 |
| Article 5 | Article 5 |
| Article 6 | Article 6 |
| Article 7 | Article 7 |
| Article 8 | Article 8 |
| Article 9 | Article 9 |
| Article 10 | Article 10 |
| Article 11 | Article 11 |
| Article 12 | Article 12 |
| Article 13 | Article 13 |
| Article 14 | Article 14 |
| Article 15 | Article 15 |
| Article 16 | Article 16 |
| Article 17 | Article 17 |
| Article 18 | Article 18 |
| Article 19 | Article 19 |
| Article 20 | Article 20 |
| Article 21 | Article 21 |
| Article 22 | Article 22 |

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| Article 23 | Article 23 |
| Article 24 | Article 24 |
| Article 25 | Article 25 |
| Article 26 | Article 26 |
| Article 27 | Article 27 |
| Article 28 | Article 28 |
| Article 29 | Article 29 |
| Article 30 | Article 30 |
| Article 31 | Article 31 |
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| Article 33 | Article 33 |
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| Article 36 | Article 36 |
| Article 37 | Article 37 |
| Article 38 | Article 38 |
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| Article 43 | Article 43 |
| Article 44 | Article 44 |
| Article 45 | Article 45 |
| Article 46 | Article 46 |
| Article 47 | Article 47 |
| Article 48 | Article 48 |
| Article 49 | Article 49 |

| | |
|------------|----------------------|
| Article 50 | Article 50 |
| Article 51 | Article 51 |
| Article 52 | New |
| Article 53 | New |
| Article 54 | Article 52 |
| Article 55 | Article 53 |
| Article 56 | Article 54 |
| Article 57 | Article 55 |
| Article 58 | Article 56 |
| Article 59 | New |
| Article 60 | Article 57 |
| Article 61 | Article 58 |
| Article 62 | Article 59 |
| Article 63 | Article 60 |
| Article 64 | Article 61 |
| Article 65 | Article 62 |
| Article 66 | Article 63 |
| Article 67 | Article 64 |
| Article 68 | Article 65 |
| | Article 66 (deleted) |
| Article 69 | New |
| Article 70 | New |
| Article 71 | Articles 67 and 68 |
| Article 72 | New |
| Article 73 | New |
| Article 74 | Article 69 |
| | Article 70 (deleted) |

| | |
|------------|-----------------------|
| Article 75 | New |
| Article 76 | Article 71 |
| Article 77 | Articles 72 and 73 |
| Article 78 | New |
| Article 79 | Article 74 |
| Annex I | Annex (Parts A and B) |

FINANCIAL STATEMENT

1. TITLE OF OPERATION

Proposal for a Regulation of the Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products

2. BUDGET HEADING(S) INVOLVED

B5-3120 European Agency for the Evaluation of Medicinal Products

3. LEGAL BASIS

Article 95 EC

4. DESCRIPTION OF OPERATION

4.1 General objective

To guarantee a high level of human and animal health protection, in particular through increased market surveillance and a stepping-up of pharmacovigilance procedures.

To increase the number of medicinal products available.

To complete the internal market in pharmaceutical products and to establish a legislative and regulatory framework promoting the competitiveness of the pharmaceutical industry.

To adapt the operation of the Agency and its administrative structure so as to cope with the consequences of the enlargement of the European Union.

4.2 Period covered and arrangements for renewal

Implementation of proposed measures scheduled for 2005, there being no specific target date.

5. CLASSIFICATION OF EXPENDITURE OR REVENUE

5.1 Non-compulsory expenditure

5.2 Non-differentiated appropriations

5.3 Type of revenue involved

Not applicable

6. TYPE OF EXPENDITURE OR REVENUE

Balancing subsidy to the Medicinal Products Agency

7. FINANCIAL IMPACT

7.1 Method of calculating the total cost of the operation (link between individual costs and total cost)

The cost of the operation for the Commission is calculated on the basis of the actual number of meetings of expert committee meetings per year for the type of operations considered for the proposal.

The cost of the operation for the Agency has to be based on the following assumptions:

- an increase in the level of revenue accruing from fees, as a result of greater responsibilities in respect of the evaluation of new categories of medicinal products, including in the event of the current level of these fees being maintained; however, the number of products involved each year and the relationship between cost and the difficulty of carrying out scientific evaluations remain unknown to date;
- an increase in expenditures as a result of the enlargement of the European Union, particularly because of:
 - a greater number of experts having to be convened each budget year, depending on the number of new Member States during each respective year (impossible to estimate as the timetables for accession by candidate countries are not known);
 - higher costs linked to the expansion of telematic networks and databases to accommodate new Member States (impossible to estimate for the same reasons).

On account of the uncertainties mentioned above, it is thus impossible to estimate the cost of the measures for the Agency. In particular, the possible adjustment of the Community subsidy in line with the increased activities of the Agency due to enlargement will have to be taken into account during the general review of Financial Perspectives in this regard.

7.2 Itemised breakdown of cost

Commitment appropriations in EUR million (at current prices)

| Breakdown | Year n | n+1 | [n+2] | [n+3] | [n+4] | n+ 5 and subsequent financial years | Total |
|---|--------|-----|-------|-------|--|-------------------------------------|-------|
| Enlargement-related increase in Agency's activities | | | | | Cost to be calculated at time of accession | | |
| Total | | | | | | | |

8. FRAUD PREVENTION MEASURES

- Specific checks envisaged

No

9. ELEMENTS OF COST-EFFECTIVENESS ANALYSIS

9.1 Specific and quantified objectives: target population

Not applicable

9.2 Justification of the measure

- Need for a contribution from the Community budget, particularly in view of the subsidiarity principle

Amendment of existing legislation in order to take account of scientific and technical progress, as well as the future enlargement of the European Union

- Choice of ways and means

Amendment of existing legislation on the basis of Article 71 of Council Regulation (EEC) No 2309/93 following an evaluation of the implementation of existing legislation which is the subject of a report by the Commission to the Council and the European Parliament.

- Main factors of uncertainty which could affect the specific results of the operation

The chief factor of uncertainty ties in with the arrangements for enlargement of the European Union, in terms both of the countries concerned and the timetable involved. Another factor of uncertainty relates to the use which the industry will make of the procedures put in place: the number of products concerned per year and the relationship between cost and the difficulty of carrying out scientific evaluations remain unknown to date.

9.3 Monitoring and assessment

- Performance indicators

Number of products authorised in accordance with the procedures, progress of the work on technical harmonisation, timetable for the expansion procedures, database and computer networks to include candidate countries.

- Details and frequency of planned evaluations

Report by the Commission at least once every ten years following the first report, based on this proposal, to be prepared after six years.

- Assessment of the results obtained (where the operation is to be continued or renewed)

The results obtained since 1 January 1995 (data of entry into force of the present system) will be the subject of a report by the Commission to the Council and the European Parliament (adoption by written procedure)

10. ADMINISTRATIVE EXPENDITURE (PART A OF SECTION III OF THE GENERAL BUDGET)

The effective mobilisation of the requisite administrative resources will depend on the Commission's annual decision on how to allocate resources, bearing in mind in particular the additional amounts of money authorised by the budget authority.

10.1 Effect on the number of jobs

| Type of job | | Staff to be assigned to the operation | | of whom | | duration |
|-------------------------------|-------------|---------------------------------------|----------------|---|----------------------------------|----------|
| | | Permanent jobs | Temporary jobs | by using existing resources in the DG or department concerned | by using supplementary resources | |
| Officials or temporary agents | A B C | 2A, 1B, 1C | | 2A, 1B, 1C | not applicable | |
| Other resources | | | | | | |
| Total | | 2A, 1B, 1C | | 2A, 1B, 1C | not applicable | |

Indicate when additional resources should be made available.

10.2 Aggregate cost of additional staffing requirements

(EUR)

| | Cost | Method of calculation |
|---------------------------------------|---------|------------------------------|
| Officials | 432 000 | 4 times EUR 108 000 per year |
| Temporary agents | | |
| Other resources(state budget heading) | | |
| Total | 432 000 | |

The figures represent the total costs of the additional posts for the duration of the operation, where stipulated, or for 12 months if the duration is not stipulated.

10.3 Increase in other operating expenditure involved in operation, in particular costs incurred by committee and expert group meetings

(EUR)

| Budget heading(No and title) | Cost | Method of calculation |
|------------------------------|---------|--|
| A0-7031 | 150 000 | Without taking into account figures linked to enlargement (the annual number of experts from candidate countries not being known), the method of calculation is based on a cost of approximately EUR 10 000 per meeting for a number of experts from the 15 Member States. |
| Total | 150 000 | 15 meetings per year |

The amounts must correspond to the total cost of the operation if it is of fixed duration or for 12 months if the duration is not fixed.

IMPACT ASSESSMENT FORM
IMPACT OF THE PROPOSAL ON BUSINESSES, PARTICULARLY ON SMALL
AND MEDIUM-SIZED ENTERPRISES (SMEs)

TITLE OF THE PROPOSAL

Proposal for a Regulation of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products

REFERENCE NUMBER OF THE DOCUMENT:

THE PROPOSAL

1. In view of the principle of subsidiarity, why is Community legislation necessary in this field and what are its main objectives?

The proposed legislation introduces new provisions and amends, in a number of respects, the existing legislation relating to the functioning of the centralised and decentralised procedures for approving and suspending the marketing of medicinal products for human and veterinary use.

Pursuant to Article 71 of Regulation (EEC) No 2309/93, the Commission is obliged to report within six years of the entry into force of the Regulation on the experience acquired as a result of the operation of the centralised and decentralised procedures. An audit report prepared on behalf of the Commission¹ has identified the aspects of the authorisation procedures that were operating satisfactorily and those where it was considered that improvement could be achieved.

From a business viewpoint, the proposed measures are intended to:

- increase the level of harmonisation across Member States of the rules governing medicinal products;
- increase the efficiency of operation of the centralised and decentralised procedures;
- thereby improve access and speed of access to the whole of the European market for both innovative and generic medicinal products; and
- allow industry to respond more quickly to the needs of the market.

¹ Evaluation of the operation of Community procedures for the authorisation of medicinal products, CMS Cameron McKenna and Andersen Consulting, October 2000.

The “new systems” for licensing which were introduced in 1995 have contributed to the creation of a single market in pharmaceuticals but, notwithstanding the progress that has been made, there is evidence that the procedures contain shortcomings. The findings of the audit report on the operation of the authorisation procedures show that there is a need to refine, and in some areas make more substantial changes to, the existing regimes. In particular, there is recognition that the centralised procedure is capable of working well and that broadening the scope of the procedure to other products would be beneficial, both in terms of patient access and economies of scale for the companies.

The decentralised procedure was acknowledged as having significant advantages in terms of optionality but any such advantage is tempered to an extent by the failure of the system to operate on the basis of effective mutual recognition involving a significant number of Member States.

The pharmaceutical industry is populated by different types of company and a significant proportion of the industry comprises non-R&D-intensive companies, notably those which focus on their own national markets and those which rely upon the manufacture of generic versions of existing products. The existing regimes do not, at present, fully meet all the needs of these sectors of the industry.

Instituting authorisation procedures that properly protect public health while promoting an innovative profitable pharmaceutical industry is critical for Europe. The pharmaceutical industry is a strategic sector for Europe but there is evidence that over the last decade the industry in Europe is losing competitiveness compared to the USA and that its growth is more erratic than in the US or Japan². The reasons underlying this trend are complex but the ability of companies to compete effectively is influenced, at least in part, by the nature of the regulatory environment.

The forthcoming enlargement of the European Union over the next decade will see the accession of further Member States. In principle, enlargement has the potential to contribute to the overall competitiveness of the European industry, but an important step in realising increased competitiveness is eradication of the shortcomings identified in the existing procedures prior to enlargement.

It is considered appropriate to maintain a balance between the centralised and decentralised authorisation procedures. Both systems have hitherto contributed – though not to the same extent - to the development of a single market in pharmaceuticals and provided a high degree of safety for patients and animals. However, the emergence of new technologies is delivering sophisticated medicinal products which are best suited to centralised approval.

² See "Global competitiveness in Pharmaceuticals", Report prepared for the Enterprise DG of the European Commission by Gambardella A, Orsenigol and Pammolli F., November 2000.

THE IMPACT ON BUSINESSES

2. Who will be affected by the proposal?

- What business sectors?

The measures primarily concern pharmaceutical manufacturers and to a lesser extent wholesalers and distributors of medicinal products.

The pharmaceutical industry in the EU consists of companies with a range of different businesses conducted often with a different geographical focus. The total number of pharmaceutical businesses in the EU is estimated at approximately 3 000³. Large multinational companies dominate the market accounting for approximately 60-65% of the market for pharmaceutical sales. Medium-sized companies (by international standards) make up approximately 30-35% of the market, with small local companies accounting for the balance. In terms of business types, the biotechnology element of the European pharmaceutical industry is still young, but the number of companies is growing with just over 1 000 company units. Generic medicines currently account for around 10% of total pharmaceutical sales in the non-hospital market with penetration highest in Germany, Denmark, UK and the Netherlands⁴. Finally, the veterinary sector accounts for approximately 5% of the value of the human pharmaceutical market⁵. This sector of the market is far more diverse than that relating to medicines for human use, reflecting differences in livestock distribution, methods of production and climate across the EU.

The legislative proposals cover a number of aspects of the regulation of medicinal products and consequently the proposals will impact to some extent upon all pharmaceuticals manufacturers. A number of the proposals will therefore affect all pharmaceutical companies irrespective of the nature of the pharmaceutical business. For example, the provisions relating to the validity of marketing authorisations, compassionate use of medicines, the application of good manufacturing practice to starting materials and pharmacovigilance. A number of the measures are sector-specific or specific to one or other of the authorisation procedures and accordingly the effect of such measures will be more selective. The centralised procedure tends to be used predominantly by large multinational companies and smaller innovation-specialist companies. Accordingly, the proposed changes to the centralised system such as the introduction of conditional authorisations and a fast-track procedure will be relevant for these types of company.

³ The pharmaceutical industry in figures, European Federation of Pharmaceutical Industries Associations, November 2000.

⁴ Generic Medicines: How to ensure their effective contribution to health care, Euro Health Vol 2 No 3, September 1996.

⁵ Fountain R and Thurman D: Animal Health Market to Face Opportunities and Challenges in 98, Feedstuffs Vol. 69 No 48, November 1997.

- What sizes of company (proportion of small and medium-sized enterprises)?

The decentralised (mutual recognition) procedure, although used by the large multinational companies, is also used by a significant proportion of small and medium-sized enterprises (“SMEs”). Accordingly, these companies will be impacted by the proposed amendments to the operation of the decentralised system. The principal sector-specific measures are directed towards manufacturers of products for veterinary use, manufacturers of generic medicines and manufacturers of homeopathic medicines.

- Are there particular geographical regions in the Community where such companies are established?

No, there are no differences.

3. What measures will companies have to take in order to comply with the proposal?

The majority of the proposal measures concern procedural changes and fine-tuning of existing procedures. Accordingly, a number of the measures do not impose direct obligations upon business. The majority of the obligations which are imposed impact at the time of application for a marketing authorisation.

Companies seeking to place a product containing a new chemical entity (“NCE”) on the market will be required to use the centralised authorisation procedure. This will remove, therefore, in respect of some medicinal products, the element of choice which companies currently enjoy when obtaining an authorisation from Member States. It should however, be noted that many products containing an NCE⁶ are already obliged to use the centralised route because they have been developed using biotechnological processes. Moreover, in circumstances where a company has a choice of procedure for a product containing an NCE, most of the companies already opt for the centralised route. It is intended that generic copies of centrally-authorized products may be authorised through either the centralised or the decentralised route. All other medicinal products may do likewise provided they show significant innovation over existing therapies. The broadening in scope of the centralised procedure will bring administrative savings for companies able to benefit from the single-application procedure. Some companies, particularly those in the veterinary sector with NCE-containing products which are relevant to only a limited geographical area of the European market, may be subject to an increase in the overall cost of preparing a centralised application for a marketing authorisation. This is why a derogation has been introduced.

Applicants pursuing an authorisation under the decentralised procedure will be compelled to enter arbitration proceedings if an issue cannot be resolved by the Member States concerned in the case of veterinary medicinal products. Companies may incur some costs in handling arbitration proceedings which they would otherwise avoid by withdrawal of the application. However, any such costs should be outweighed by the fact that companies may be permitted to market a medicinal product which is the subject of arbitration proceedings in the Member States that

⁶ Taken here in broader sense as meaning any new active substance.

have agreed to authorise the product, thus permitting companies to begin to recoup investment costs earlier than at present.

The harmonisation to ten years (plus, for medicines for human use, one year for new therapeutic indications) of the period of data protection afforded to innovator companies will prevent an applicant for a generic (copy) product from making abridged applications in Austria⁷, Denmark, Greece, Finland, Ireland, Luxembourg, Portugal, and Spain on the expiry of six years from the date of first authorisation of the innovator product in the EU. An abridged application is one where the applicant does not present the results of his/her own safety and efficacy testing but relies upon the data underlying the authorisation of the innovator product. However, this restriction is balanced by the fact that companies intending to seek an authorisation for a generic product will be permitted, under a "Bolar-type" provision, to conduct the testing required prior to the expiry of the originator product's period of patent protection.

There is recognition that in some respects the veterinary sector of the pharmaceutical industry has different requirements and faces different issues and the proposal, therefore, seeks to address matters which are a concern in this area of the business. The incremental periods of protection available for data used to extend a marketing authorisation to additional food-producing species, the 13-year period of protection for honey bees and fish, and the introduction of a limited period of data protection for certain MRL data will encourage innovation by providing greater protection for the results of research by delaying somewhat the date at which applicants seeking an authorisation for a generic (copy) product may obtain approval without themselves investing in the research required to obtain and maintain a marketing authorisation. However, consistent with the position for medicines for human use, generic manufacturers will be able to take advantage of a "Bolar-type" provision.

The removal of the requirement for companies to renew marketing authorisations every five years will reduce the cost burden for companies. This amendment is balanced by increased pharmacovigilance reporting requirements; overall, a cost saving is expected for companies, since companies already have established pharmacovigilance systems in place.

4. What economic effects is the proposal likely to have:

- on employment?
- on investment and the creation of new businesses?
- on the competitiveness of businesses?

The proposed package is expected to benefit the pharmaceutical industry in Europe and provide earlier access for patients in the Community to important new medicines.

⁷ Currently in this Member State the period of data protection will not be applied beyond the date of expiry of the patent. This link will cease to exist under the proposed amendment.

The examination in the report by Pammolli *et al*⁸ of the competitive position of the European pharmaceutical business compared with the USA reveals that, in general, the profile of the pharmaceutical industry in Europe is different from that in the USA. The European industry is less specialised in Research and Development activities and has a much larger presence of companies specialising in low value-added activities. The US has developed an industry which is effective not only in the “exploration” of new technologies but also in their “exploitation”. This vertical specialisation enhances innovation – a key driver of competitiveness – by exploiting the advantages of both the small biotechnology firms and the larger multinational firms.

Strengthening the scientific advice procedure within the centralised system will enable companies’ research to be better focused and will reduce the investment risk for small biotechnology companies and thereby provide encouragement for this sector of the industry. In addition, extension of the period of data protection to ten years in all Member States, with an additional year for subsequent clinically-important indications, will encourage innovation by providing a greater opportunity for research-based companies to recoup the costs of their research investment. The Pammolli *et al.* Report⁹ showed that there was too little competition in some Member States, which in turn led to inefficiencies within the industry. Accordingly, the measures to encourage innovation are balanced by those intended to stimulate generic competition - for example, the introduction of a “Bolar-type” provision and the availability of the centralised procedure for generic copies of centrally-authorized products.

A strengthening of innovation and competition within the industry will ultimately promote growth and enhance employment opportunities within the sector. Following the expiry of patent and data protection periods, the proposals aimed at stimulating the prompt approval of generic copies, will provide competition that will exert downward pressure on pricing, thereby helping to facilitate the supply of affordable medicinal products to Member States’ healthcare systems.

The proposal is expected to benefit patients by supplying medicinal products more quickly to the market and, in particular, making available important new treatments at an earlier stage. This will be achieved by a combination of the reduction by half of the length of time available for the consultation of Member States on Commission decisions, the introduction of conditional authorisations and a fast-track procedure, together with a more formalised approach to the availability of medicinal products on a compassionate-use basis. Earlier access to medicines is likely to bring economic benefits by reducing morbidity and mortality and thereby have some influence on national healthcare budgets.

The veterinary sector of the pharmaceutical industry has encountered problems in the availability of medicines for minor species and, following the introduction of the MRL requirement for food-producing animals, for certain therapeutic areas. The increased periods of protection for data used to extend an authorisation for use in additional food-producing species and the increased period for minor species will encourage businesses to exploit their products for use in a broader range of species.

⁸ See note 2.

⁹ See note 2.

This will benefit agricultural producers active in these areas and reduce the hitherto unacceptable level of off-label use.

5. Does the proposal contain measures to take account of the specific situation of small and medium-sized enterprises (reduced or different requirements, etc.)?

The proposal does not contain specific measures for SMEs, but a number of the measures will be particularly beneficial for SMEs. For example, those measures designed to promote innovation, those improving the scientific advice procedure (biotechnology SMEs) and those requiring the introduction of a simplified registration procedure for homeopathic products.

CONSULTATION

6. List the organisations which have been consulted about the proposal and outline their main views.

There has been extensive consultation with interested parties on the operation of the rules governing medicinal products in the European Union and on the amendments which would improve the system. As part of the survey undertaken for the Commission on the operation of the Community procedures, the consultants concerned sought written and oral comments from a broad range of respondents, as follows:

- all holders of a centralised marketing authorisation at the time of the review;
- 159 marketing-authorisation holders (including large multinationals, SMEs, manufacturers of generics and non-prescription and veterinary medicines from different Member States) who had used the decentralised procedure;
- European trade associations representing the interests of human and veterinary medicines including those concerned with NCEs, generics, non-prescription medicines, and homeopathic and herbal medicinal products;
- 15 national consumer organisations and 134 patient associations;
- professional associations responsible for the regulation of doctors, dentists, pharmacists and veterinary practitioners;
- competent authorities responsible for authorising medicinal products;
- chairmen of the Committee for Proprietary Medicinal Products, the Committee for Veterinary Medicinal Products, the Mutual Recognition Facilitation Group and the Veterinary Mutual Recognition Facilitation Group; and
- the ministries responsible for health, social affairs, finance and agriculture.

Many companies were in favour, in principle, of opening up the centralised procedure to other products. There was broad acceptance from businesses of the need to reduce the procedural delays in the Commission decision-making procedure and also for the concept of a formal fast-track procedure.

In relation to the decentralised procedure, although companies were generally satisfied with the performance of the Member States there was dissatisfaction with the limited adherence to the principle of mutual recognition. Many respondents supported the introduction of a dialogue between the Member States prior to the granting of an authorisation in order to encourage greater acceptance of the principles of mutual recognition. Most companies were not in favour of compulsory arbitration in circumstances where Member States were unable to reach agreement, but there was strong support for permitting the marketing of a product pending arbitration in the Member States concerned that felt able to authorise the product.

There was strong support from business for the abolition of the renewal procedure for marketing authorisations.

Finally, there was very strong support for harmonising the periods of data protection, but less consensus on what the harmonised level of protection should be or how it should be applied to products derived from incremental research.

2001/0253 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

**amending Directive 2001/83/EC on the Community code relating to medicinal products
for human use**

EXPLANATORY MEMORANDUM

I. GENERAL CONSIDERATIONS

The purpose of the Community provisions concerning the placing on the market of medicinal products for human use is to guarantee a high level of public health protection and to enable the rules of the internal market to operate effectively. No medicinal product may be placed on the market unless its quality, safety and efficacy have been previously demonstrated. These guarantees must be maintained when it is actually placed on the market.

II. JUSTIFICATION

A. Aims

1. On 1 January 1995, new authorisation and monitoring procedures for medicinal products came into force¹ which replaced various procedures based on voluntary cooperation between the competent national authorities. The centralised procedure enables applicants to obtain from the Commission authorisation to place medicinal products on the Community market after evaluation by the European Agency for the Evaluation of Medicinal Products. This procedure is compulsory for biotechnological medicinal products and optional for innovative medicinal products. Where applicants wish to obtain authorisation to place other medicinal products on the market in more than one Member State, the mutual recognition procedure has been compulsory since 1998. This procedure is based on the evaluation carried out by the Member State (the "reference Member State") which granted marketing authorisation, which is normally recognised by the Member States concerned by the same application for authorisation ("concerned Member States"). The European Agency for the Evaluation of Medicinal Products and the competent authorities in the Member States pursue a number of objectives, in particular the pooling of the Member States' potential in terms of scientific expertise in order to guarantee a high degree of public health protection, the free movement of pharmaceutical products, and more rapid access for the people of Europe to medicinal products and in particular to new generations of medicinal products. Now, six years later, these objectives are still valid. However, as a result of international and European developments, scientific progress and the forthcoming advent of new therapies, the existing legislation needs to be adapted and consideration must be given to the main features of future marketing authorisation procedures.

Regulation (EEC) No 2309/93 provided for the possibility of changing these procedures, since its Article 71 states that "within six years of the entry into force of this Regulation, the Commission shall publish a general report on the experience acquired as a result of the operation of the procedures laid down in this Regulation, in Chapter III of Directive 75/319/EEC [*medicinal products for human use*] and in Chapter IV of Directive 81/851/EEC [*veterinary medicinal products*]".

¹ Directives 93/39/EEC, 93/40/EEC, 93/41/EEC and Regulation (EEC) No 2309/93.

On the basis of the provisions of this Article 71, an audit of the procedures and the operation of the Agency was commissioned from Cameron McKenna and Andersen Consulting. The results of this work are being analysed and developed in the "Commission Report on the operation of Community marketing authorisation procedures for medicinal products" (COM....).

2. In the light of the experience acquired between 1995 and 2000 and of the analysis of the comments by the various parties concerned (the competent authorities in the Member States, pharmaceutical companies, associations of the pharmaceutical industry, professional associations of doctors and pharmacists, and associations of patients and consumers), the Commission felt it necessary to adapt certain provisions of Regulation (EEC) No 2309/93. It also appears necessary to adapt in an appropriate manner the general provisions relating to the placing on the market of medicinal products for human use, which have been consolidated in Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, which is the subject of this proposal for amendment. The word "adaptation" must be particularly stressed in this connection since, although procedural arrangements or other provisions need to be amended or added, neither the general principles nor the basic architecture of the system, as laid down by the original 1993 Regulation establishing the Agency, are disputed. The Commission is aware that, in view of the growth of the battery of therapeutic products available, and of the growing necessity for information and transparency with respect to medicinal products and their use, a number of Member States have developed a system for evaluating the relative efficacy of medicinal products, intended to allow a new medicinal product to be positioned with respect to those already on the market. Accordingly, in its Conclusions of 29 June 2000 on Medicinal Products and Public Health², the Council has underlined the importance of the identification of medicines with significant added therapeutic value. The Commission is of the opinion that this type of assessment should not be undertaken within the marketing authorisation framework, where it is essential to maintain the fundamental criteria of quality, safety and efficacy. Even though it appears that action at a Community level may be useful, the Commission has not, therefore at this stage, made any proposals in this regard. After having conducted large consultations on this issue, the Commission will reflect on the possibility of making a proposal in the appropriate legal context.
3. The necessary adaptation must take account of the experience acquired in the six years during which the procedures have been implemented and of the rapid scientific developments in the pharmaceutical field. These considerations must also be seen in the light of ever-increasing globalisation, in particular between the world's three major pharmaceutical "regions" of Europe, North America and Japan. Scientific globalisation is being accompanied by the globalisation of certain regulatory practices and in particular of the scientific and technical criteria for evaluating medicinal products. The increasingly rapid introduction of new technologies in the field of research and development relating to medicinal products requires an adaptable regulatory environment based on stable, well defined principles which are nevertheless truly international in scope. This "global" dimension of regulatory requirements is surely one of the main new factors to be considered in comparison

² OJ C 218, 31.7.2000, p. 10.

with the early 1990s, when the present Community marketing authorisation system was devised. Any regulatory environment applying to the authorisation of medicinal products can no longer be regarded as modern, effective and lasting if it develops in isolation. The Commission and the Member States are already very actively involved, through their participation in ICH³ and VICH⁴, in the international discussions on technical and scientific requirements in the field of human and veterinary medicinal products. However, it is also very important that the regulatory framework of the Community marketing authorisation system should take due account of this new global environment so that the European Community can play a full part on the international stage alongside its – particularly American and Japanese – partners.

4. There is another new dimension in relation to the 1993 context which now has to be considered: the enlargement of the European Union. As in other areas, the future enlargement obviously raises the question of whether certain procedural arrangements for the regulation of medicinal products are appropriate and particularly whether it will be possible, in a context designed for 15 countries, for 20, 25 or 28 Member States to conduct scientific debates and take decisions effectively.
5. As part of all these regulatory and technical considerations, it will obviously be necessary to bear in mind the primary purpose of developing and subsequently marketing medicinal products: to achieve health benefits for patients. While the centralised authorisation system has proved to be effective for evaluating medicinal products, the effectiveness of the mutual recognition system should be improved, since it concerns to some extent new medicinal products but also medicinal products on which the files go back further or generic medicinal products. Particular account should be taken of generic medicinal products since, in the overall context of health systems, it should be made easier to place them on the market.
6. Any changes in the rules must maintain safety of use for the patient, market surveillance and pharmacovigilance. The analysis of the risk/benefit balance must remain the basis for any administrative decision on a medicinal product, irrespective of the authorisation procedures applied. Although the provisions in force have helped to ensure a high level of safety, it is necessary to improve certain existing arrangements with a view to speeding up action in emergencies and to increasing the effectiveness of the system of pharmacovigilance and market surveillance in order, *inter alia*, to take account of the fact that the market subject to such surveillance will increase in size as a result of the forthcoming enlargement of the European Union.
7. Lastly, the regulations must be adapted in order to take account of the experience acquired during these years of intensive cooperation between the Member States, the European Agency for the Evaluation of Medicinal Products and the Commission.

³ International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

⁴ International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Pharmaceuticals.

8. In general terms, the pharmaceutical legislation must be revised in the light of the objectives set out in the conclusions of the Commission Report:
- to provide a high level of health protection for the people of Europe and tighter surveillance of the market;
 - to complete the internal market in pharmaceutical products taking account of the implications of globalisation and to establish a regulatory and legislative framework that favours the competitiveness of the European pharmaceuticals industry sector;
 - to meet the challenges of the future enlargement of the European Union;
 - to rationalise and simplify the system as far as possible, thus improving its overall consistency and visibility, and the transparency of procedures and decision-making.

B. Legal basis and procedure

The legal basis of this proposal is Article 95 of the Treaty. This Article, which provides for recourse to the co-decision procedure under Article 251, is the legal basis for achieving the objectives set out in Article 14 of the Treaty, which include the free movement of goods and hence of medicinal products for human use. The prime objective of all rules on the production and distribution of medicinal products must be to safeguard public health, but it must be achieved by means which do not restrict the free movement of medicinal products within the Community. Following the entry into force of the Treaty of Amsterdam, all the legislative provisions adopted by the European Parliament and the Council – except directives adopted on the basis of the executive powers conferred on the Commission and seeking to align the provisions on medicinal products – are adopted on the basis of this Article. This is because the differences between national laws, regulations and administrative provisions on medicinal products result in obstacles to intra-Community trade which directly affect the operation of the internal market. Legislative action by the Community is therefore justified in order to prevent or remove such obstacles.

III. DETAILED CONTENT OF THE PROPOSAL

(For greater ease of consultation, the Articles quoted as references are those of Directive 2001/83/EC as amended by this proposal).

A. Adaptation of definitions, terminology and certain concepts

1. The definition of medicinal product is adapted to take account of new therapies and their particular method of administration (*Articles 1 and 2*) (cellular therapy in particular).
2. In order to bring the text into line with current practice, it is proposed that both in the summary of the product characteristics (*Article 11*) and on the packaging (*Articles 54 and 59*), the name of the medicinal product be followed by the strength and the pharmaceutical form in order to improve the information for patients and practitioners.

3. The criteria for refusing, suspending and withdrawing marketing authorisations have been adapted and harmonised so that the key evaluation criteria of quality, safety and efficacy go hand in hand with the concept of risk/benefit balance, which is the basis of the authorisation and its continued validity (*Articles 26, 116 and 117*).
4. Since the possible duality of certain "borderline" products (medical devices, cosmetics, biocides etc.) has led to differences of interpretation as to the applicable legislation, it is proposed that, when a product fully meets the definition of a medicinal product, but may also meet the definition of other regulated products, the pharmaceutical legislation should apply (*Article 2(2)*).
5. Adaptations are proposed to certain provisions relating to the marketing authorisation application file. These adaptations do not involve any substantive changes to the present provisions but are intended to bring certain legal provisions, the wording of which is sometimes outdated, more into line with current administrative, scientific and technical practices. Furthermore, they take account of the guidelines finalised by the ICH.
6. In order to ensure, as in the case of the centralised procedure, that the procedures are transparent, it is proposed that assessment reports and authorisations accompanied by summaries of the characteristics of the medicinal products authorised under the decentralised or mutual recognition procedure be made available to any interested party (*Article 21*).

B. Generic medicinal products

1. In the case of abridged marketing authorisation procedures, it is proposed that the concept of "essentially similar" medicinal product be abandoned since it actually refers to generic medicinal products. A definition of generic medicinal product is inserted into the text, together with a definition of reference medicinal product in relation to which the generic medicinal product is defined, in order to bring the text into line with the commonly accepted terminology (*Article 10(2)*).
2. Again to bring the text into line with practice, it is proposed that, for the reference medicinal product, the concept of actual placing on the market be abandoned and that only the requirement for it to have a marketing authorisation be retained (*Article 10(1)*). This is necessary in order to make it easier for generic medicinal products to gain access to the market.
3. The administrative protection period for data on the reference medicinal product must be harmonised at ten years (*Article 10(1)*). This period has been chosen in order to stipulate the same period irrespective of the type of marketing authorisation procedure and is the same as the period adopted under the centralised procedure. However, in order to promote research on new therapeutic indications with a significant clinical benefit and bringing an improvement to the quality of life and welfare of the patient, it is proposed that the applicant be granted an extra year of data protection in the case of therapeutic indications which meet the abovementioned conditions and are granted during this ten-year period. It is however necessary to maintain an appropriate balance between such innovations and the need to favour the production of generic medicines. It is therefore foreseen that this extra year will only be granted in the cases where the new indication is authorised during the first eight

years of the ten years data protection period, with the aim of not hindering the emergence of a generic market (*Article 10(1)*).

4. Applicants for a marketing authorisation for a generic medicinal product may carry out the tests necessary for submitting the file before the end of the exclusivity period without this being regarded as an infringement of the rules on the protection of industrial and commercial property (*Article 10(4)*). The purpose of this provision is to prevent a large proportion of the requisite tests being conducted outside the Community, as is currently the case, but without affecting the date on which the generic medicinal products arrive on the market.
5. Lastly, in order to facilitate the harmonisation of existing reference medicinal products, it is proposed that an annual plan for gradual harmonisation be introduced (*Article 30(2)*). This will simplify the procedures for applying for a marketing authorisation for generic versions of these reference medicinal products under the mutual recognition or decentralised procedure.

C. The decentralised procedure and the mutual recognition procedure (*Chapter 4*)

1. The scope of these procedures is linked to that of the centralised procedure. In the proposal to amend Regulation (EEC) No 2309/93, it is proposed that the scope provided for in the original Regulation be maintained on the whole, except for certain amendments rendered necessary by the experience acquired during the past six years and by scientific and technological developments. Since the main amendment proposed is to make the centralised procedure compulsory for all new active substances appearing on the Community market, this means a significant change in the scope of the decentralised or mutual recognition procedure. Any medicinal product not compulsorily subject to the centralised procedure will be covered by the decentralised or mutual recognition procedure, on condition that it is intended for the markets of more than one Member State⁵.

These procedures are thus still optional for other medicinal products which represent a therapeutic innovation and will be the procedure of choice for generic medicinal products. It should be stressed in this connection that the procedures will also be open to generic medicinal products whose reference medicinal product has been authorised under the centralised procedure, since it is proposed that the Member States be given the option of authorising at national level the generic versions of medicinal products authorised by the Community on condition that they maintain the harmonisation achieved at Community level. In particular, the summary of the characteristics of the generic product must comply with that of the medicinal product authorised by the Community.

2. The mutual recognition procedure has been criticised because of difficulties encountered in practice. Under the present system, the Member States must recognise an initial authorisation granted by the reference Member State. It is always more difficult to go back on a scientific decision than to take an initial decision jointly as part of a scientific cooperation procedure. It is also proposed (a) to maintain the general principles of the mutual recognition procedure as laid down in the present rules on medicinal products which have already been granted a marketing

⁵ The national procedure still applies to medicinal products strictly confined to a national market.

authorisation in one of the Member States but whose holder wishes to make the product available to other Member States (*Article 28(1) and (2)*), and (b) to add to it a new decentralised procedure for medicinal products not yet authorised in the Community (*Article 28(1) and (3)*). There would be cooperation between Member States before the decision is taken on the basis of the evaluation conducted by one of them. This procedure is modelled on an existing procedure which has proved its worth, namely the procedure applied to the authorisation of major amendments to an existing authorisation.

3. The introduction of the mutual recognition procedure was facilitated by an informal working group, the "Mutual Recognition Facilitation Group" (MRFG), in which representatives of the Member States meet. Since this group has proved to be effective and the amendment proposed to the procedure involves considerable cooperation between Member States, it is proposed that the group be given formal status and be called a co-ordination group (*Article 27*). Under the new mutual recognition or decentralised procedures, disagreements would be referred to this committee (*Article 29(1) and (2)*) and, if it fails to arrive at a consensus, the matter would be referred to the European Agency for the Evaluation of Medicinal Products (*Article 29(3)*).
4. It is proposed in the case of both Regulation (EEC) No 2309/93 and the mutual recognition or decentralised procedure that the obligation to renew the marketing authorisation every five years be removed (*Article 24(1)*). However, to take account of this removal of the obligation to renew the authorisation every five years, the present proposal stipulates that any marketing authorisation which is not followed within two consecutive years by the actual placing on the market of the medicinal product concerned shall cease to be valid (*Article 24(2) and (3)*). The removal of the obligation of renewal goes hand in hand with a strengthening of the pharmacovigilance and market-surveillance procedures.

D. Referral procedures

The referral procedures come into play if a Member State cannot agree with the assessment report and the summary of product characteristics drawn up by another Member State (*Article 29*), if there is a lack of harmonisation in the decisions taken by the Member States (*Article 30*), or if the interests of the Community are involved (*Article 31*). Although few procedures are referred in this way, such referrals have given rise to very many discussions, particularly regarding interpretation and practical application. In particular in cases where a Member State cannot agree with the evaluation or authorisation by another Member State, it is proposed that referral be made automatic, since experience has shown that, in order to avoid referral, firms systematically withdraw their applications in Member States which are not in favour of granting authorisation. However, it is proposed that in such cases the Member States which are in favour of granting authorisation be allowed to do so on the understanding that, depending on the result of the referral, they may subsequently have to amend it. With regard to referrals on matters of Community interest, and in the light of the experience acquired, it is necessary to provide for an appropriate procedure, particularly in the case of referrals concerning an entire therapeutic class or all medicinal products containing the same active substance (*Article 31*). In both these cases, the number of medicinal products concerned may be very large, and the aim is to ensure that the procedure is effective.

Lastly, in order to make this procedure more effective in terms of deadlines, it is proposed that its overall length be reduced from 90 days to 60 days (*Article 32(1)*).

Following referral procedures, the Commission must take a decision, which must be applied by the Member States (*Articles 33 and 34*). The Commission decision-making process has been the subject of much criticism, in particular on account of its length. As in the case of the decisions which the Commission must take following applications for marketing authorisation under the centralised procedure, this process needs to be reorganised. At present the decision-making procedure is subject to a type III (b) "comitology" procedure⁶. It should be noted first of all that from the outset the Commission has always followed the Agency's opinion on highly scientific matters. Furthermore, the opinions have generally been obtained by written procedure without a formal meeting of the regulatory committee, since this possibility is provided for by the legislation. The rare cases requiring a formal vote during a meeting arose during the system's "running-in" period.

In view of the experience acquired and of the adoption of a new "comitology" Decision by the Council on 28 June 1999 (1999/468/EC)⁷, this decision-making procedure now needs to be re-assessed. It is also proposed that decision-making be subject to a consultation procedure under Decision 1999/468/EEC if the draft submitted by the Commission follows the Agency's scientific opinion or, in all other cases, to a management procedure under this Decision. In both cases, the deadlines are adapted in order to shorten the phase in which the Member States are consulted (*Article 34(2)*).

E. Inspection and surveillance

1. The overall quality of medicinal products is based both on the evaluation of the information submitted as part of the application for marketing authorisation and on the constant monitoring of the quality of the manufactured and marketed medicinal products to establish whether they comply with the data supplied. The monitoring of the quality of the manufacture and control of medicinal products must broadly take account of consumer protection, the completion of the internal market and the international dimension, in particular the agreements with non-member countries on mutual recognition. Quality guarantees are based mainly on a quality-assurance system which includes compliance with good manufacturing practice and on inspections by the competent authorities to ensure that all the legal requirements are complied with. The present Regulation covers medicinal products but is not specifically intended to apply to starting materials. It is therefore proposed that it be extended to cover active substances used as starting materials in the manufacture of medicinal products (*Article 111(1)*). Since the Member States adopt differing approaches, the harmonisation of the application of good manufacturing practice for these substances should be proposed. Detailed guidelines setting out appropriate practical provisions will be adopted. The same applies to the system for inspecting the manufacture of these active substances. Lastly, it is proposed that provision be made for issuing certificates of good manufacturing practice attesting compliance with the relevant requirements.
2. It is also necessary to reinforce the general provisions on inspection of medicinal products, if necessary in conjunction with the European Pharmacopoeia (*Article 111(1) and (5)*), and to increase Community coordination by introducing a Community information register on good manufacturing practice (*Article 111(6) and (7)*) and setting up a Community system of data on manufacturing authorisations

⁶ Within the meaning of Council Decision 87/373/EEC (OJ L 197, 18.7.1987, p. 33).

⁷ OJ L 184, 17.7.1999, p. 23.

(*Article 40(4)*)). It is proposed that the inspection system based on the recognition of inspections carried out by one of the Member States be supplemented by a procedure for settling disagreements between Member States on the results of an inspection (*Article 122*). It is also proposed that the possibility of inspecting pharmacovigilance sites and conducting inspections in non-member countries be added (*Article 111(4)*).

F. Pharmacovigilance

On the basis of the experience acquired, it is necessary to place greater emphasis on the need for a preventive approach with regard to pharmacovigilance. There has been considerable technical progress at both Community and international level. Exchanges of data between the Member States, marketing authorisation holders and the European Agency for the Evaluation of Medicinal Products are increasingly dependent on information technologies. There should be a rapid exchange of the data collected by all the partners. Following the agreement on the MedDRA, the use of this medical terminology, drawn up by ICH and officially launched in 1999, should be made compulsory in the interests of public health and to ensure that notifications of adverse reactions to medicinal products are consistent in a multilingual environment (*Article 106*). It is also important to ensure that the Member States' pharmacovigilance systems are harmonised and consistent so that all medicinal products authorised in the Community can be effectively monitored. In connection with the proposal to abolish the five-yearly renewal requirement, and to increase the efficacy of the system, it is proposed that the deadlines for the compulsory submission of periodic safety update reports be shortened (*Article 104*). It is also proposed that the Commission should, where urgent action is necessary, be able to request the Member States to adopt temporary measures with immediate effect (*Article 107*). Furthermore, it is proposed that the inspections regarding the obligations on marketing authorisation holders be reinforced (*Article 111*). Lastly, it is proposed that the coordination between Member States for the pharmacovigilance of medicinal products subject to the mutual recognition or decentralised procedure be improved (*Article 104(5)*).

G. Homeopathy (*Chapter 2*)

In order to create an additional stage in the harmonisation of this category of medicinal products, the proposal provides for the introduction of a limited mutual recognition procedure. Furthermore, in order to make it easier to place them on the market, invented names may be used, and it is proposed that the blanket prohibition of public advertising be removed (*Article 100*).

H. Packaging

The rules stipulate that the packaging of medicinal products must contain a package leaflet for patients. The order of the headings which must figure in this package leaflet is compulsory. On the basis of the experience acquired, it is necessary to adapt the rules and to propose an order of headings corresponding to patients' needs and habits (*Article 59*).

I. Information

In view of the spread of new information technologies and of growing consumer demand for information, it is proposed that, on an experimental basis, the possibilities of disseminating information on prescription-only medicinal products be extended. Public advertising is not currently authorised for prescription-only medicinal products. This provision has been interpreted as forbidding also all kind of information to the public, and only advertising and

information addressed to health professionals being possible. It is proposed that there should be public advertising of three classes of medicinal products. This type of information would be subject to the principles of good practice to be adopted by the Commission and to the drafting of a code of conduct by the industry. After five years of operation, an evaluation would be carried out in order to determine what action should be taken (*Article 88(2)*) in the wake of this trial.

IV. ADMINISTRATIVE AND LEGISLATIVE SIMPLIFICATION

The present proposal takes due account of the vast amount of work to consolidate the directives in the field of Community legislation on medicinal products for human use (*31 consolidated texts*). It also introduces provisions to rationalise and speed up the procedures relating to marketing authorisations for medicinal products for human use

V. CONSULTATIONS PRIOR TO THE DRAFTING OF THE PROPOSAL

The Commission has had an audit carried out by an external consultant, as stated in the explanatory memorandum. There have been several consultations, meetings and hearings with all the parties concerned. The Commission has also received numerous reports and discussion papers from these parties, particularly the Member States, patients' associations, European federations of the pharmaceutical industry, pharmacists and distributors. All these documents and their analysis have been taken up in the Commission report to the European Parliament and the Council on the operation of the abovementioned marketing authorisation procedures in the Community (COM).