

## I

*(Acts whose publication is obligatory)*

**REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL  
of 31 March 2004**

**laying down Community procedures for the authorisation and supervision of medicinal products  
for human and veterinary use and establishing a European Medicines Agency**

**(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 Commission <sup>(1)</sup>,

Having regard to the Opinion of the European Economic and Social Committee <sup>(2)</sup>,

After consulting the Committee of the Regions,

In accordance with the procedure laid down in Article 251 of the Treaty <sup>(3)</sup>,

Whereas:

(1) Article 71 of Council Regulation (EEC) 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 Products <sup>(4)</sup> provides 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 report 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. In addition, the name of that Agency should be simplified and changed to the European Medicines Agency, (hereinafter referred to as the 'Agency').

(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 6 November 2001 on the Community code relating to medicinal products for human use <sup>(5)</sup> and Directive 2001/82/EC of 6 November 2001 on the Community code relating to veterinary medicinal products <sup>(6)</sup>, all the references to the codified Directives in Regulation (EEC) No 2309/93 should be updated.

(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.

<sup>(1)</sup> OJ C 75 E, 26.3.2002, p. 189 and OJ C ... (not yet published in the Official Journal).

<sup>(2)</sup> OJ C 61, 14.3.2003, p. 1.

<sup>(3)</sup> Opinion of the European Parliament of 23 October 2002 (OJ C 300 E, 11.12.2003, p. 308), Council Common Position of 29 September 2003 (OJ C 297 E, 9.12.2003, p. 1), Position of the European Parliament of 17 December 2003 (not yet published in the Official Journal) and Council Decision of 11 March 2004.

<sup>(4)</sup> OJ L 214, 24.8.1993, p. 1. Regulation as last amended by Regulation (EC) No 1647/2003 (OJ L 245, 29.9.2003, p. 19).

<sup>(5)</sup> OJ L 311, 28.11.2001, p. 67. Directive as last amended by Council Directive 2004/27/EC (see p. 34 of this Official Journal).

<sup>(6)</sup> OJ L 311, 28.11.2001, p. 1. Directive as amended by Council Directive 2004/28/EC (see p. 58 of this Official Journal).

- (7) Experience gained since the adoption of Council Directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology<sup>(1)</sup> 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 orphan medicinal products and any medicinal product for human use containing an entirely new active substance, i.e. one that has not yet been authorised in the Community, and for which the therapeutic indication is the treatment of acquired immune deficiency syndrome, cancer, neurodegenerative disorder or diabetes. Four years after the date of entry into force of this Regulation, the procedure should also become compulsory for medicinal products for human use containing a new active substance, and for which the therapeutic indication is for the treatment of auto-immune diseases and other immune dysfunctions and viral diseases. It should be possible to review the provisions in point 3 of the Annex via a simplified decision-making procedure not earlier than four years after the entry into force of this Regulation.
- (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 therapeutically innovative. It is also appropriate to allow access to this procedure for medicinal products 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 can 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 achieved when the reference medicinal product was evaluated or the results of that evaluation.
- (10) In the field of veterinary medicinal products, administrative measures should be laid down in order to take account of the specific features of this field, particularly those due to the regional distribution of certain diseases. It should be possible to use the centralised procedure for the authorisation of veterinary medicinal products used within the framework of Community provisions regarding prophylactic measures for epizootic diseases. Optional access to the centralised procedure should be maintained for veterinary medicinal products containing a new active substance.
- (11) For medicinal products for human use, the period for protection of data relating to pre-clinical tests and clinical trials should be the same as that provided for in Directive 2001/83/EC. For medicinal products for veterinary use, the period for protection of data relating to pre-clinical tests and clinical trials as well as safety and residue tests should be the same as that provided for in Directive 2001/82/EC.
- (12) In order to reduce the cost for small and medium-sized enterprises of marketing medicinal products authorised via the centralised procedure, provisions should be adopted to allow for a reduction of fees, deferring the payment of fees, taking over responsibility for translations and offering administrative assistance in respect of these enterprises.
- (13) In the interest of public health, authorisation decisions under the centralised procedure should 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 in their territory of medicinal products for human use which infringe objectively defined concepts of public policy and public morality. Moreover, a veterinary medicinal product is not to be authorised by the Community if its use would contravene the rules laid down within the framework of the Common Agricultural Policy or if presented for a use prohibited under other Community provisions, inter alia Directive 96/22/EC<sup>(2)</sup>.
- (14) Provision should be made for the quality, safety and efficacy criteria in Directives 2001/83/EC and 2001/82/EC to apply to medicinal products authorised by the Community and it should be possible to assess the risk-benefit balance of all medicinal products when they are placed on the market, at the time of the renewal of the authorisation and at any other time the competent authority deems appropriate.

<sup>(1)</sup> OJ L 15, 17.1.1987, p. 38. Directive repealed by Directive 93/41/EEC (OJ L 214, 24.8.1993, p. 40).

<sup>(2)</sup> Council Directive 96/22/EC of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of  $\beta$ -agonists (OJ L 125, 23.5.1996, p. 3).

- (15) The Community is required, pursuant to Article 178 of the Treaty, to take account of the development policy aspects of any measure and to promote the creation of conditions fit for human beings worldwide. Pharmaceutical law should continue to ensure that only efficacious, safe and top-quality medicinal products are exported, and the Commission should consider creating further incentives to carry out research into medicinal products against widespread tropical diseases.
- (16) There is also a need to provide for the ethical requirements of Directive 2001/20/EC of 4 April 2001 of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use <sup>(1)</sup> to apply to medicinal products authorised by the Community. In particular, with respect to clinical trials conducted outside the Community on medicinal products destined to be authorised within the Community, at the time of the evaluation of the application for authorisation, it should be verified that these trials were conducted in accordance with the principles of good clinical practice and the ethical requirements equivalent to the provisions of the said Directive.
- (17) The Community should have the means to carry out a scientific assessment of the medicinal products presented in accordance with the decentralised 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 decentralised 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.
- (18) The structure and operation of the various 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 bodies, the need for adequate involvement of civil society, and the future enlargement of the European Union. The various bodies of the Agency should establish and develop appropriate contacts with the parties concerned, in particular representatives of patients and health-care professionals.
- (19) 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, and this should be done by means of a rapid procedure ensuring close cooperation between the Commission and Member States.
- (20) In order to ensure close cooperation between the Agency and scientists operating in Member States, the composition of the Management Board should be such 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.
- (21) The Agency's budget should be composed of fees paid by the private sector and contributions paid out of the Community budget to implement Community policies.
- (22) Paragraph 25 of the Interinstitutional Agreement of 6 May 1999 between the European Parliament, the Council and the Commission on budgetary discipline and improvement of budgetary procedure <sup>(2)</sup> provides for the Financial Perspective to be adjusted in order to cover the new needs resulting from enlargement.
- (23) 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 Medicinal Products for Veterinary Use. 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 1999 on orphan medicinal products <sup>(3)</sup>. 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.
- (24) 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.

<sup>(1)</sup> OJ L 121, 1.5.2001, p. 34.

<sup>(2)</sup> OJ C 172, 18.6.1999, p. 1.

<sup>(3)</sup> OJ L 18, 22.1.2000, p. 1.

- (25) 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, in particular small and medium-sized enterprises, 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 re-examination procedures should be amended to provide a better guarantee for applicants' rights.
- (26) 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 an efficient size after the enlargement of the European Union.
- (27) It is also necessary to reinforce the role of the Scientific Committees in such a way as to enable the Agency to participate actively in 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.
- (28) 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 event of failure to observe the provisions of this Regulation and the conditions contained in the authorisations granted under the procedures it establishes.
- (29) 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 a negative risk-benefit balance under normal conditions of use.
- (30) 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.
- (31) 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.
- (32) 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 harmonised to a considerable degree by Directives 2001/83/EC and 2001/82/EC. It is appropriate that the operation of the procedures laid down by this Regulation be re-examined by the Commission every ten years on the basis of experience gained.
- (33) 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.
- (34) Member States have developed an evaluation of the comparative efficacy of medicinal products aimed at positioning a new medicinal product with respect to those that already exist in the same therapeutic class. Similarly, the Council, in its Conclusions on medicinal products and public health<sup>(1)</sup>, adopted on 29 June 2000, emphasised the importance of identifying medicinal products that presented an added therapeutic value. However this evaluation should not be conducted in the context of the marketing authorisation, for which it is agreed that the fundamental criteria should be retained. It is useful in this respect to allow for the possibility of gathering information on the methods used by the Member States to determine the therapeutic benefit obtained by each new medicinal product.

(1) OJ C 218, 31.7.2000, p. 10.

- (35) 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 limited initially to a period of five years, upon the expiry of which it should be renewed. Thereafter the marketing authorisation should normally be of unlimited validity. Furthermore, any authorisation not used for three 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 of maintaining such authorisations. However, this rule should be subject to exemptions when these are justified on public health grounds.
- (36) 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<sup>(1)</sup>, to be conducted in parallel with the evaluation, under a single Community procedure, of the quality, safety and efficacy of the product concerned.
- (37) The measures necessary for the implementation of this Regulation should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission<sup>(2)</sup>.
- (38) The provisions of Regulation (EC) No 1647/2003<sup>(3)</sup> amending Regulation (EC) No 2309/93 as regards the budgetary and financial rules applicable to the Agency and access to the Agency's documents should be fully incorporated into this Regulation,
- 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 Medicines Agency (hereinafter referred to as 'the Agency').

The provisions of this Regulation shall not affect the powers of 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 medicinal products covered by this Regulation must be established in the Community. The holder shall be responsible for the placing on the market of those medicinal products, whether he does it himself or via one or more persons designated to that effect.

## Article 3

1. No medicinal product appearing in the Annex 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 the Annex may be granted a marketing authorisation by the Community in accordance with the provisions of this Regulation, if:

- (a) the medicinal product contains a new active substance which, on the date of entry into force of this Regulation, was not authorised in the Community; or
- (b) the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorisation in accordance with this Regulation is in the interests of patients or animal health at Community level.

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

<sup>(1)</sup> OJ L 106, 17.4.2001, p. 1. Directive as last amended by Regulation (EC) No 1830/2003 of the European Parliament and of the Council (OJ L 268, 18.10.2003, p. 24).

<sup>(2)</sup> OJ L 184, 17.7.1999, p. 23.

<sup>(3)</sup> OJ L 245, 29.9.2003, p. 19.

3. A generic medicinal product of a reference 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 product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the Community except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed; and
- (c) the generic medicinal product is authorised under the same name in all the Member States where the application has been made. For the purposes of this provision, all the linguistic versions of the INN (international non-proprietary name) shall be considered to be the same name.

4. After the competent committee of the Agency has been consulted, the Annex may be re-examined in the light of technical and scientific progress, with a view to making any necessary amendments without extending the scope of the centralised procedure. Such amendments shall be adopted in accordance with the procedure referred to in Article 87(2).

#### Article 4

1. Applications for the marketing authorisations referred to in Article 3 shall be submitted to the Agency.
2. The Community shall grant and supervise marketing authorisations for medicinal products for human use in accordance with Title II.
3. The Community shall grant and supervise marketing authorisations for veterinary medicinal products 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 Medicinal Products for Human Use is hereby established. The Committee shall be part of the Agency.
2. Without prejudice to Article 56 or to other tasks which Community law may confer on it, the Committee for Medicinal Products for Human Use shall be responsible for drawing up 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 revocation 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 Medicinal Products for Human Use shall also draw up an opinion on any scientific matter concerning the evaluation of medicinal products for human use. The Committee shall take due account of any requests by Member States for an opinion. The Committee shall also formulate an opinion whenever there is disagreement in the evaluation of medicinal products through the mutual recognition procedure. The opinion of the Committee shall be made publicly accessible.

#### Article 6

1. Each application for the authorisation of a medicinal product for human use shall specifically and completely include the particulars and documents as referred to in Articles 8(3), 10, 10a, 10b or 11 of, and Annex I to, Directive 2001/83/EC. The documents must include a statement to the effect that clinical trials carried out outside the European Union meet the ethical requirements of Directive 2001/20/EC. These particulars and documents shall take account of the unique, Community nature of the authorisation requested and, otherwise than in exceptional cases relating to the application of the law on trade marks, shall include 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 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 Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms <sup>(1)</sup>;

<sup>(1)</sup> OJ L 117, 8.5.1990, p. 15. Directive repealed by Directive 2001/18/EC, but continues to have certain legal effects.

- (b) the complete technical dossier supplying the information required by 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 medicinal products for human use containing or consisting of genetically modified organisms.

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

The duration of the analysis of the scientific data in the file concerning the application for marketing authorisation must be at least 80 days, except in cases where the rapporteur and co-rapporteur declare that they have completed their assessment before that time.

On the basis of a duly reasoned request, the said Committee may call for the duration of the analysis of the scientific data in the file concerning the application for marketing authorisation to be extended.

In the case of a medicinal product for human use containing or consisting of genetically modified organisms, the opinion of the said 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 rapporteur shall carry out necessary consultations of bodies that the Community or Member States have set up in accordance with Directive 2001/18/EC.

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

#### Article 7

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

- (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 granting a marketing authorisation are satisfied;

- (b) may request that an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose 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 request that the applicant supplement the particulars accompanying the application within a specific time period. Where the said Committee avails itself of this option, the time-limit laid down in Article 6(3), first subparagraph, 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 for the applicant to prepare oral or written explanations.

#### Article 8

1. Upon receipt of a written request from the Committee for Medicinal Products for Human Use, a Member State shall forward the information showing that the manufacturer of a medicinal product or the importer from a third 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 said Committee may require the applicant to undergo a specific inspection of the manufacturing site of the medicinal product concerned. Such inspections may be made unannounced.

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; they may be accompanied by a rapporteur or an expert appointed by the Committee.

#### Article 9

1. The Agency shall forthwith inform the applicant if the opinion of the Committee for Medicinal Products for Human Use 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 14(7) and (8).

2. Within 15 days after receipt of the opinion referred to in paragraph 1, the applicant may give written notice to the Agency that he wishes to request a re-examination of the opinion. In that case, the applicant shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

Within 60 days following receipt of the grounds for the request, the said Committee shall re-examine its opinion in accordance with the conditions laid down in the fourth subparagraph of Article 62(1). The reasons for the conclusion reached shall be annexed to the final opinion.

3. Within 15 days after its adoption, the Agency shall send the final opinion of the said Committee 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 granting 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, in accordance with the criteria laid down in Title VI of Directive 2001/83/EC;
- (c) details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product;
- (d) the draft text of the labelling and package leaflet proposed by the applicant, presented in accordance with Title V of Directive 2001/83/EC;
- (e) the assessment report.

#### Article 10

1. Within 15 days after 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.

Where a draft decision envisages the granting of a marketing authorisation, it shall include or make reference to the documents mentioned in Article 9(4)(a), (b), (c) and (d).

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 Member States and the applicant.

2. The Commission shall take a final decision in accordance with, and within 15 days after the end of, the procedure referred to in Article 87(3).

3. The Standing Committee on Medicinal Products for Human Use referred to in Article 87(1) shall adjust its rules of procedure so as to take account of the tasks incumbent upon it under this Regulation.

The adjustments shall provide that:

- (a) the opinion of the said Standing Committee is to be given in writing;
- (b) Member States shall have 22 days to forward their 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. This time-limit shall not, otherwise than in exceptional circumstances, be shorter than 5 days;
- (c) Member States may request in writing that the draft decision referred to in paragraph 1 be discussed by a plenary meeting of the said Standing Committee, stating their reasons in detail.

4. Where, in the opinion of the Commission, a Member State's written observations raise important new questions of a scientific or technical nature which the opinion delivered by the Agency has not addressed, 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 4 in accordance with the procedure referred to in Article 87(2).

6. The Agency shall disseminate the documents referred to in Article 9(4)(a), (b), (c) and (d).

#### Article 11

If an applicant withdraws an application for a marketing authorisation submitted to the Agency before an opinion has been given on the application, the applicant shall communicate its reasons for doing so to the Agency. The Agency shall make this information publicly accessible and shall publish the assessment report, if available, after deletion of all information of a commercially confidential nature.



#### Article 12

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

Authorisation shall likewise be refused if particulars or documents provided by the applicant in accordance with Article 6 are incorrect or if the labelling and package leaflet 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.

3. Information about all refusals and the reasons for them shall be made publicly accessible.

#### Article 13

1. Without prejudice to Article 4(4) of Directive 2001/83/EC, a marketing authorisation which has been granted 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 6 of Directive 2001/83/EC.

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 Union*, quoting in particular the date of authorisation and the registration number in the Community Register, any International Non-proprietary Name (INN) of the active substance of the medicinal product, its pharmaceutical form, and any Anatomical Therapeutic Chemical Code (ATC).

3. The Agency shall immediately publish the assessment report on the medicinal product for human use drawn up by the Committee for Medicinal Products for Human Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

The European Public Assessment Report (EPAR) shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

4. After a 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 notify the Agency if the product ceases to be placed on the market, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than 2 months before the interruption in the placing on the market of the product.

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 the medicinal product at Community level, broken down by Member State, and any data in the holder's possession relating to the volume of prescriptions.

#### Article 14

1. Without prejudice to paragraphs 4, 5 and 7 a marketing authorisation shall be valid for five years.

2. The marketing authorisation may be renewed after five years on the basis of a re-evaluation by the Agency of the risk-benefit balance.

To this end, the marketing authorisation holder shall provide the Agency with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, at least six months before the marketing authorisation ceases to be valid in accordance with paragraph 1.

3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal in accordance with paragraph 2.

4. Any authorisation which is not followed by the actual placing of the medicinal product for human use on the Community market within three years after authorisation shall cease to be valid.

5. When an authorised medicinal product previously placed on the market is no longer actually present on the market for three consecutive years, the authorisation shall cease to be valid.

6. In exceptional circumstances and on public health grounds the Commission may grant exemptions from paragraphs 4 and 5. Such exemptions must be duly justified.

7. Following consultation with the applicant, an authorisation may be granted subject to certain specific obligations, to be reviewed annually by the Agency. The list of these obligations shall be made publicly accessible.

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

The provisions for granting such authorisation shall be laid down in a Commission Regulation adopted in accordance with the procedure referred to in Article 87(2).

8. In exceptional circumstances and following consultation with the applicant, the authorisation may be granted subject to a requirement for the applicant to introduce specific procedures, in particular concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. This authorisation may be granted only for objective, verifiable reasons and must be based on one of the grounds set out in Annex I to Directive 2001/83/EC. Continuation of the authorisation shall be linked to the annual reassessment of these conditions.

9. When an application is submitted 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. The request shall be duly substantiated.

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

10. When adopting its opinion, the Committee for Medicinal Products for Human Use shall include a proposal concerning the criteria for the prescription or use of the medicinal products in accordance with Article 70(1) of Directive 2001/83/EC.

11. Without prejudice to the law on the protection of industrial and commercial property, medicinal products for human use which have been authorised in accordance with the provisions of this Regulation shall benefit from an eight-year period of data protection and a ten-year period of marketing protection, in which connection the latter period shall be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies.

#### Article 15

The granting of authorisation shall not affect the civil or criminal liability of the manufacturer or of the holder of the

marketing authorisation pursuant to the applicable national law in Member States.

## Chapter 2

### Supervision and penalties

#### Article 16

1. After an authorisation has been granted 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 Article 8(3)(d) and (h) of Directive 2001/83/EC, take account of technical and scientific progress and make any variations that may be required to enable the medicinal products to be manufactured and checked by means of generally accepted scientific methods. He shall apply for approval of such variations 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 variation of the particulars or documents referred to in Articles 8(3), 10, 10a, 10b and 11 of Directive 2001/83/EC, in Annex I thereto, or in Article 9(4) of this Regulation.

In particular, he 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 medicinal product for human use is marketed and of any other new information which might influence the evaluation of the benefits and risks of the medicinal product for human use concerned.

In order that the risk-benefit balance may be continuously assessed, the Agency may at any time ask the holder of the marketing authorisation to forward data demonstrating that the risk-benefit balance remains favourable.

3. If the holder of the authorisation for a medicinal product for human use proposes to make any variation of the particulars and documents referred to in paragraph 2, he shall submit the relevant application to the Agency.

4. The Commission shall, after consulting the Agency, adopt appropriate provisions for the examination of variations to marketing authorisations in the form of a regulation in accordance with the procedure referred to in Article 87(2).

#### Article 17

The applicant or the holder of a marketing authorisation shall be responsible for the accuracy of the documents and of the data submitted.

#### Article 18

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 granted the manufacturing authorisation provided for in Article 40(1) of Directive 2001/83/EC in respect of the medicinal product concerned.

2. In the case of medicinal products imported from third countries, the supervisory authorities shall be the competent authorities of the Member State or Member States that granted the authorisation provided for in Article 40(3) of Directive 2001/83/EC to the importer, unless appropriate agreements 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 19

1. The supervisory authorities shall be responsible 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 established within the Community satisfies the requirements laid down in Titles IV, IX and XI of Directive 2001/83/EC.

2. Where, in accordance with 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 or by two experts nominated by the Committee for Medicinal Products for Human Use.

3. Subject to any agreements which may have been concluded between the Community and third countries in accordance with Article 18(2), the Commission may, following a reasoned request from a Member State or from the said Committee, or on its own initiative, require a manufacturer established in a third country to submit to an inspection.

The inspection shall be undertaken by inspectors from the Member States who possess the appropriate qualifications; they may be accompanied by a rapporteur or expert

appointed by the said Committee. The report of the inspectors shall be made available to the Commission, the Member States and the said Committee.

#### Article 20

1. Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established within the Community territory is no longer fulfilling the obligations laid down in Title IV of Directive 2001/83/EC, they shall forthwith inform the Committee for Medicinal Products for Human Use 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 said Committee 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 procedure referred to in Article 87(3).

4. Where urgent action is essential to protect human health or the environment, a Member State may, on its own initiative or at the Commission's request, suspend the use in 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. In this case, the Member State shall ensure that health-care professionals are rapidly informed of its action and the reasons for the action. Networks set up by professional associations may be used to this effect. The Member States shall inform the Commission and the Agency of actions taken for this purpose.

6. 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 procedure referred to in Article 87(3).

7. The Agency shall, upon request, inform any person concerned of the final decision and make the decision publicly accessible immediately after it has been taken.

### Chapter 3

#### Pharmacovigilance

##### Article 21

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

##### Article 22

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 concerning suspected adverse reactions to medicinal products for human use which have been authorised by the Community in accordance with this Regulation. Where appropriate, the Committee for Medicinal Products for Human Use shall, in accordance with Article 5 of this Regulation, draw up opinions on the measures necessary. These opinions shall be made publicly accessible.

The measures referred to in the first paragraph may include amendments to the marketing authorisation granted in accordance with Article 10. They shall be adopted in accordance with the procedure referred to in Article 87(3).

The holder of the marketing authorisation and the competent authorities of Member States shall ensure that all relevant information concerning 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. Patients shall be encouraged to communicate any adverse reaction to health-care professionals.

##### Article 23

The holder of an authorisation for a medicinal product for human use 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 reside in the Community and shall be responsible for the following:

(a) establishing and managing a system which ensures that information concerning 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) preparing the reports referred to in Article 24(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 risks and benefits of a medicinal product is answered fully and promptly, including the provision of information regarding 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 24

1. The holder of the marketing authorisation for a medicinal product for human use shall ensure that all suspected serious adverse reactions to a medicinal product authorised in accordance with this Regulation occurring within the Community which a health-care professional brings to his attention are recorded and reported promptly to Member States within the territory of which the incident occurred, and no later than 15 days following the receipt of the information.

The holder of the marketing authorisation shall record any other suspected serious adverse reactions occurring within the Community, in accordance with the guide referred to in Article 26, of which he may reasonably be expected to be aware, and promptly notify the competent authority of Member States in the territory of which the incident occurred and the Agency, and no later than 15 days following receipt of the information.

2. The holder of the marketing authorisation for a medicinal product for human use shall ensure that all suspected serious unexpected adverse reactions and any suspected transmission via a medicinal product of any infectious agent occurring in the territory of a third country are reported promptly to Member States and the Agency, and no later than 15 days following receipt of the information. The provisions for the reporting of suspected unexpected adverse reactions which are not serious, whether occurring in the Community or in a third country, shall be adopted in accordance with the procedure referred to in Article 87(2).

Save in exceptional circumstances, these reactions shall be transmitted electronically in the form of a report and in accordance with the guide referred to in Article 26.

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

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

These reports shall be accompanied by a scientific evaluation, particularly of the risk-benefit balance of the medicinal product.

4. The Commission may lay down provisions to amend paragraph 3 in view of experience gained with its operation. The Commission shall adopt any such provisions in accordance with the procedure referred to in Article 87(2).

5. The holder of a marketing authorisation may not communicate information relating to pharmacovigilance concerns to the general public in relation to its authorised medicinal product without giving prior or simultaneous notification to the Agency.

In any case, the marketing authorisation holder shall ensure that such information is presented objectively and is not misleading.

Member States shall take the necessary measures to ensure that a marketing authorisation holder who fails to discharge these obligations is subject to effective, proportionate and dissuasive penalties.

#### Article 25

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 this Regulation which are brought to their attention are recorded and reported promptly to the Agency and the marketing authorisation holder, and no later than 15 days following receipt of the information.

The Agency shall forward the information to the national pharmacovigilance systems set up in accordance with Article 102 of Directive 2001/83/EC.

#### Article 26

The Commission, in consultation with the Agency, Member States and interested parties, shall draw up a guide on the collection, verification and presentation of adverse-reaction reports. This guide shall contain, in particular, for the benefit of health-care professionals, recommendations concerning the communication of information on adverse reactions.

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

The Agency, in consultation with Member States and the Commission, shall set up a data-processing network for the rapid transmission of information to 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. Such data shall be made publicly accessible, if relevant, after evaluation.

For a period of five years following the initial placing on the market in the Community, the Agency may request that the marketing authorisation holder arrange for specific pharmacovigilance data to be collected from targeted groups of patients. The Agency shall state the reasons for the request. The marketing authorisation holder shall collate and assess the data collected and submit it to the Agency for evaluation.

#### Article 27

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 third countries; it shall send a copy thereof to the Commission and the Member States.

#### Article 28

The Agency and Member States' competent authorities shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of routes of authorisation, including the use of collaborative approaches, to maximise use of resources available within the Community.

#### Article 29

Any amendment which may be necessary to update the provisions of this Chapter in order to take account of scientific and technical progress shall be adopted in accordance with the procedure referred to in Article 87(2).

## TITLE III

## AUTHORISATION AND SUPERVISION OF VETERINARY MEDICINAL PRODUCTS

## Chapter 1

**Submission and examination of applications —  
Authorisations***Article 30*

1. A Committee for Medicinal Products for Veterinary Use is hereby established. The Committee shall be part of the Agency.

2. Without prejudice to Article 56 and other tasks which Community law may confer on it, in particular under Regulation (EEC) No 2377/90<sup>(1)</sup>, the Committee for Medicinal Products for Veterinary Use shall be responsible for drawing up the opinion of the Agency on any question concerning the admissibility of files submitted in accordance with the centralised procedure, the granting, variation, suspension or revocation 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 Medicinal Products for Veterinary Use shall also draw up opinions on any scientific matters concerning the evaluation of veterinary medicinal products. The Committee shall take due account of any requests from Member States for an opinion. The Committee shall also formulate an opinion whenever there is disagreement in the assessment of a veterinary medicinal product through the mutual recognition procedure. The opinion of the Committee shall be made publicly accessible.

*Article 31*

1. Each application for the authorisation of a medicinal product for veterinary use shall specifically and exhaustively include the particulars and documents as referred to in Articles 12(3), 13, 13a, 13b and 14 of, and Annex I to, Directive 2001/82/EC. These particulars and documents shall take account of the unique, Community nature of the authorisation requested and, otherwise than in exceptional cases relating to the application of the law on trade marks, shall include 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 the written consent of the competent authorities to the deliberate release into the environment of the genetically modified organisms for research and development purposes, as 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 required under 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 Medicinal Products for Veterinary Use is given within 210 days after 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 said Committee must 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, Member States and interested parties, draw up a detailed guide regarding the form in which applications for authorisation are to be presented.

*Article 32*

1. In order to prepare its opinion, the Committee for Medicinal Products for Veterinary Use:

- (a) shall verify that the particulars and documents submitted in accordance with Article 31 comply with the requirements of Directive 2001/82/EC and examine whether the conditions specified in this Regulation for granting a marketing authorisation are satisfied;

<sup>(1)</sup> Council Regulation (EEC) No 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin (OJ L 224, 18.8.1990, p. 1). Regulation as last amended by Commission Regulation (EC) No 1029/2003 (OJ L 149, 17.6.2003, p. 15).

(b) may request that an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose test the veterinary medicinal product, its starting materials and, where appropriate, 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, Official Medicines Control Laboratory or laboratory that a Member State has designated for that purpose to verify, using samples provided by the applicant, that the analytical detection method proposed by the applicant for the purposes of Article 12(3)(j), second indent, 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 said Committee avails itself of this option, the time-limit laid down in Article 31(3), first subparagraph 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 under the procedures established by Regulation (EEC) No 2377/90, the verification shall be carried out within the framework of this Article.

#### Article 33

1. Upon receipt of a written request from the Committee for Medicinal Products for Veterinary Use, a Member State shall forward the information establishing that the manufacturer of a veterinary medicinal product or the importer from a third 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 31.

2. Where it considers it necessary in order to complete its examination of the application, the said Committee may require the applicant to undergo a specific inspection of the manufacturing site of the veterinary medicinal product concerned. Such inspections may be made unannounced.

The inspection, which shall be completed within the time-limit referred to in Article 31(3), first subparagraph, shall be undertaken by inspectors from the Member State who possess the appropriate qualifications; they may be accompanied by a rapporteur or expert appointed by the said Committee.

#### Article 34

1. The Agency shall forthwith inform the applicant if the opinion of the Committee for Medicinal Products for Veterinary Use 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 39(7).

2. Within 15 days after receipt of the opinion referred to in paragraph 1, the applicant may provide written notice to the Agency that he wishes to request a re-examination of the opinion. In that case the applicant shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

Within 60 days after receipt of the grounds for the request, the said Committee shall re-examine its opinion in accordance with the conditions laid down in Article 62(1), fourth subparagraph. The reasons for the conclusion reached shall be annexed to the final opinion.

3. Within 15 days after its adoption, the Agency shall forward the final opinion of the said Committee to the Commission, to 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. If an opinion is favourable to the granting of 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 appropriate, this draft shall reflect differences in the veterinary conditions in the Member States;
- (b) in 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) details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product;
- (e) the draft text of the labelling and package leaflet proposed by the applicant, presented in accordance with Title V of Directive 2001/82/EC;
- (f) the assessment report.

#### Article 35

1. Within 15 days after receipt of the opinion referred to in Article 30(2), the Commission shall prepare a draft of the decision to be taken in respect of the application.

Where a draft decision envisages the granting of marketing authorisation, it shall include or make reference to the documents mentioned in Article 34(4)(a) to (e).

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 Member States and the applicant.

2. The Commission shall take a final decision in accordance with, and within 15 days after the end of, the procedure referred to in Article 87(3).

3. The Standing Committee for Veterinary Medicinal Products referred to in Article 87(1) shall adjust its rules of procedure so as to take account of the tasks assigned to it by this Regulation.

The adjustments shall provide that:

- (a) the opinion of the said Standing Committee is to be given in writing;
- (b) Member States shall have 22 days to forward their 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. This time-limit shall not, otherwise than in exceptional circumstances, be shorter than 5 days;

(c) Member States may request in writing that the draft decision referred to in paragraph 1 be discussed at a plenary meeting of the said Standing Committee, stating their 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 delivered by 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 4 shall be adopted by the Commission in accordance with the procedure referred to in Article 87(2).

6. The Agency shall disseminate the documents referred to in Article 34(4) (a) to (e).

#### Article 36

If an applicant withdraws an application for a marketing authorisation submitted to the Agency before an opinion has been given on the application, the applicant shall communicate its reasons for doing so to the Agency. The Agency shall make this information publicly accessible and shall publish the assessment report, if available, after deletion of all information of a commercially confidential nature.

#### Article 37

1. The marketing authorisation shall be refused if, after verification of the particulars and documents submitted in accordance with Article 31, it appears that:

- (a) the applicant has not properly or sufficiently demonstrated the quality, safety or efficacy of the veterinary medicinal product;
- (b) in the case of zootechnical veterinary medicinal products and performance enhancers, when the safety and welfare of the animals and/or consumer safety have not been sufficiently taken into account;
- (c) the withdrawal period 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 particulars or documents provided by the applicant in accordance with Article 31 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.

3. Information about all refusals and the reasons for them shall be made publicly accessible.

#### Article 38

1. Without prejudice to Article 71 of Directive 2001/82/EC, a marketing authorisation which has been granted 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.

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 Union*, quoting in particular the date of authorisation and the number in the Community Register, any International Non-proprietary Name (INN) of the active substance of the medicinal product, its pharmaceutical form, and any Anatomical Therapeutic Chemical Veterinary Code (ATC Vet Code).

3. The Agency shall immediately publish the assessment report on the veterinary medicinal product drawn up by the Committee for Medicinal Products for Veterinary Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

The European Public Assessment Report (EPAR) shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

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

The holder shall also notify the Agency if the product ceases to be placed on the market, either temporarily or permanently. Such notification shall, other than in exceptional circumstances, be made no less than 2 months before the interruption in the placing of the product on the market.

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 the medicinal product at Community level, broken down by Member State, and any data in the holder's possession relating to the volume of prescriptions.

#### Article 39

1. Without prejudice to paragraphs 4 and 5, a marketing authorisation shall be valid for five years.

2. The marketing authorisation may be renewed after five years on the basis of a re-evaluation by the Agency of the risk-benefit balance.

To this end, the marketing authorisation holder shall submit a consolidated list of all documents submitted in respect of quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, at least six months before the marketing authorisation ceases to be valid in accordance with paragraph 1. The Agency may require the applicant to submit the listed documents at any time.

3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal in accordance with paragraph 2.

4. Any authorisation which is not followed by the actual placing of the medicinal product for veterinary use on the Community market within three years after authorisation shall cease to be valid.

5. When an authorised medicinal product previously placed on the market is no longer actually present on the market for three consecutive years, the authorisation shall cease to be valid.

6. In exceptional circumstances and on public and/or animal health grounds the Commission may grant exemptions from the provisions of paragraphs 4 and 5. Such exemptions must be duly justified.

7. In exceptional circumstances and following consultation with the applicant, authorisation may be granted subject to a requirement for the applicant to introduce specific procedures, in particular concerning product safety, notification to the relevant authorities of any incident relating to its use, and action to be taken. This authorisation may be granted only for objective, verifiable reasons. Continuation of the authorisation shall be linked to the annual reassessment of these conditions.

8. When an application is submitted 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. The request shall be duly substantiated.

If the Committee for Medicinal Products for Veterinary Use accepts the request, the time-limit laid down in Article 31(3), first subparagraph, shall be reduced to 150 days.

9. When adopting its opinion, the said Committee shall include a proposal concerning the conditions for the prescription or use of the veterinary medicinal products.

10. Veterinary medicinal products which have been authorised in accordance with the provisions of this Regulation shall benefit from the provisions on protection in Articles 13 and 13a of Directive 2001/82/EC.

#### Article 40

The granting of authorisation shall not affect the civil or criminal liability of the manufacturer or the holder of the marketing authorisation pursuant to the applicable national law in Member States.

### Chapter 2

#### Supervision and sanctions

##### Article 41

1. After an authorisation has been granted in accordance with this Regulation, the holder of the marketing authorisation shall, in respect of the methods of manufacture and control provided for in Article 12(3)(d) and (i) of Directive 2001/82/EC, take account of technical and scientific progress and make any variations that may be required to enable the medicinal products to be manufactured and checked by means of generally accepted scientific methods. He shall apply for approval of these variations in accordance with this Regulation.

2. The competent authority of a Member State or the Agency may require the holder of the marketing authorisation 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 technical expertise to facilitate the implemen-

tation of the analytical method for detecting residues of veterinary medicinal products by the Community reference laboratory or, where appropriate, national reference laboratories designated in accordance with Council Directive 96/23/EC of 29 April 1996 on measures to monitor certain substances and residues thereof in live animals and animal products<sup>(1)</sup>.

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 variation of the particulars or documents referred to in Articles 12(3), 13, 13a, 13b and 14 of Directive 2001/82/EC, in Annex I thereto, or in Article 34(4) of this Regulation.

He 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.

In order that the risk-benefit balance may be continuously assessed, the Agency may at any time ask the holder of the marketing authorisation to forward data justifying that the risk-benefit balance remains favourable.

5. If the holder of the marketing authorisation for the veterinary medicinal product proposes to make any variation of the particulars and documents referred to in paragraph 4, he shall submit the relevant application to the Agency.

6. The Commission shall, after consulting the Agency, adopt appropriate provisions for the examination of variations to marketing authorisations in the form of a regulation in accordance with the procedure referred to in Article 87(2).

##### Article 42

The applicant or the holder of a marketing authorisation shall be responsible for the accuracy of the documents and of the data submitted.

##### Article 43

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 granted the manufacturing authorisation provided for in Article 44(1) of Directive 2001/82/EC in respect of the manufacture of the medicinal product concerned.

<sup>(1)</sup> OJ L 125, 23.5.1996, p. 10. Directive as amended by Regulation (EC) No 806/2003 (OJ L 122, 16.5.2003, p. 1).

2. In the case of veterinary medicinal products imported from third countries, the supervisory authorities shall be the competent authorities of the Member State or Member States that granted the authorisation provided for in Article 44(3) of Directive 2001/82/EC to the importer, unless appropriate agreements 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 44

1. The supervisory authorities shall be responsible 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 within the Community satisfies the requirements laid down in Titles IV, VII and VIII of Directive 2001/82/EC.

2. Where, in accordance with 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 holder of the marketing authorisation, 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 Medicinal Products for Veterinary Use.

3. Subject to any agreements which may have been concluded between the Community and third countries in accordance with Article 43(2), the Commission may, upon receipt of a reasoned request from a Member State or from the said Committee, or on its own initiative, require a manufacturer established in a third country to submit to an inspection.

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

#### Article 45

1. Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established within the Community is

no longer fulfilling the obligations laid down in Title VII of Directive 2001/82/EC, they shall forthwith inform the Committee for Medicinal Products for Veterinary Use 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 said Committee has delivered an opinion to that effect in accordance with Article 30 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 marketing authorisation for the medicinal product 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 procedure referred to in Article 87(3).

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, the Member State 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. In this case, the Member State shall ensure that health-care professionals are rapidly informed of its action and the reasons for the action. Networks set up by professional associations may be used to this effect. Member States shall inform the Commission and the Agency of actions taken for this purpose.

6. 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 procedure referred to in Article 87(3).

7. The Agency shall, upon request, inform any person concerned of the final decision and make the decision publicly accessible, immediately after it has been taken.

### Chapter 3

#### Pharmacovigilance

##### Article 46

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

##### Article 47

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. Where appropriate the Committee for Medicinal Products for Veterinary Use shall, in accordance with Article 30 of this Regulation, draw up opinions on the measures necessary. These opinions shall be made publicly accessible.

These measures may include amendments to the marketing authorisation granted in accordance with Article 35. They shall be adopted in accordance with the procedure referred to in Article 87(3).

The holder of the marketing authorisation and the competent authorities of the Member States shall ensure all relevant information about suspected adverse reactions to the veterinary medicinal products authorised under this Regulation is brought to the attention of the Agency in accordance with the provisions of this Regulation. Animal owners and breeders shall be encouraged to communicate any adverse reaction to health-care professionals or to the competent national authorities responsible for pharmacovigilance.

##### Article 48

The holder of the marketing authorisation for a veterinary medicinal product 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 reside in the Community and shall be responsible for the following:

- (a) establishing and managing 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) preparing the reports referred to in Article 49(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 risks and benefits 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-authorisation safety studies, including information regarding the validity of the withdrawal period or lack of expected efficacy or potential environmental problems.

##### Article 49

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

The holder of the marketing authorisation shall record any other suspected serious adverse reactions and human adverse reactions occurring within the Community, in accordance with the guidelines referred to in Article 51, of which he may reasonably be expected to be aware, and promptly notify Member States in the territory of which the incident occurred and the Agency, and no later than 15 days following receipt of the information.

2. The holder of the marketing authorisation for a veterinary medicinal product shall ensure that all suspected serious unexpected adverse reactions, and adverse human reactions, and any suspected transmission via a medicinal product of any infectious agent occurring in the territory of a third country are reported promptly to the Member States and the Agency, and no later than 15 days following receipt of the information. The provisions for the reporting of suspected unexpected adverse reactions which are not serious, whether occurring in the Community or in a third country, shall be adopted in accordance with the procedure referred to in Article 87(2).

Save in exceptional circumstances, these reactions shall be transmitted electronically in the form of a report and in accordance with the guide referred to in Article 51.

3. The holder of the marketing authorisation for a veterinary medicinal product shall maintain detailed records of all suspected adverse reactions occurring within or outside the Community which are reported to him.

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

These reports shall be accompanied by a scientific evaluation, particularly of the risk-benefit balance of the medicinal product.

4. The Commission may lay down provisions to amend paragraph 3 in view of experience gained with its operation. The Commission shall adopt any such provisions in accordance with the procedure referred to in Article 87(2).

5. The holder of a marketing authorisation may not communicate information relating to pharmacovigilance concerns to the general public in relation to its authorised medicinal product without giving prior or simultaneous notification to the Agency.

In any case, the marketing authorisation holder shall ensure that such information is presented objectively and is not misleading.

Member States shall take the necessary measures to ensure that a marketing authorisation holder who fails to discharge these obligations is subject to effective, proportionate and dissuasive penalties.

#### Article 50

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 promptly to the Agency and the holder of the marketing authorisation for the veterinary medicinal product, and no later than 15 days following 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 51

The Commission, in consultation with the Agency, Member States and interested parties, shall draw up a guide on the collection, verification and presentation of adverse-reaction reports. This guide shall contain, in particular, for the benefit of health-care professionals, recommendations concerning the communication of information on adverse reactions.

In accordance with this guide, holders of marketing authorisations 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.

For a period of five years following the initial placing on the market in the Community, the Agency may request that the marketing authorisation holder arrange for specific pharmacovigilance data to be collected from targeted groups of animals. The Agency shall state the reasons for the request. The marketing authorisation holder shall collate and assess the data collected and submit it to the Agency for evaluation.

#### Article 52

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

#### Article 53

The Agency and the Member States' competent authorities shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of routes of authorisation, including the use of collaborative approaches, to maximise use of resources available within the Community.

#### Article 54

Any amendment which may be necessary to update the provisions of this Chapter in order to take account of scientific and technical progress shall be adopted in accordance with the procedure referred to in Article 87(2).

## TITLE IV

## THE EUROPEAN MEDICINES AGENCY — RESPONSIBILITIES AND ADMINISTRATIVE STRUCTURE

## Chapter 1

## Tasks of the Agency

## Article 55

A European Medicines Agency is hereby established.

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

## Article 56

1. The Agency shall comprise:

- (a) the Committee for Medicinal Products for Human Use, 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 Medicinal Products for Veterinary Use, 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, scientific 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 64;
- (g) a Management Board, which shall exercise the responsibilities set out in Articles 65, 66 and 67.

2. The committees referred to in paragraph 1(a) to (d) may each establish standing and temporary working parties. The committees referred to in paragraph 1(a) and (b) may establish scientific advisory groups in connection with the evaluation of specific types of medicinal products or treatments, to which the committee concerned may delegate certain tasks associated with drawing up the scientific opinions referred to in Articles 5 and 30.

When establishing working parties and scientific advisory groups, the committees shall in their rules of procedures referred to in Article 61(8) provide for:

(a) the appointment of members of these working parties and scientific advisory groups on the basis of the lists of experts referred to in the second subparagraph of Article 62(2); and

(b) consultation of these working parties and scientific advisory groups.

3. The Executive Director, in close consultation with the Committee for Medicinal Products for Human Use and the Committee for Medicinal Products for Veterinary Use, shall set up the administrative structures and procedures allowing the development of advice for undertakings, as referred to in Article 57(1)(n), particularly regarding the development of new therapies.

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

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

## Article 57

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, safety and 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) 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 publicly available assessment reports, summaries of product characteristics, labels and package leaflets or inserts for these medicinal products;
- (c) 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 such implementation;

- (d) ensuring 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; health-care professionals, marketing authorisation holders and the public shall have appropriate levels of access to these databases, with personal data protection being guaranteed;
- (e) assisting Member States with the rapid communication of information concerning pharmacovigilance to health-care professionals.
- (f) distributing appropriate pharmacovigilance information to the general public;
- (g) 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;
- (h) providing scientific advice on the use of antibiotics in food-producing animals in order to minimise the occurrence of bacterial resistance in the Community; this advice shall be updated when needed;
- (i) coordinating the verification of compliance with the principles of good manufacturing practice, good laboratory practice, good clinical practice and the verification of compliance with pharmacovigilance obligations;
- (j) upon request, providing technical and scientific support in order to improve cooperation between the Community, its Member States, international organisations and third 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;
- (k) recording the status of marketing authorisations for medicinal products granted in accordance with Community procedures;
- (l) creating a database on medicinal products, to be accessible to the general public, and ensuring that it is updated, and managed independently of pharmaceutical companies; the database shall facilitate the search for information already authorised for package leaflets; it shall include a section on medicinal products authorised for the treatment of children; the information provided to the public shall be worded in an appropriate and comprehensible manner;
- (m) 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;
- (n) advising undertakings on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products;
- (o) 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;
- (p) 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;
- (q) with a view to the protection of public health, compilation of scientific information concerning pathogenic agents which might be used in biological warfare, including the existence of vaccines and other medicinal products available to prevent, or to treat, the effects of such agents;
- (r) coordination of the supervision of the quality of medicinal products placed on the market by requesting testing of compliance with their authorised specifications by an Official Medicines Control Laboratory or by a laboratory that a Member State has designated for that purpose;
- (s) forwarding annually to the budgetary authority any information relevant to the outcome of the evaluation procedures.
2. The database provided for in paragraph 1(l) 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 Chapter 4 of Title III of Directive 2001/83/EC and of Directive 2001/82/EC respectively. The database shall subsequently be extended to include any medicinal product placed on the market within the Community.
- Where appropriate, the database shall also include references to data on clinical trials currently being carried out or already completed, contained in the clinical trials database provided for in Article 11 of Directive 2001/20/EC. The Commission shall, in consultation with the Member States, issue guidelines on data fields which could be included and which may be accessible to the public.

*Article 58*

1. The Agency may give a scientific opinion, in the context of cooperation with the World Health Organisation, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the Community. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with Articles 6 to 9. The provisions of Article 10 shall not apply.

2. The said Committee shall establish specific procedural rules for the implementation of paragraph 1, as well as for the provision of scientific advice.

*Article 59*

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 potentially conflict.

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 resolve the conflict or to submit a joint document to the Commission clarifying the scientific points of conflict. This document shall be published immediately after its adoption.

4. Save as otherwise provided 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 resolve the conflict or to prepare a joint document clarifying the scientific points of conflict. This document shall be published immediately after its adoption.

*Article 60*

At the request of the Commission, the Agency shall, in respect of authorised medicinal products, collect any available information on methods that Member States' competent authorities use to determine the added therapeutic value that any new medicinal product provides.

*Article 61*

1. Each Member State shall, after consultation of the Management Board, appoint, for a three-year term which may be renewed, one member and one alternate to the Committee for Medicinal Products for Human Use and one member and one alternate to the Committee for Medicinal Products for Veterinary Use.

The alternates shall represent and vote for the members in their absence and may act as rapporteurs in accordance with Article 62.

Members and alternates shall be chosen for their role and experience in the evaluation of medicinal products for human and veterinary use as appropriate and shall represent the competent national authorities.

2. The committees may co-opt 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 may be renewed, and shall not have alternates.

With a view to the co-opting of such members, the committees shall identify the specific complementary scientific competence of the additional member(s). Co-opted members shall be chosen among experts nominated by Member States or the Agency.

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

4. The Executive Director of the Agency or his representative and representatives of the Commission shall be entitled to attend all meetings of the committees, working parties and scientific advisory groups and all other meetings convened by the Agency or its committees.

5. 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.

6. Members of the committees and experts responsible for evaluating medicinal products shall rely on the scientific evaluation and resources available to 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 nominated committee members and experts. Member States shall refrain from giving committee members and experts any instruction which is incompatible with their own individual tasks or with the tasks and responsibilities of the Agency.



7. 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 divergent positions, with the grounds on which they are based.

8. Each committee shall establish its own rules of procedure.

These rules shall, in particular, lay down:

- (a) procedures for appointing and replacing the Chairman;
- (b) procedures relating to working parties and scientific advisory groups; and
- (c) a procedure for the urgent adoption of opinions, particularly in relation to the provisions of this Regulation on market surveillance and pharmacovigilance.

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

#### Article 62

1. Where, in accordance with the provisions of this Regulation, the Committee for Medicinal Products for Human Use, the Committee on Herbal Medicinal Products or the Committee for Medicinal Products for Veterinary Use 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.

When consulting the scientific advisory groups referred to in Article 56(2), the Committee shall forward to them the draft assessment report(s) drawn up by the rapporteur or the co-rapporteur. The opinion issued by the scientific advisory group shall be forwarded to the chairman of the relevant Committee in such a way as to ensure that the deadlines laid down in Article 6(3) and Article 31(3) are met.

The substance of the opinion shall be included in the assessment report published pursuant to Article 13(3) and Article 38(3).

If there is a request for re-examination of 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. The re-examination

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 when the Committee adopted the initial opinion. The applicant may request that the Committee consult a scientific advisory group in connection with the re-examination.

2. Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products who would be available to serve on working parties or scientific advisory groups of the Committee for Medicinal Products for Human Use, the Committee on Herbal Medicinal Products or the Committee for Medicinal Products for Veterinary Use, 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 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 tasks of the Agency, in particular to ensure 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 Article 56(1) may use the services of experts for the discharge of other specific tasks for which they are responsible.

#### Article 63

1. The membership of the committees referred to in Article 56(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 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, and shall make an annual declaration of their financial interests. All indirect interests which could relate to this industry shall be entered in a register held by the Agency which is accessible to the public, on request, at the Agency's offices.

The Agency's code of conduct shall provide for the implementation of this Article with particular reference to the acceptance of gifts.

Members of the Management 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 items on the agenda. These declarations shall be made available to the public.

#### Article 64

1. The Executive Director shall be appointed by the Management Board, on a proposal from the Commission, for a period of five years on the basis of a list of candidates proposed by the Commission following a call for expressions of interest published in the *Official Journal of the European Union* and elsewhere. Before appointment, the candidate nominated by the Management Board shall be invited forthwith to make a statement to the European Parliament and to answer any questions put by its Members. His mandate may be renewed once. The Management Board may, upon a proposal from the Commission, remove the Executive Director from his post.

2. The Executive Director shall be the legal representative of the Agency. He 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 Article 56(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 Article 56(1);
- (e) for the preparation of the draft statement of estimates of the Agency's revenue and expenditure, and execution of its budget;

(f) for all staff matters;

(g) for providing the secretariat for the Management Board.

3. Each year the Executive Director shall submit a draft report covering the activities of the Agency in the previous year and a draft work programme for the coming year to the Management Board for approval, making a distinction between the Agency's activities concerning medicinal products for human use, those concerning herbal medicinal products and those concerning veterinary medicinal products.

The draft report covering the activities of the Agency in the previous year shall include 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.

#### Article 65

1. The Management Board shall consist of one representative of each Member State, two representatives of the Commission and two representatives of the European Parliament.

In addition, two representatives of patients' organisations, one representative of doctors' organisations and one representative of veterinarians' organisations shall be appointed by the Council in consultation with the European Parliament on the basis of a list drawn up by the Commission which includes appreciably more names than there are posts to be filled. The list drawn up by the Commission shall be forwarded to the European Parliament, together with the relevant background documents. As quickly as possible, and within three months of notification, the European Parliament may submit its views for consideration to the Council, which shall then appoint the Management Board.

The members of the Management Board shall be appointed in such a way as to guarantee the highest levels of specialist qualifications, a broad spectrum of relevant expertise and the broadest possible geographic spread within the European Union.

2. The members of the Management Board shall be appointed on the basis of their relevant expertise in management and, if appropriate, experience in the field of medicinal products for human or veterinary use.

3. Each Member State and the Commission shall appoint their members of the Management Board as well as an alternate who will replace the member in his absence and vote on his behalf.

4. The term of office of the representatives shall be three years. The term of office may be renewed.

5. The Management Board shall elect its Chairman from among its members.

The term of office of the Chairman shall be three years and shall expire when he ceases to be a member of the Management Board. The term of office may be renewed once.

6. Decisions of the Management Board shall be adopted by a majority of two-thirds of its members.

7. The Management Board shall adopt its rules of procedure.

8. The Management Board may invite the chairmen of the scientific committees to attend its meetings, but they shall not have the right to vote.

9. The Management Board shall approve the annual work programme of the Agency programme and forward it to the European Parliament, the Council, the Commission and the Member States.

10. The Management Board shall adopt the annual report on the Agency's activities and forward it by 15 June at the latest to the European Parliament, the Council, the Commission, the European Economic and Social Committee, the Court of Auditors and the Member States.

#### Article 66

The Management Board shall:

- (a) adopt an opinion on the rules of procedures of the Committee for Medicinal Products for Human Use and the Committee for Medicinal Products for Veterinary Use (Article 61);
- (b) adopt procedures for the performance of scientific services (Article 62);
- (c) appoint the Executive Director (Article 64);
- (d) adopt the annual work programme and forward it to the European Parliament, the Council, the Commission and the Member States (Article 65);
- (e) approve the annual report on the Agency's activities and forward it by 15 June at the latest to the European Parliament, the Council, the Commission, the European Economic and Social Committee, the Court of Auditors and the Member States (Article 65);
- (f) adopt the budget of the Agency (Article 67);

(g) adopt the internal financial provisions (Article 67);

(h) adopt provisions implementing the Staff Regulations (Article 75);

(i) develop contacts with stakeholders and stipulate the conditions applicable (Article 78);

(j) adopt provisions for providing assistance to pharmaceutical companies (Article 79);

(k) adopt rules to ensure the availability to the public of information concerning the authorisation or supervision of medicinal products (Article 80).

## Chapter 2

### Financial Provisions

#### Article 67

1. Estimates of all the revenue and expenditure of the Agency shall be prepared for each financial year, corresponding to the calendar year, and shall be shown in the budget of the Agency.

2. The revenue and expenditure shown in the budget shall be in balance.

3. The Agency's revenue shall consist of a contribution from the Community and fees paid by undertakings for obtaining and maintaining Community marketing authorisations and for other services provided by the Agency.

The European Parliament and the Council (hereinafter referred to as 'the budgetary authority') shall re-examine, when necessary, the level of the Community contribution on the basis of an evaluation of needs and taking account of the level of fees.

4. Activities relating to pharmacovigilance, to the operation of communications networks and to market surveillance shall receive adequate public funding commensurate with the tasks conferred.

5. The expenditure of the Agency shall include staff remuneration, administrative and infrastructure costs, and operating expenses as well as expenses resulting from contracts entered into with third parties.

6. Each year the Management Board, on the basis of a draft drawn up by the Executive Director, shall produce an estimate of revenue and expenditure for the Agency for the following financial year. This estimate, which shall include a draft establishment plan, shall be forwarded by the Management Board to the Commission by 31 March at the latest.

7. The estimate shall be forwarded by the Commission to the budgetary authority together with the preliminary draft general budget of the European Union.

8. On the basis of the estimate, the Commission shall enter in the preliminary draft general budget of the European Union the estimates it deems necessary for the establishment plan and the amount of the subsidy to be charged to the general budget, which it shall place before the budgetary authority in accordance with Article 272 of the Treaty.

9. The budgetary authority shall authorise the appropriations for the subsidy to the Agency.

The budgetary authority shall adopt the establishment plan for the Agency.

10. The budget shall be adopted by the Management Board. It shall become final following final adoption of the general budget of the European Union. Where appropriate, it shall be adjusted accordingly.

11. Any modification of the establishment plan and of the budget shall be the subject of an amending budget, which is forwarded for the purposes of information to the budgetary authority.

12. The Management Board shall, as soon as possible, notify the budgetary authority of its intention to implement any project which may have significant financial implications for the funding of its budget, in particular any projects relating to property such as the rental or purchase of buildings. It shall inform the Commission thereof.

Where a branch of the budgetary authority has notified its intention to deliver an opinion, it shall forward its opinion to the Management Board within a period of six weeks from the date of notification of the project.

#### Article 68

1. The Executive Director shall implement the budget of the Agency.

2. By 1 March at the latest following each financial year, the Agency's accounting officer shall communicate the provisional accounts to the Commission's accounting officer together with a report on the budgetary and financial management for that financial year. The Commission's accounting officer shall consolidate the provisional accounts of the institutions and decentralised bodies in accordance with Article 128 of the Financial Regulation applicable to the general budget of the European Communities<sup>(1)</sup> (hereinafter referred to as the 'general Financial Regulation').

3. By 31 March at the latest following each financial year, the Commission's accounting officer shall submit the Agency's provisional accounts to the Court of Auditors, together with a report on the budgetary and financial management for that financial year. The report on the budgetary and financial management for the financial year shall also be forwarded to the European Parliament and the Council.

4. On receipt of the Court of Auditors' observations on the Agency's provisional accounts, pursuant to Article 129 of the general Financial Regulation, the Executive Director shall draw up the Agency's final accounts under his own responsibility and submit them to the Management Board for an opinion.

5. The Management Board of the Agency shall deliver an opinion on the Agency's final accounts.

6. The Executive Director shall, by 1 July at the latest following each financial year, forward the final accounts to the European Parliament, the Council, the Commission and the Court of Auditors, together with the Management Board's opinion.

7. The final accounts shall be published.

8. The Agency's Executive Director shall send the Court of Auditors a reply to its observations by 30 September at the latest. He shall also send this reply to the Management Board.

9. The Executive Director shall submit to the European Parliament, at the latter's request, any information required for the smooth application of the discharge procedure for the financial year in question, as laid down in Article 146(3) of the general Financial Regulation.

10. The European Parliament, on a recommendation from the Council acting by a qualified majority, shall, before 30 April of year N + 2, give a discharge to the Executive Director in respect of the implementation of the budget for year N.

11. The financial rules applicable to the Agency shall be adopted by the Management Board after the Commission has been consulted. They may not depart from Commission Regulation (EC, Euratom) No 2343/2002 of 19 November 2002 on the framework Financial Regulation for the bodies referred to in Article 185 of Council Regulation (EC, Euratom) No 1605/2002 on the Financial Regulation applicable to the general budget of the European Communities<sup>(2)</sup>, unless specifically required for the Agency's operation and with the Commission's prior consent.

<sup>(1)</sup> Council Regulation (EC, Euratom) No 1605/2002 of 25 June 2002 on the Financial Regulation applicable to the general budget of the European Communities (OJ L 248, 16.9.2002, p. 1).

<sup>(2)</sup> OJ L 357, 31.12.2002, p. 72.

*Article 69*

1. In order to combat fraud, corruption and other unlawful activities the provisions of Regulation (EC) No 1073/1999 of the European Parliament and of the Council of 25 May 1999 concerning investigations conducted by the European Anti-Fraud Office (OLAF) <sup>(1)</sup> shall apply without restriction.

2. The Agency shall accede to the Interinstitutional Agreement of 25 May 1999 concerning internal investigations by the European Anti-Fraud Office (OLAF) and shall issue, without delay, the appropriate provisions applicable to all the employees of the Agency.

*Article 70*

1. The structure and the level of the fees referred to in Article 67(3) shall be established by the Council acting under the conditions provided for by the Treaty on a proposal from the Commission, once the Commission has consulted organisations representing the interests of the pharmaceutical industry at Community level.

2. However, provisions shall be adopted in accordance with the procedure referred to in Article 87(2), establishing the circumstances in which small and medium-sized enterprises may pay reduced fees, defer payment of the fee, or receive administrative assistance.

**Chapter 3****General Provisions governing the Agency***Article 71*

The Agency shall have legal personality. In all Member States it shall enjoy the most extensive legal capacity accorded to legal persons under their laws. It may in particular acquire or dispose of movable and immovable property and may be a party to legal proceedings.

*Article 72*

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 by its servants in the performance of their duties.

<sup>(1)</sup> OJ L 136, 31.5.1999, p. 1.

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

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 73*

Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents <sup>(2)</sup> shall apply to documents held by the Agency.

The Agency shall set up a register pursuant to Article 2(4) of Regulation (EC) No 1049/2001 to make available all documents that are publicly accessible pursuant to this Regulation.

The Management Board shall adopt the arrangements for implementing Regulation (EC) No 1049/2001 within six months of entry into force of this Regulation.

Decisions taken by the Agency pursuant to Article 8 of Regulation (EC) No 1049/2001 may give rise to the lodging of a complaint with the Ombudsman or form the subject of an action before the Court of Justice, under the conditions laid down in Articles 195 and 230 of the Treaty respectively.

*Article 74*

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

*Article 75*

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 76*

Members of the Management Board, members of the committees referred to in Article 56(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 obligation of professional secrecy.

<sup>(2)</sup> OJ L 145, 31.5.2001, p. 43.

*Article 77*

The Commission may, in agreement with the Management Board and the relevant committee, invite representatives of international organisations with an interest 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 78*

1. 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.

2. The committees referred to in Article 56(1) and any working parties and scientific advisory groups established in accordance with that Article shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and health-care professionals' associations. Rapporteurs appointed by these committees may, on an advisory basis,

establish contacts with representatives of patient organisations and health-care professionals' associations relevant to the indication of the medicinal product concerned.

*Article 79*

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 measures to provide assistance to companies at the time of submission of their applications.

*Article 80*

To ensure an appropriate level of transparency, the Management Board, on the basis of a proposal by the Executive Director and 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.

The internal rules and procedures of the Agency, its committees and its working groups shall be made available to the public at the Agency and on the Internet.

## TITLE V

## GENERAL AND FINAL PROVISIONS

*Article 81*

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, withdrawn or revoked except through the procedures and on the grounds set out in this Regulation.

*Article 82*

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

However, the Commission shall authorise the same applicant to submit more than one application to the Agency for that medicinal product when there are objective verifiable reasons relating to public health regarding the availability of medicinal products to health-care professionals and/or patients, or for co-marketing reasons.

2. As regards medicinal products for human use, Article 98(3) of Directive 2001/83/EC shall 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 Article 9(4)(a), (b), (c) and (d) and in Article 34(4)(a) to (e), this Regulation shall not prohibit the use of two or more commercial designs for a given medicinal product covered by a single authorisation.

*Article 83*

1. By way of exemption from Article 6 of Directive 2001/83/EC Member States may make a medicinal product for human use belonging to the categories referred to in Article 3(1) and (2) of this Regulation available for compassionate use.

2. For the purposes of this Article, 'compassionate use' shall mean making a medicinal product belonging to the categories referred to in Article 3(1) and (2) available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who can not be treated satisfactorily by an authorised medicinal product. The medicinal product concerned must either be the subject of an application for a marketing authorisation in accordance with Article 6 of this Regulation or must be undergoing clinical trials.

3. When a Member State makes use of the possibility provided for in paragraph 1 it shall notify the Agency.

4. When compassionate use is envisaged, the Committee for Medicinal Products for Human Use, after consulting the manufacturer or the applicant, may adopt opinions on the conditions for use, the conditions for distribution and the patients targeted. The opinions shall be updated on a regular basis.

5. Member States shall take account of any available opinions.

6. The Agency shall keep an up-to-date list of the opinions adopted in accordance with paragraph 4, which shall be published on its website. Article 24(1) and Article 25 shall apply *mutatis mutandis*.

7. The opinions referred to in paragraph 4 shall not affect the civil or criminal liability of the manufacturer or of the applicant for marketing authorisation.

8. Where a compassionate use programme has been set up, the applicant shall ensure that patients taking part also have access to the new medicinal product during the period between authorisation and placing on the market.

9. This Article shall be without prejudice to Directive 2001/20/EC and to Article 5 of Directive 2001/83/EC.

#### Article 84

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 infringement of the provisions of this Regulation or the regulations adopted pursuant to it and shall take all measures necessary for their implementation. The penalties shall be effective, proportionate and dissuasive.

Member States shall inform the Commission of these provisions no later than 31 December 2004. They shall notify any subsequent alterations as soon as possible.

2. Member States shall inform the Commission immediately of any litigation instituted for 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 in accordance with the procedure referred to in Article 87(2).

The Commission shall publish the names of the marketing authorisation holders involved and the amounts of and reasons for the financial penalties imposed.

#### Article 85

This Regulation shall not affect the competences vested in the European Food Safety Authority created by Regulation (EC) No 178/2002<sup>(1)</sup>.

#### Article 86

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 and in Chapter 4 of Title III of Directive 2001/82/EC.

#### Article 87

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, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The period laid down in Article 5(6) of Decision 1999/468/EC shall be set at three months.

3. Where reference is made to this paragraph, Articles 4 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The period laid down in Article 4(3) of Decision 1999/468/EC shall be set at one month.

4. The committees shall adopt their Rules of Procedure.

<sup>(1)</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (OJ L 31, 1.2.2002, p. 1).

*Article 88*

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

References to the repealed Regulation shall be construed as references to this Regulation.

*Article 89*

The periods of protection provided for in Articles 14(11) and 39(10) shall not apply to reference medicinal products for

which an application for authorisation has been submitted before the date referred to in Article 90, second paragraph.

*Article 90*

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

By way of derogation from the first paragraph, Titles I, II, III and V shall apply from 20 November 2005 and point 3, fifth and sixth indent of the Annex shall apply from 20 May 2008.

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

Done at Strasbourg 31 March 2004.

*For the European Parliament*

*The President*

P. COX

*For the Council*

*The President*

D. ROCHE



## ANNEX

**MEDICINAL PRODUCTS TO BE AUTHORISED BY THE COMMUNITY**

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. Medicinal products for veterinary use 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 for human use containing a new active substance which, on the date of entry into force of this Regulation, was not authorised in the Community, for which the therapeutic indication is the treatment of any of the following diseases:
  - acquired immune deficiency syndrome,
  - cancer,
  - neurodegenerative disorder,
  - diabetes,and with effect from 20 May 2008
  - auto-immune diseases and other immune dysfunctions,
  - viral diseases.
4. Medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

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