ISSN 1725-2555

Official Journal

of the European Union

L 136

Volume 47

30 April 2004

English edition

Legislation

Contents

Price: EUR 18,00

(1) Text with EEA relevance

EN

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(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 [1],

Having regard to the Opinion of the European Economic and Social Committee [2],

After consulting the Committee of the Regions,

In accordance with the procedure laid down in Article 251 of the Treaty [3],

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 [4] 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 [5] and Directive 2001/82/EC of 6 November 2001 on the Community code relating to veterinary medicinal products [6], 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.

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[1] OJ C 75 E, 26.3.2002, p. 189 and OJ C ... (not yet published in the Official Journal).

[2] OJ C 61, 14.3.2003, p. 1.

[3] 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.

[4] 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).

[5] 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).

[6] 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 [1] 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 autoimmune 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 [2].

(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.

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 Directive repealed by Directive 93/41/EEC (OJ L 214, 24.8.1993, p. 40).

[2] 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 β-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 [1] 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 [2] 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 [3]. 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.

[1] OJ L 121, 1.5.2001, p. 34.

[2] OJ C 172, 18.6.1999, p. 1.

[3] 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 [1], 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 [1], 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 [2].

(38) The provisions of Regulation (EC) No 1647/2003 [3] 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.

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[1] 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).
[2] OJ L 184, 17.7.1999, p. 23.
[3] 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 [1];

[1] 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 [1], 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;

[1] 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 implementation 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 [1].

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.

[1] 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 [1] (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 [2], unless specifically required for the Agency's operation and with the Commission's prior consent.

[1] 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).

[2] 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) [1] 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. 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 [2] 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.

[1] OJ L 136, 31.5.1999, p. 1.

[2] 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 [1].

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.

[1] 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.

   After 20 May 2008, the Commission, having consulted the Agency, may present any appropriate proposal modifying this point and the Council shall take a decision on that proposal by qualified majority.

4. Medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

DIRECTIVE 2004/27/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

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

(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 thereof,

Having regard to the proposal by the Commission [1],

Having regard to the Opinion of the European Economic and Social Committee [2],

After consulting the Committee of the Regions,

Acting in accordance with the procedure laid down in Article 251 of the Treaty [3],

Whereas:

(1) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [4], codified and consolidated in a single text the texts of Community legislation on medicinal products for human use, in the interests of clarity and rationalisation.

(2) The Community legislation so far adopted has made a major contribution to the achievement of the objective of the free and safe movement of medicinal products for human use and the elimination of obstacles to trade in such products. However, in the light of the experience acquired, it has become clear that new measures are necessary to eliminate the remaining obstacles to free movement.

(3) It is therefore necessary to align the national laws, regulations and administrative provisions which contain differences with regard to the basic principles in order to promote the operation of the internal market while realising a high level of human health protection.

(4) The main purpose of any regulation on the manufacture and distribution of medicinal products for human use should be to safeguard public health. However, this objective should be achieved by means which do not hinder the development of the pharmaceutical industry or trade in medicinal products in the Community.

(5) 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 [5] provided that, within six years of its entry into force, the Commission was required to publish a general report on the experience acquired as a result of the operation of the marketing authorisation procedures laid down in that Regulation and in other Community legal provisions.

(6) In the light of the Commission's report on the experience acquired, it has proved necessary to improve the operation of the marketing authorisation procedures for medicinal products in the Community.

(7) Particularly as a result of scientific and technical progress, the definitions and scope of Directive 2001/83/EC should be clarified in order to achieve high standards for the quality, safety and efficacy of medicinal products for human use. In order to take account both of the emergence of new therapies and of the growing number of so-called 'borderline' products between the medicinal product sector and other sectors, the definition of 'medicinal product' should be modified so as to avoid any doubt as to the applicable legislation when a product, whilst fully falling within the definition of a medicinal product, may also fall within the definition of other regulated products. This definition should specify the type of action that the medicinal product may exert on physiological functions. This enumeration of actions will also make it possible to cover medicinal products such as gene therapy, radiopharmaceutical products as well as certain medicinal products for topical use. Also, in view of the characteristics of pharmaceutical legislation, provision should be made for such legislation to apply. With the same objective of clarifying situations, where a given product comes under the definition of a medicinal product but could also fall within the definition of other regulated products, it is necessary, in case of doubt and in order to ensure legal certainty, to state explicitly which provisions have to be complied with. Where a product comes clearly under the definition of other product categories, in particular food, food supplements,

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[1] OJ C 75 E, 26.3.2002, p. 216 and OJ C ... (not yet published in the Official Journal).

[2] OJ C 61, 14.3.2003, p. 1.

[3] Opinion of the European Parliament of 23 October 2002 (OJ C 300 E, 11.12.2003, p. 353), Council Common Position of 29 September 2003 (OJ C 297 E, 9.12.2003, p. 41), Position of the European Parliament of 17 December 2003 (not yet published in the Official Journal) and Council Decision of 11 March 2004.

[4] OJ L 311, 28.11.2001, p. 67. Directive as last amended by Commission Directive 2003/63/EC (OJ L 159, 27.6.2003, p. 46).

[5] OJ L 214, 21.8.1993, p. 1. Regulation repealed by Regulation (EC) No 726/2004 (see p. 1 of this Official Journal).

medical devices, biocides or cosmetics, this Directive should not apply. It is also appropriate to improve the consistency of the terminology of pharmaceutical legislation.

(8) Wherever it is proposed to change the scope of the centralised procedure, it should no longer be possible to opt for the mutual-recognition procedure or the decentralised procedure in respect of orphan medicinal products and medicinal products which contain new active substances 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 Regulation (EC) No 726/2004 [1], it should no longer be possible to opt for the mutual-recognition procedure or the decentralised procedure in respect of medicinal products which contain new active substances and for which the therapeutic indication is the treatment of auto-immune diseases and other immune dysfunctions and viral diseases.

(9) On the other hand, in the case of generic medicinal products of which the reference medicinal product has been granted a marketing authorisation under the centralised procedure, applicants seeking marketing authorisation should be able to choose either of the two procedures, on certain conditions. Similarly, the mutual-recognition or decentralised procedure should be available as an option for medicinal products which represent a therapeutic innovation or which are of benefit to society or to patients.

(10) In order to increase availability of medicinal products, in particular on smaller markets, it should, in cases where an applicant does not apply for an authorisation for a medicinal product in the context of the mutual-recognition procedure in a given Member State, be possible for that Member State, for justified public health reasons, to authorise the placing on the market of the medicinal product.

(11) Evaluation of the operation of marketing authorisation procedures has revealed the need to revise, in particular, the mutual-recognition procedure in order to improve the opportunities for cooperation between Member States. This cooperation process should be formalised by setting up a coordination group for this procedure and by defining its operation so as to settle disagreements within the framework of a revised decentralised procedure.

(12) With regard to referrals, the experience acquired reveals the need for an appropriate procedure, particularly in the case of referrals relating to an entire therapeutic class or to all medicinal products containing the same active substance.

(13) There is a need to provide for the ethical requirements of Directive 2001/20/EC of the European Parliament and the Council of 4 April 2001 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 [2] to apply to all medicinal products authorised within the Community. In particular, with respect to clinical trials conducted outside the Community on medicinal products destined to be authorised within the Community, it should be verified, at the time of the evaluation of the application for authorisation, that these trials were conducted in accordance with the principles of good clinical practice and the ethical requirements equivalent to the provisions of that Directive.

(14) Since generic medicines account for a major part of the market in medicinal products, their access to the Community market should be facilitated in the light of the experience acquired. Furthermore, the period for protection of data relating to pre-clinical tests and clinical trials should be harmonised.

(15) Biological medicinal products similar to a reference medicinal product do not usually meet all the conditions to be considered as a generic medicinal product mainly due to manufacturing process characteristics, raw materials used, molecular characteristics and therapeutic modes of action. When a biological medicinal product does not meet all the conditions to be considered as a generic medicinal product, the results of appropriate tests should be provided in order to fulfil the requirements related to safety (pre-clinical tests) or to efficacy (clinical tests) or to both.

(16) The criteria of quality, safety and efficacy should enable the risk-benefit balance of all medicinal products to be assessed both when they are placed on the market and at any other time the competent authority deems this appropriate. In this connection, it is necessary to harmonise and adapt the criteria for refusal, suspension and revocation of marketing authorisations.

(17) A marketing authorisation should be renewed once five years after the granting of the marketing authorisation. 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 Member States concerned during that period, should be considered invalid, in order, in particular, to avoid the administrative burden of maintaining such authorisations. However, exemptions from this rule should be granted when these are justified on public health grounds.

[1] See p. 1 of this Official Journal.

[2] OJ L 121, 1.5.2001, p. 34.

(18) The environmental impact should be assessed and, on a case-by-case basis, specific arrangements to limit it should be envisaged. In any event this impact should not constitute a criterion for refusal of a marketing authorisation.

(19) The quality of medicinal products for human use manufactured or available in the Community should be guaranteed by requiring that the active substances used in their composition comply with the principles of good manufacturing practice in relation to those medicinal products. It has proved necessary to reinforce the Community provisions on inspections and to compile a Community register of the results of those inspections.

(20) Pharmacovigilance and, more generally, market surveillance and sanctions in the event of failure to comply with the provisions should be stepped up. In the field of pharmacovigilance, account should be taken of the facilities offered by new information technologies to improve exchanges between Member States.

(21) As part of the proper use of medicinal products, the rules on packaging should be adapted to take account of the experience acquired.

(22) The measures necessary for the implementation of this Directive 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 [1].

(23) Directive 2001/83/EC should be amended accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Directive 2001/83/EC is hereby amended as follows:

1) Article 1 shall be amended as follows:

(a) point 1 shall be deleted;

(b) point 2 shall be replaced by the following:

'2. *Medicinal product:*

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.'

(c) point 5 shall be replaced by the following:

'5. *Homeopathic medicinal product:*

Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.';

(d) the Title of point 8 shall be replaced by 'Kit';

(e) the following point shall be inserted:

'18a *Representative of the marketing authorisation holder:*

The person, commonly known as local representative, designated by the marketing authorisation holder to represent him in the Member State concerned'.

(f) point 20 shall be replaced by the following:

'20. *Name of the medicinal product:*

The name, which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trade mark or the name of the marketing authorisation holder.';

(g) the heading of point 26 shall be replaced by the following:

(only concerns the Portuguese version);

(h) point 27 shall be replaced by the following:

'27. *Agency:*

The European Medicines Agency established by Regulation (EC) No 726/2004 (*);

[1] OJ L 184, 17.7.1999, p. 23.

(*) OJ L 136, 30.4.2004, p. 1.';

(i) point 28 shall be replaced by the following points:

'28. *Risks related to use of the medicinal product:*

— any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health;

— any risk of undesirable effects on the environment;

28a. *Risk-benefit balance:*

An evaluation of the positive therapeutic effects of the medicinal product in relation to the risks as defined in point 28, first indent.';

2) Article 2 shall be replaced by the following:

'*Article 2*

1. This Directive shall apply to medicinal products for human use intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process.

2. In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a "medicinal product" and within the definition of a product covered by other Community legislation the provisions of this Directive shall apply.

3. Notwithstanding paragraph 1 and Article 3(4), Title IV of this Directive shall apply to medicinal products intended only for export and to intermediate products.';

3) Article 3 shall be amended as follows:

(a) point 2 shall be replaced by the following:

'2. Any medicinal product which is prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and is intended to be supplied directly to the patients served by the pharmacy in question (commonly known as the officinal formula).'

(b) point 3 shall be replaced by the following:

'3. Medicinal products intended for research and development trials, but without prejudice to the provisions of Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 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 (*).

(*) OJ L 121, 1.5.2001, p. 34.';

(c) point 6 shall be replaced by the following:

'6. Whole blood, plasma or blood cells of human origin, except for plasma which is prepared by a method involving an industrial process.';

4) Article 5 shall be replaced by the following:

'*Article 5*

1. A Member State may, in accordance with legislation in force and to fulfil special needs, exclude from the provisions of this Directive medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health-care professional and for use by an individual patient under his direct personal responsibility.

2. Member States may temporarily authorise the distribution of an unauthorised medicinal product in response to the suspected or confirmed spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm.

3. Without prejudice to paragraph 1, Member States shall lay down provisions in order to ensure that marketing authorisation holders, manufacturers and health professionals are not subject to civil or administrative liability for any consequences resulting from the use of a medicinal product otherwise than for the authorised indications or from the use of an unauthorised medicinal product, when such use is recommended or required by a competent authority in response to the suspected or confirmed spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm. Such provisions shall apply whether or not national or Community authorisation has been granted.

4. Liability for defective products, as provided for by Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States, concerning liability for defective products (*), shall not be affected by paragraph 3.

(*) OJ L 210, 7.8.1985, p. 29. Directive as last amended by Directive 1999/34/EC of the European Parliament and of the Council (OJ L 141, 4.6.1999, p. 20).';

5) Article 6 shall be amended as follows:

(a) in paragraph 1, the following subparagraph shall be added:

'When a medicinal product has been granted an initial marketing authorisation in accordance with the first subparagraph, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 10(1).';

(b) the following paragraph shall be inserted:

'1a The marketing authorisation holder shall be responsible for marketing the medicinal product. The designation of a representative shall not relieve the marketing authorisation holder of his legal responsibility.';

(c) in paragraph 2, 'radionuclide kits' shall be replaced by 'kits';

6) in Article 7, 'radionuclide kits' shall be replaced by 'kits';

7) Article 8(3) shall be amended as follows:

(a) points (b) and (c) shall be replaced by the following:

'(b) Name of the medicinal product.

(c) Qualitative and quantitative particulars of all the constituents of the medicinal product, including the reference to its international non-proprietary name (INN) recommended by the WHO, where an INN for the medicinal product exists, or a reference to the relevant chemical name;';

(b) the following point shall be inserted:

'(ca) Evaluation of the potential environmental risks posed by the medicinal product. This impact shall be assessed and, on a case-by-case basis, specific arrangements to limit it shall be envisaged.';

(c) points (g), (h), (i) and (j) shall be replaced by the following points:

'(g) Reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for the disposal of waste products, together with an indication of potential risks presented by the medicinal product for the environment.

(h) Description of the control methods employed by the manufacturer.

(i) Results of:

— pharmaceutical (physico-chemical, biological or microbiological) tests,

— pre-clinical (toxicological and pharmacological) tests,

— clinical trials.

(ia) A detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant will introduce.

(ib) A statement to the effect that clinical trials carried out outside the European Union meet the ethical requirements of Directive 2001/20/EC.

(j) A summary, in accordance with Article 11, of the product characteristics, a mock-up of the outer packaging, containing the details provided for in Article 54, and of the immediate packaging of the medicinal product, containing the details provided for in Article 55, together with a package leaflet in accordance with Article 59.';

(d) the following points shall be added:

'(m) A copy of any designation of the medicinal product as an orphan medicinal product under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (*), accompanied by a copy of the relevant Agency opinion.

(n) Proof that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

(*) OJ L 18, 22.1.2000, p. 1.';

(e) the following subparagraph shall be added:

'The documents and information concerning the results of the pharmaceutical and pre-clinical tests and the clinical trials referred to in point (i) of the first subparagraph shall be accompanied by detailed summaries in accordance with Article 12.';

8) Article 10 shall be replaced by the following:

'*Article 10*

1. By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the Community.

A generic medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.

The first subparagraph shall also apply if the reference medicinal product was not authorised in the Member State in which the application for the generic medicinal product is submitted. In this case, the applicant shall indicate in the application form the name of the Member State in which the reference medicinal product is or has been authorised. At the request of the competent authority of the Member State in which the application is submitted, the competent authority of the other Member State shall transmit within a period of one month, a confirmation that the reference medicinal product is or has been authorised together with the full composition of the reference product and if necessary other relevant documentation.

The ten-year period referred to in the second subparagraph shall be extended to a maximum of eleven 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.

2. For the purposes of this Article:

(a) "reference medicinal product" shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8;

(b) "generic medicinal product" shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required of the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.

3. In cases where the medicinal product does not fall within the definition of a generic medicinal product as provided in paragraph 2(b) or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration, vis-à-vis the reference medicinal product, the results of the appropriate pre-clinical tests or clinical trials shall be provided.

4. Where a biological medicinal product which is similar to a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided. The type and quantity of supplementary data to be provided must comply with the relevant criteria stated in Annex I and the related detailed guidelines. The results of other tests and trials from the reference medicinal product's dossier shall not be provided.

5. In addition to the provisions laid down in paragraph 1, where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication.

6. Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.';

9) the following Articles shall be inserted:

'*Article 10a*

By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests or clinical trials if he can demonstrate that the active substances of the medicinal product have been in well-established medicinal use within the Community for at least ten years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in Annex I. In that event, the test and trial results shall be replaced by appropriate scientific literature.

Article 10b

In the case of medicinal products containing active substances used in the composition of authorised medicinal products but not hitherto used in combination for therapeutic purposes, the results of new pre-clinical tests or new clinical trials relating to that combination shall be provided in accordance with Article 8(3)(i), but it shall not be necessary to provide scientific references relating to each individual active substance.

Article 10c

Following the granting of a marketing authorisation, the authorisation holder may allow use to be made of the pharmaceutical, pre-clinical and clinical documentation contained in the file on the medicinal product, with a view to examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form.';

10) Article 11 shall be replaced by the following:

'*Article 11*

The summary of the product characteristics shall contain, in the order indicated below, the following information:

1. name of the medicinal product followed by the strength and the pharmaceutical form.

2. qualitative and quantitative composition in terms of the active substances and constituents of the excipient, knowledge of which is essential for proper administration of the medicinal product. The usual common name or chemical description shall be used.

3. pharmaceutical form.

4. clinical particulars:

   4.1. therapeutic indications,

   4.2. posology and method of administration for adults and, where necessary for children,

   4.3. contra-indications,

   4.4. special warnings and precautions for use and, in the case of immunological medicinal products, any special precautions to be taken by persons handling such products and administering them to patients, together with any precautions to be taken by the patient,

   4.5. interaction with other medicinal products and other forms of interactions,

   4.6. use during pregnancy and lactation,

   4.7. effects on ability to drive and to use machines,

   4.8. undesirable effects,

   4.9. overdose (symptoms, emergency procedures, antidotes).

5. pharmacological properties:

   5.1. pharmacodynamic properties,

   5.2. pharmacokinetic properties,

   5.3. preclinical safety data.

6. pharmaceutical particulars:

   6.1. list of excipients,

   6.2. major incompatibilities,

   6.3. shelf life, when necessary after reconstitution of the medicinal product or when the immediate packaging is opened for the first time,

   6.4. special precautions for storage,

   6.5. nature and contents of container,

   6.6. special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product, if appropriate.

7. marketing authorisation holder.

8. marketing authorisation number(s).

9. date of the first authorisation or renewal of the authorisation.

10. date of revision of the text.

11. for radiopharmaceuticals, full details of internal radiation dosimetry.

12. for radiopharmaceuticals, additional detailed instructions for extemporaneous preparation and quality control of such preparation and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready-to-use pharmaceutical will conform with its specifications.

For authorisations under Article 10, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed need not be included.';

11) Article 12 shall be replaced by the following:

'*Article 12*

1. The applicant shall ensure that, before the detailed summaries referred to in the last subparagraph of Article 8(3) are submitted to the competent authorities, they have been drawn up and signed by experts with the necessary technical or professional qualifications, which shall be set out in a brief curriculum vitae.

2. Persons having the technical and professional qualifications referred to in paragraph 1 shall justify any use made of scientific literature under Article 10a in accordance with the conditions set out in Annex I.

3. The detailed summaries shall form part of the file which the applicant submits to the competent authorities.';

12) Article 13 shall be replaced by the following:

'*Article 13*

1. Member States shall ensure that homeopathic medicinal products manufactured and placed on the market within the Community are registered or authorised in accordance with Articles 14, 15 and 16, except where such medicinal products are covered by a registration or authorisation granted in accordance with national legislation on or before 31 December 1993. In case of registrations, Article 28 and Article 29(1) to (3) shall apply.

2. Member States shall establish a special simplified registration procedure for the homeopathic medicinal products referred to in Article 14.';

13) Article 14 shall be amended as follows:

(a) in paragraph 1, the following second subparagraph shall be inserted:

'If new scientific evidence so warrants, the Commission may amend the third indent of the first subparagraph by the procedure referred to in Article 121(2).';

(b) paragraph 3 shall be deleted;

14) Article 15 shall be amended as follows:

(a) the second indent shall be replaced by the following:

'— dossier describing how the homeopathic stock or stocks is/are obtained and controlled, and justifying its/their homeopathic use, on the basis of an adequate bibliography,';

(b) the sixth indent shall be replaced by the following:

'— one or more mock-ups of the outer packaging and the immediate packaging of the medicinal products to be registered,';

15) Article 16 shall be amended as follows:

(a) in paragraph 1, 'Articles 8, 10 and 11' shall be replaced by 'Articles 8, 10, 10a, 10b, 10c and 11'.

(b) in paragraph 2, 'toxicological and pharmacological tests' shall be replaced by 'pre-clinical tests';

16) Articles 17 and 18 shall be replaced by the following:

'*Article 17*

1. Member States shall take all appropriate measures to ensure that the procedure for granting a marketing authorisation for medicinal products is completed within a maximum of 210 days after the submission of a valid application.

Applications for marketing authorisations in two or more Member States in respect of the same medicinal product shall be submitted in accordance with Articles 27 to 39.

2. Where a Member State notes that another marketing authorisation application for the same medicinal product is being examined in another Member State, the Member State concerned shall decline to assess the application and shall advise the applicant that Articles 27 to 39 apply.

Article 18

Where a Member State is informed in accordance with Article 8(3)(1) that another Member State has authorised a medicinal product which is the subject of a marketing authorisation application in the Member State concerned, it shall reject the application unless it was submitted in compliance with Articles 27 to 39.';

17) Article 19 shall be amended as follows:

(a) in the introductory sentence, 'Articles 8 and 10(1)' shall be replaced by 'Articles 8, 10, 10a, 10b and 10c';

(b) in point 1, 'Articles 8 and 10(1)' shall be replaced by 'Articles 8, 10, 10a, 10b and 10c';

(c) in point 2, 'a State laboratory or a laboratory designated for that purpose' shall be replaced by 'an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose';

(d) in point 3, 'Articles 8(3) and 10(1)' shall be replaced by 'Articles 8(3), 10, 10a, 10b and 10c';

18) in point (b) of Article 20, 'in exceptional and justifiable cases' shall be replaced by 'in justifiable cases';

19) in Article 21, paragraphs 3 and 4 shall be replaced by the following:

'3. The competent authorities shall make publicly available without delay the marketing authorisation together with the summary of the product characteristics for each medicinal product which they have authorised.

4. The competent authorities shall draw up an assessment report and comments on the file as regards the results of the pharmaceutical and pre-clinical tests and the clinical trials of the medicinal product concerned. The assessment report shall be updated whenever new information becomes available which is of importance for the evaluation of the quality, safety or efficacy of the medicinal product concerned.

The competent authorities shall make publicly accessible without delay the assessment report, together with the reasons for their opinion, after deletion of any information of a commercially confidential nature. The justification shall be provided separately for each indication applied for.';

20) Article 22 shall be replaced by the following:

'*Article 22*

In exceptional circumstances and following consultation with the applicant, the authorisation may be granted subject to a requirement for the applicant to meet certain conditions, 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. Continuation of the authorisation shall be linked to the annual reassessment of these conditions. The list of these conditions shall be made publicly accessible without delay, together with deadlines and dates of fulfilment.';

21) in Article 23, the following paragraphs shall be added:

'The authorisation holder shall forthwith supply to the competent authority any new information which might entail the amendment of the particulars or documents referred to in Articles 8(3), 10, 10a, 10b and 11, or 32(5), or Annex I.

In particular, he shall forthwith inform the competent authority 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 competent authority may at any time ask the holder of the marketing authorisation to forward data demonstrating that the risk-benefit balance remains favourable.';

22) the following Article shall be inserted:

'*Article 23a*

After a marketing authorisation has been granted, the holder of the authorisation shall inform the competent authority of the authorising Member State of the date of actual marketing of the medicinal product for human use in that Member State, taking into account the various presentations authorised.

The holder shall also notify the competent authority if the product ceases to be placed on the market of the Member State, 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 competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the volume of sales of the medicinal product, and any data in his possession relating to the volume of prescriptions.';

23) Article 24 shall be replaced by the following:

'*Article 24*

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 of the risk-benefit balance by the competent authority of the authorising Member State.

To this end, the marketing authorisation holder shall provide the competent authority 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 competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal in accordance with paragraph 2.

4. Any authorisation which within three years of its granting is not followed by the actual placing on the market of the authorised product in the authorising Member State shall cease to be valid.

5. When an authorised product previously placed on the market in the authorising Member State is no longer actually present on the market for a period of three consecutive years, the authorisation for that product shall cease to be valid.

6. The competent authority may, in exceptional circumstances and on public health grounds grant exemptions from paragraphs 4 and 5. Such exemptions must be duly justified.';

24) Article 26 shall be replaced by the following:

'*Article 26*

1. The marketing authorisation shall be refused if, after verification of the particulars and documents listed in Articles 8, 10, 10a, 10b and 10c, it is clear that:

(a) the risk-benefit balance is not considered to be favourable; or

(b) its therapeutic efficacy is insufficiently substantiated by the applicant; or

(c) its qualitative and quantitative composition is not as declared.

2. Authorisation shall likewise be refused if any particulars or documents submitted in support of the application do not comply with Articles 8, 10, 10a, 10b and 10c.

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

25) the heading of Chapter 4 of Title III shall be replaced by the following:

'*CHAPTER 4*

Mutual recognition procedure and decentralised procedure';

26) Articles 27 to 32 shall be replaced by the following:

'*Article 27*

1. A coordination group shall be set up for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States in accordance with the procedures laid down in this Chapter. The Agency shall provide the secretariat of this coordination group.

2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of three years. Members of the coordination group may arrange to be accompanied by experts.

3. The coordination group shall draw up its own Rules of Procedure, which shall enter into force after a favourable opinion has been given by the Commission. These Rules of Procedure shall be made public.

Article 28

1. With a view to the granting of a marketing authorisation for a medicinal product in more than one Member State, an applicant shall submit an application based on an identical dossier in these Member States. The dossier shall contain the information and documents referred to in Articles 8, 10, 10a, 10b, 10c and 11. The documents submitted shall include a list of Member States concerned by the application.

The applicant shall request one Member State to act as "reference Member State" and to prepare an assessment report on the medicinal product in accordance with paragraphs 2 or 3.

2. Where the medicinal product has already received a marketing authorisation at the time of application, the concerned Member States shall recognise the marketing authorisation granted by the reference Member State. To this end, the marketing authorisation holder shall request the reference Member State either to prepare an assessment report on the medicinal product or, if necessary, to update any existing assessment report. The reference Member State shall prepare or update the assessment report within 90 days of receipt of a valid application. The assessment report together with the approved summary of product characteristics, labelling and package leaflet shall be sent to the concerned Member States and to the applicant.

3. In cases where the medicinal product has not received a marketing authorisation at the time of application, the applicant shall request the reference Member State to prepare a draft assessment report, a draft summary of product characteristics and a draft of the labelling and package leaflet. The reference Member State shall prepare these draft documents within 120 days after receipt of a valid application and shall send them to the concerned Member States and to the applicant.

4. Within 90 days of receipt of the documents referred to in paragraphs 2 and 3, the Member States concerned shall approve the assessment report, the summary of product characteristics and the labelling and package leaflet and shall inform the reference Member State accordingly. The reference Member State shall record the agreement of all parties, close the procedure and inform the applicant accordingly.

5. Each Member State in which an application has been submitted in accordance with paragraph 1 shall adopt a decision in conformity with the approved assessment report, the summary of product characteristics and the labelling and package leaflet as approved, within 30 days after acknowledgement of the agreement.

Article 29

1. If, within the period laid down in Article 28(4), a Member State cannot approve the assessment report, the summary of product characteristics, the labelling and the package leaflet on the grounds of potential serious risk to public health, it shall give a detailed exposition of the reasons for its position to the reference Member State, to the other Member States concerned and to the applicant. The points of disagreement shall be forthwith referred to the coordination group.

2. Guidelines to be adopted by the Commission shall define a potential serious risk to public health.

3. Within the coordination group, all Member States referred to in paragraph 1 shall use their best endeavours to reach agreement on the action to be taken. They shall allow the applicant the opportunity to make his point of view known orally or in writing. If, within 60 days of the communication of the points of disagreement, the Member States reach an agreement, the reference Member State shall record the agreement, close the procedure and inform the applicant accordingly. Article 28(5) shall apply.

4. If the Member States fail to reach an agreement within the 60-day period laid down in paragraph 3, the Agency shall be immediately informed, with a view to the application of the procedure under Articles 32, 33 and 34. The Agency shall be provided with a detailed statement of the matters on which the Member States have been unable to reach agreement and the reasons for their disagreement. A copy shall be forwarded to the applicant.

5. As soon as the applicant is informed that the matter has been referred to the Agency, he shall forthwith forward to the Agency a copy of the information and documents referred to in the first subparagraph of Article 28(1).

6. In the circumstances referred to in paragraph 4, Member States that have approved the assessment report, the draft summary of product characteristics and the labelling and package leaflet of the reference Member State may, at the request of the applicant, authorise the medicinal product without waiting for the outcome of the procedure laid down in Article 32. In that event, the authorisation granted shall be without prejudice to the outcome of that procedure.

Article 30

1. If two or more applications submitted in accordance with Articles 8, 10, 10a, 10b, 10c and 11 have been made for marketing authorisation for a particular medicinal product, and if Member States have adopted divergent decisions concerning the authorisation of the medicinal product or its suspension or revocation, a Member State, the Commission or the applicant or the marketing authorisation holder may refer the matter to the Committee for Medicinal Products for Human Use, hereinafter referred to as "the Committee", for the application of the procedure laid down in Articles 32, 33 and 34.

2. In order to promote harmonisation of authorisations for medicinal products authorised in the Community, Member States shall, each year, forward to the coordination group a list of medicinal products for which a harmonised summary of product characteristics should be drawn up.

The coordination group shall lay down a list taking into account the proposals from all Member States and shall forward this list to the Commission.

The Commission or a Member State, in agreement with the Agency and taking into account the views of interested parties, may refer these products to the Committee in accordance with paragraph 1.

Article 31

1. The Member States or the Commission or the applicant or the marketing authorisation holder shall, in specific cases where the interests of the Community are involved, refer the matter to the Committee for application of the procedure laid down in Articles 32, 33 and 34 before any decision is reached on a request for a marketing authorisation or on the suspension or revocation of an authorisation, or on any other variation to the terms of a marketing authorisation which appears necessary, in particular to take account of the information collected in accordance with Title IX.

The Member State concerned or the Commission shall clearly identify the question which is referred to the Committee for consideration and shall inform the applicant or the marketing authorisation holder.

The Member States and the applicant or the marketing authorisation holder shall supply the Committee with all available information relating to the matter in question.

2. Where the referral to the Committee concerns a range of medicinal products or a therapeutic class, the Agency may limit the procedure to certain specific parts of the authorisation.

In that event, Article 35 shall apply to those medicinal products only if they were covered by the authorisation procedures referred to in this Chapter.

Article 32

1. When reference is made to the procedure laid down in this Article, the Committee shall consider the matter concerned and shall issue a reasoned opinion within 60 days of the date on which the matter was referred to it.

However, in cases submitted to the Committee in accordance with Articles 30 and 31, this period may be extended by the Committee for a further period of up to 90 days, taking into account the views of the applicants or the marketing authorisation holders concerned.

In an emergency, and on a proposal from its Chairman, the Committee may agree to a shorter deadline.

2. In order to consider the matter, the Committee shall appoint one of its members to act as rapporteur. The Committee may also appoint individual experts to advise it on specific questions. When appointing experts, the Committee shall define their tasks and specify the time-limit for the completion of these tasks.

3. Before issuing its opinion, the Committee shall provide the applicant or the marketing authorisation holder with an opportunity to present written or oral explanations within a time limit which it shall specify.

The opinion of the Committee shall be accompanied by a draft summary of product characteristics for the product and a draft text of the labelling and package leaflet.

If necessary, the Committee may call upon any other person to provide information relating to the matter before it.

The Committee may suspend the time-limits referred to in paragraph 1 in order to allow the applicant or the marketing authorisation holder to prepare explanations.

4. The Agency shall forthwith inform the applicant or the marketing authorisation holder where the opinion of the Committee is that:

(a) the application does not satisfy the criteria for authorisation; or

(b) the summary of the product characteristics proposed by the applicant or the marketing authorisation holder in accordance with Article 11 should be amended; or

(c) the authorisation should be granted subject to certain conditions, in view of conditions considered essential for the safe and effective use of the medicinal product including pharmacovigilance; or

(d) a marketing authorisation should be suspended, varied or revoked.

Within 15 days after receipt of the opinion, the applicant or the marketing authorisation holder may notify the Agency in writing of his intention to request a re-examination of the opinion. In that case, he 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 Committee shall re-examine its opinion in accordance with the fourth subparagraph of Article 62(1) of Regulation (EC) No 726/2004. The reasons for the conclusion reached shall be annexed to the assessment report referred to in paragraph 5 of this Article.

5. Within 15 days after its adoption, the Agency shall forward the final opinion of the Committee to the Member States, to the Commission and to the applicant or the marketing authorisation holder, together with a report describing the assessment of the medicinal product and stating the reasons for its conclusions.

In the event of an opinion in favour of granting or maintaining an 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;

(b) any conditions affecting the authorisation within the meaning of paragraph 4(c);

(c) details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product;

(d) the proposed text of the labelling and leaflet.'

27) Article 33 shall be amended as follows:

(a) in the first paragraph, '30 days' shall be replaced by '15 days';

(b) in the second paragraph, 'Article 32(5)(a) and (b)' shall be replaced by 'Article 32(5), second subparagraph';

(c) in the fourth paragraph, the words 'or the marketing authorisation holder' shall be added after the word 'applicant';

28) Article 34 shall be replaced by the following:

'*Article 34*

1. The Commission shall take a final decision in accordance with, and within 15 days after the end of, the procedure referred to in Article 121(3).

2. The rules of procedure of the Standing Committee established by Article 121(1) shall be adjusted to take account of the tasks incumbent upon it under this Chapter.

Those adjustments shall entail the following provisions:

(a) except in cases referred to in the third paragraph of Article 33, the opinion of the Standing Committee shall 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 shall have the option of submitting a written request that the draft Decision be discussed in a plenary meeting of the Standing Committee.

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.

The provisions necessary for the implementation of this paragraph shall be adopted by the Commission in accordance with the procedure referred to in Article 121(2).

3. The decision as referred to in paragraph 1 shall be addressed to all Member States and reported for information to the marketing authorisation holder or applicant. The concerned Member States and the reference Member State shall either grant or revoke the marketing authorisation, or vary its terms as necessary to comply with the decision within 30 days following its notification, and they shall refer to it. They shall inform the Commission and the Agency accordingly.';

29) the third subparagraph of Article 35(1) shall be deleted;

30) in Article 38, paragraph 2 shall be replaced by the following:

'2. At least every ten years the Commission shall publish a report on the experience acquired on the basis of the procedures described in this Chapter and shall propose any amendments which may be necessary to improve those procedures. The Commission shall submit this report to the European Parliament and to the Council.';

31) Article 39 shall be replaced by the following:

'*Article 39*

Article 29(4), (5) and (6) and Articles 30 to 34 shall not apply to the homeopathic medicinal products referred to in Article 14.

Articles 28 to 34 shall not apply to the homeopathic medicinal products referred to in Article 16(2).';

32) the following paragraph shall be added to Article 40:

'4. The Member States shall forward to the Agency a copy of the authorisation referred to in paragraph 1. The Agency shall enter that information on the Community database referred to in Article 111(6).';

33) in Article 46, point (f) shall be replaced by the following:

'(f) to comply with the principles and guidelines of good manufacturing practice for medicinal products and to use as starting materials only active substances, which have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials.

This point shall also be applicable to certain excipients, the list of which as well as the specific conditions of application shall be established by a Directive adopted by the Commission in accordance with the procedure referred to in Article 121(2).';

34) the following Article shall be inserted:

'*Article 46a*

1. For the purposes of this Directive, manufacture of active substances used as starting materials shall include both total and partial manufacture or import of an active substance used as a starting material as defined in Part I, point 3.2.1.1 (b) Annex I, and the various processes of dividing up, packaging or presentation prior to its incorporation into a medicinal product, including repackaging or re-labelling, such as are carried out by a distributor of starting materials.

2. Any amendments necessary to adapt paragraph 1 to new scientific and technical developments shall be laid down in accordance with the procedure referred to in Article 121(2).';

35) in Article 47, the following paragraphs shall be added:

'The principles of good manufacturing practice for active substances used as starting materials referred to in point (f) of Article 46 shall be adopted in the form of detailed guidelines.

The Commission shall also publish guidelines on the form and content of the authorisation referred to in Article 40(1), on the reports referred to in Article 111(3) and on the form and content of the certificate of good manufacturing practice referred to in Article 111(5).';

36) in Article 49(1), 'minimum' shall be deleted;

37) in Article 49(2), fourth subparagraph, first indent 'Applied physics' shall be replaced by 'Experimental physics';

38) in Article 50(1), 'in the State concerned' shall be replaced by 'within the Community';

39) in Article 51(1), point (b) shall be replaced by the following:

'(b) in the case of medicinal products coming from third countries, irrespective of whether the product has been manufactured in the Community, that each production batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products in accordance with the requirements of the marketing authorisation.';

40) Article 54 shall be amended as follows:

(a) point (a) shall be replaced by the following:

'(a) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults; where the product contains up to three active substances, the international non-proprietary name (INN) shall be included, or, if one does not exist, the common name;';

(b) in point (d), 'guidelines' shall be replaced by 'detailed guidance';

(c) Point (e) shall be replaced by the following:

'(e) the method of administration and, if necessary, the route of administration. Space shall be provided for the prescribed dose to be indicated.';

(d) point (f) shall be replaced by the following:

'(f) a special warning that the medicinal product must be stored out of the reach and sight of children;';

(e) Point (j) shall be replaced by the following:

'(j) specific precautions relating to the disposal of unused medicinal products or waste derived from medicinal products, where appropriate, as well as reference to any appropriate collection system in place;';

(f) point (k) shall be replaced by the following:

'(k) the name and address of the marketing authorisation holder and, where applicable, the name of the representative appointed by the holder to represent him;';

(g) point (n) shall be replaced by the following:

'(n) in the case of non-prescription medicinal products, instructions for use';

41) Article 55 shall be amended as follows:

(a) in paragraph 1, 'in Articles 54 and 62' shall be replaced by 'in Article 54';

(b) the first indent of paragraph 2 shall be replaced by the following:

'— the name of the medicinal product as laid down in point (a) of Article 54,';

(c) the first indent of paragraph 3 shall be replaced by the following:

'— the name of the medicinal product as laid down in point (a) of Article 54 and, if necessary, the route of administration,';

42) the following Article shall be inserted:

'*Article 56a*

The name of the medicinal product, as referred to in Article 54, point (a) must also be expressed in Braille format on the packaging. The marketing authorisation holder shall ensure that the package information leaflet is made available on request from patients' organisations in formats appropriate for the blind and partially-sighted.'

43) in Article 57, the following paragraph shall be added:

'For medicinal products authorised under Regulation (EC) No 726/2004, Member States shall, when applying this Article, observe the detailed guidance referred to in Article 65 of this Directive.';

44) Article 59 shall be replaced by the following:

'*Article 59*

1. The package leaflet shall be drawn up in accordance with the summary of the product characteristics; it shall include, in the following order:

(a) for the identification of the medicinal product:

(i) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults. The common name shall be included where the product contains only one active substance and if its name is an invented name;

(ii) the pharmaco-therapeutic group or type of activity in terms easily comprehensible for the patient;

(b) the therapeutic indications;

(c) a list of information which is necessary before the medicinal product is taken:

(i) contra-indications;

(ii) appropriate precautions for use;

(iii) forms of interaction with other medicinal products and other forms of interaction (e.g. alcohol, tobacco, foodstuffs) which may affect the action of the medicinal product;

(iv) special warnings;

(d) the necessary and usual instructions for proper use, and in particular:

(i) the dosage,

(ii) the method and, if necessary, route of administration;

(iii) the frequency of administration, specifying if necessary the appropriate time at which the medicinal product may or must be administered;

and, as appropriate, depending on the nature of the product:

(iv) the duration of treatment, where it should be limited;

(v) the action to be taken in case of an overdose (such as symptoms, emergency procedures);

(vi) what to do when one or more doses have not been taken;

(vii) indication, if necessary, of the risk of withdrawal effects;

(viii) a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product;

(e) a description of the adverse reactions which may occur under normal use of the medicinal product and, if necessary, the action to be taken in such a case; the patient should be expressly asked to communicate any adverse reaction which is not mentioned in the package leaflet to his doctor or pharmacist;

(f) a reference to the expiry date indicated on the label, with:

(i) a warning against using the product after that date;

(ii) where appropriate, special storage precautions;

(iii) if necessary, a warning concerning certain visible signs of deterioration;

(iv) the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names, for each presentation of the medicinal product;

(v) for each presentation of the product, the pharmaceutical form and content in weight, volume or units of dosage;

(vi) the name and address of the marketing authorisation holder and, where applicable, the name of his appointed representatives in the Member States;

(vii) the name and address of the manufacturer;

(g) where the medicinal product is authorised in accordance with Articles 28 to 39 under different names in the Member States concerned, a list of the names authorised in each Member State;

(h) the date on which the package leaflet was last revised.

2. The list set out in point (c) of paragraph 1 shall:

(a) take into account the particular condition of certain categories of users (children, pregnant or breastfeeding women, the elderly, persons with specific pathological conditions);

(b) mention, if appropriate, possible effects on the ability to drive vehicles or to operate machinery;

(c) list those excipients knowledge of which is important for the safe and effective use of the medicinal product and which are included in the detailed guidance published pursuant to Article 65.

3. The package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use.';

45) Article 61(1) shall be replaced by the following:

'1. One or more mock-ups of the outer packaging and the immediate packaging of a medicinal product, together with the draft package leaflet, shall be submitted to the authorities competent for authorising marketing when the marketing authorisation is requested. The results of assessments carried out in cooperation with target patient groups shall also be provided to the competent authority.';

46) in Article 61(4), 'or as appropriate' shall be replaced by 'and';

47) in Article 62, 'for health education' shall be replaced by 'for the patient';

48) Article 63 shall be amended as follows:

(a) the following subparagraph shall be added to paragraph 1:

'In the case of certain orphan medicinal products, the particulars listed in Article 54 may, on reasoned request, appear in only one of the official languages of the Community.';

(b) paragraphs 2 and 3 shall be replaced by the following:

'2. The package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals. The package leaflet must be clearly legible in the official language or languages of the Member State in which the medicinal product is placed on the market.

The first subparagraph shall not prevent the package leaflet from being printed in several languages, provided that the same information is given in all the languages used.

3. When the product is not intended to be delivered directly to the patient, the competent authorities may grant an exemption to the obligation that certain particulars should appear on the labelling and in the package leaflet and that the leaflet must be in the official language or languages of the Member State in which the product is placed on the market.';

49) Article 65 shall be replaced by the following:

'*Article 65*

In consultation with the Member States and the parties concerned, the Commission shall draw up and publish detailed guidance concerning in particular:

(a) the wording of certain special warnings for certain categories of medicinal products;

(b) the particular information needs relating to non-prescription medicinal products;

(c) the legibility of particulars on the labelling and package leaflet;

(d) the methods for the identification and authentication of medicinal products;

(e) the list of excipients which must feature on the labelling of medicinal products and the way in which these excipients must be indicated;

(f) harmonised provisions for the implementation of Article 57.';

50) Article 66(3), fourth indent shall be replaced by:

'— the name and address of the manufacturer,';

51) Article 69(1) shall be amended as follows:

(a) the first indent shall be replaced by the following:

'— the scientific name of the stock or stocks followed by the degree of dilution, making use of the symbols of the pharmacopoeia used in accordance with Article 1(5); if the homeopathic medicinal product is composed of two or more stocks, the scientific names of the stocks on the labelling may be supplemented by an invented name';

(b) the last indent shall be replaced by the following:

'— a warning advising the user to consult a doctor if the symptoms persist';

52) Article 70(2) shall be amended as follows:

(a) point (a) shall be replaced by the following:

'(a) medicinal products on medical prescription for renewable or non-renewable delivery;';

(b) point (c) shall be replaced by the following:

'(c) medicinal products on "restricted" medical prescription, reserved for use in certain specialised areas.';

53) Article 74 shall be replaced by the following:

'*Article 74*

When new facts are brought to their attention, the competent authorities shall examine and, as appropriate, amend the classification of a medicinal product by applying the criteria listed in Article 71.';

54) the following Article shall be inserted:

'*Article 74a*

Where a change of classification of a medicinal product has been authorised on the basis of significant pre-clinical tests or clinical trials, the competent authority shall not refer to the results of those tests or trials when examining an application by another applicant for or holder of marketing authorisation for a change of classification of the same substance for one year after the initial change was authorised.';

55) Article 76 shall be amended as follows:

(a) the existing text shall become paragraph 1;

(b) the following paragraphs shall be added:

'2. In the case of wholesale distribution and storage, medicinal products shall be covered by a marketing authorisation granted pursuant to Regulation (EC) No 726/2004 or by the competent authorities of a Member State in accordance with this Directive.

3. Any distributor, not being the marketing authorisation holder, who imports a product from another Member State shall notify the marketing authorisation holder and the competent authority in the Member State to which the product will be imported of his intention to import it. In the case of products which have not been granted an authorisation pursuant to Regulation (EC) No 726/2004, the notification to the competent authority shall be without prejudice to additional procedures provided for in the legislation of that Member State.';

56) the second indent of point (e) of Article 80 shall be replaced by the following:

'— name of the medicinal product,';

57) Article 81 shall be replaced by the following:

'*Article 81*

With regard to the supply of medicinal products to pharmacists and persons authorised or entitled to supply medicinal products to the public, Member States shall not impose upon the holder of a distribution authorisation which has been granted by another Member State any obligation, in particular public service obligations, more stringent than those they impose on persons whom they have themselves authorised to engage in equivalent activities.

The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.

The arrangements for implementing this Article should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition.';

58) in Article 82, the second indent of the first paragraph shall be replaced by the following:

'— the name and pharmaceutical form of the medicinal product,';

59) Article 84 shall be replaced by the following:

'*Article 84*

The Commission shall publish guidelines on good distribution practice. To this end, it shall consult the Committee for Medicinal Products for Human Use and the Pharmaceutical Committee established by Council Decision 75/320/EEC (*).

(*) OJ L 147, 9.6.1975, p. 23.';

60) Article 85 shall be replaced by the following:

'*Article 85*

This Title shall apply to homeopathic medicinal products.';

61) the fourth indent of Article 86(2) shall be replaced by the following:

'— information relating to human health or diseases, provided that there is no reference, even indirect, to medicinal products';

62) Article 88 shall be replaced by the following:

'*Article 88*

1. Member States shall prohibit the advertising to the general public of medicinal products which:

(a) are available on medical prescription only, in accordance with Title VI;

(b) contain substances defined as psychotropic or narcotic by international convention, such as the United Nations Conventions of 1961 and 1971.

2. Medicinal products may be advertised to the general public which, by virtue of their composition and purpose, are intended and designed for use without the intervention of a medical practitioner for diagnostic purposes or for the prescription or monitoring of treatment, with the advice of the pharmacist, if necessary.

3. Member States shall be entitled to ban, on their territory, advertising to the general public of medicinal products the cost of which may be reimbursed.

4. The prohibition contained in paragraph 1 shall not apply to vaccination campaigns carried out by the industry and approved by the competent authorities of the Member States.

5. The prohibition referred to in paragraph 1 shall apply without prejudice to Article 14 of Directive 89/552/EEC.

6. Member States shall prohibit the direct distribution of medicinal products to the public by the industry for promotional purposes.';

63) the following text is inserted after Article 88:

'TITLE VIIIa

INFORMATION AND ADVERTISING

Article 88a

Within three years of the entry into force of Directive 2004/726/EC, the Commission shall, following consultations with patients' and consumers' organisations, doctors' and pharmacists' organisations, Member States and other interested parties, present to the European Parliament and the Council a report on current practice with regard to information provision — particularly on the Internet — and its risks and benefits for patients.

Following analysis of the above data, the Commission shall, if appropriate, put forward proposals setting out an information strategy to ensure good-quality, objective, reliable and non-promotional information on medicinal products and other treatments and shall address the question of the information source's liability.';

64) Article 89 shall be amended as follows:

(a) the first indent of point (b) of paragraph 1 shall be replaced by the following:

(does not affect the English version);

(b) paragraph 2 shall be replaced by the following:

'2. Member States may decide that the advertising of a medicinal product to the general public may, notwithstanding paragraph 1, include only the name of the medicinal product or its international non-proprietary name, where this exists, or the trademark if it is intended solely as a reminder.';

65) in Article 90, point (l) shall be deleted;

66) in Article 91, paragraph 2 shall be replaced by the following:

'2. Member States may decide that the advertising of a medicinal product to persons qualified to prescribe or supply such products may, notwithstanding paragraph 1, include only the name of the medicinal product, or its international non-proprietary name, where this exists, or the trademark, if it is intended solely as a reminder.';

67) Article 94(2) shall be replaced by the following:

'2. Hospitality at sales promotion events shall always be strictly limited to their main purpose and must not be extended to persons other than health-care professionals.';

68) Article 95 shall be replaced by the following:

'*Article 95*

The provisions of Article 94(1) shall not prevent hospitality being offered, directly or indirectly, at events for purely professional and scientific purposes; such hospitality shall always be strictly limited to the main scientific objective of the event; it must not be extended to persons other than health-care professionals.';

69) point (d) of Article 96(1) shall be replaced by the following:

'(d) each sample shall be no larger than the smallest presentation on the market;';

70) in Article 98, the following paragraph shall be added:

'3. The Member States shall not prohibit the co-promotion of a medicinal product by the holder of the marketing authorisation and one or more companies nominated by him.';

71) Article 100 shall be replaced by the following:

'*Article 100*

Advertising of the homeopathic medicinal products referred to in Article 14(1) shall be subject to the provisions of this Title with the exception of Article 87(1).

However, only the information specified in Article 69(1) may be used in the advertising of such medicinal products.';

72) in Article 101, the second paragraph shall be replaced by the following:

'The Member States may impose specific requirements on doctors and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions.';

73) Article 102 shall be replaced by the following:

'*Article 102*

In order to ensure the adoption of appropriate and harmonised regulatory decisions concerning the medicinal products authorised within the Community, having regard to information obtained about adverse reactions to medicinal products under normal conditions of use, the Member States shall operate a pharmacovigilance system. This system shall be used to collect information useful in the surveillance of medicinal products, with particular reference to adverse reactions in human beings, and to evaluate such information scientifically.

Member States shall ensure that suitable information collected within this system is communicated to the other Member States and the Agency. The information shall be recorded in the database referred to in point (l) of the second subparagraph of Article 57(1) of Regulation (EC) No 726/2004 and shall be permanently accessible to all Member States and without delay to the public.

This system shall also take into account any available information on misuse and abuse of medicinal products which may have an impact on the evaluation of their benefits and risks.';

74) the following Article shall be inserted:

'*Article 102a*

The management of funds intended for activities connected with pharmacovigilance, the operation of communication networks and market surveillance shall be under the permanent control of the competent authorities in order to guarantee their independence.';

75) in Article 103, the introductory phrase of the second paragraph shall be replaced by the following:

'That qualified person shall reside in the Community and shall be responsible for the following:';

76) Articles 104 to 107 shall be replaced by the following:

'*Article 104*

1. The marketing authorisation holder shall be required to maintain detailed records of all suspected adverse reactions occurring either in the Community or in a third country.

Save in exceptional circumstances, these reactions shall be communicated electronically in the form of a report in accordance with the guidelines referred to in Article 106(1).

2. The marketing authorisation holder shall be required to record all suspected serious adverse reactions which are brought to his attention by a health-care professional and to report them promptly to the competent authority of the Member State on whose territory the incident occurred, and no later than 15 days following the receipt of the information.

3. The marketing authorisation holder shall be required to record and report all other suspected serious adverse reactions which meet the notification criteria in accordance with the guidelines referred to in Article 106(1), of which he can reasonably be expected to have knowledge, promptly to the competent authority of the Member State in whose territory the incident occurred, and no later than 15 days following the receipt of the information.

4. The marketing authorisation holder 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 in accordance with the guidelines referred to in Article 106(1), so that the Agency and the competent authorities of the Member States in which the medicinal product is authorised are informed of them, and no later than 15 days following the receipt of the information.

5. By way of derogation from paragraphs 2, 3 and 4, in the case of medicinal products which are covered by Directive 87/22/EEC or which have qualified for the procedures laid down in Articles 28 and 29 of this Directive or which have been the subject of the procedures under Articles 32, 33 and 34 of this Directive, the marketing authorisation holder shall also ensure that all suspected serious adverse reactions occurring in the Community are reported in such a way as to be accessible to the reference Member State or to any competent authority acting as reference Member State. The reference Member State shall assume the responsibility of analysing and monitoring such adverse reactions.

6. Unless other requirements have been laid down as a condition for the granting of the marketing authorisation, or subsequently as indicated in the guidelines referred to in Article 106(1), reports of all adverse reactions shall be submitted to the competent authorities in the form of a periodic safety update report, immediately upon request or at least every six months after authorisation and 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 market and once a year for the following two years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request.

The periodic safety update reports shall include a scientific evaluation of the risk-benefit balance of the medicinal product.

7. The Commission may lay down provisions to amend paragraph 6 in view of experience gained through its operation. The Commission shall adopt the provisions in accordance with the procedure referred to in Article 121(2).

8. Following the granting of a marketing authorisation, the marketing authorisation holder may request the amendment of the periods referred to in paragraph 6 in accordance with the procedure laid down by Commission Regulation (EC) No 1084/2003 (*).

9. 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 competent authority.

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 105

1. The Agency, in collaboration with the Member States and the Commission, shall set up a data-processing network to facilitate the exchange of pharmacovigilance information regarding medicinal products marketed in the Community in order to allow all competent authorities to share the information at the same time.

2. Making use of the network referred to in paragraph 1, Member States shall ensure that reports of suspected serious adverse reactions that have taken place on their territory are promptly made available to the Agency and the other Member States, and in any case within 15 days after their notification at the latest.

3. The Member States shall ensure that reports of suspected serious adverse reactions that have taken place on their territory are promptly made available to the marketing authorisation holder, and in any case within 15 days after their notification at the latest.

Article 106

1. In order to facilitate the exchange of information on pharmacovigilance within the Community, the Commission, after consulting the Agency, the Member States and interested parties, shall draw up guidelines on the collection, verification and presentation of adverse reaction reports, including technical requirements for electronic exchange of pharmacovigilance information in accordance with internationally agreed formats, and shall publish a reference to an internationally agreed medical terminology.

Acting in accordance with the guidelines, marketing authorisation holders shall use internationally agreed medical terminology for the reporting of adverse reactions.

These guidelines shall be published in Volume 9 of The Rules governing Medicinal Products in the European Community and shall take account of international harmonisation work carried out in the field of pharmacovigilance.

2. For the interpretation of the definitions referred to in points (11) to (16) of Article 1 and of the principles outlined in this Title, the marketing authorisation holder and the competent authorities shall follow the guidelines referred to in paragraph 1.

Article 107

1. Where, as a result of the evaluation of pharmacovigilance data, a Member State considers that a marketing authorisation should be suspended, revoked or varied in accordance with the guidelines referred to in Article 106(1), it shall forthwith inform the Agency, the other Member States and the marketing authorisation holder.

2. Where urgent action to protect public health is necessary, the Member State concerned may suspend the marketing authorisation of a medicinal product, provided that the Agency, the Commission and the other Member States are informed no later than the following working day.

When the Agency is informed in accordance with paragraph 1 in relation to suspensions and revocation, or the first subparagraph of this paragraph, the Committee shall prepare an opinion within a time-frame to be determined depending on the urgency of the matter. In relation to variations, the Committee may upon request from a Member State prepare an opinion.

Acting on the basis of this opinion, the Commission may request all Member States in which the product is being marketed to take temporary measures immediately.

The final measures shall be adopted in accordance with the procedure referred to in Article 121(3).

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(*) OJ L 159, 27.6.2003, p. 1.';

77) Article 111 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. The competent authority of the Member State concerned shall ensure, by means of repeated inspections, and if necessary unannounced inspections, and, where appropriate, by asking an Official Medicines Control Laboratory or a laboratory designated for that purpose to carry out tests on samples, that the legal requirements governing medicinal products are complied with.

The competent authority may also carry out unannounced inspections at the premises of manufacturers of active substances used as starting materials, or at the premises of marketing authorisation holders whenever it considers that there are grounds for suspecting non-compliance with the principles and guidelines of good manufacturing practice referred to in Article 47. These inspections may also be carried out at the request of a Member State, the Commission or the Agency.

In order to verify whether the data submitted in order to obtain a conformity certificate comply with the monographs of the European Pharmacopoeia, the standardisation body of the nomenclatures and the quality norms within the meaning of the Convention relating to the elaboration of the European Pharmacopoeia (*) (European Directorate for the quality of Medicinal Products) may ask the Commission or the Agency to request such an inspection when the starting material concerned is the subject of a European Pharmacopoeia monograph.

The competent authority of the Member State concerned may carry out inspections of starting material manufacturers at the specific request of the manufacturer himself.

Such inspections shall be carried out by officials representing the competent authority who shall be empowered to:

(a) inspect the manufacturing or commercial establishments of manufacturers of medicinal products or of active substances used as starting materials, and any laboratories employed by the holder of the manufacturing authorisation to carry out checks pursuant to Article 20;

(b) take samples including with a view to independent tests being carried out by an Official Medicines Control Laboratory or a laboratory designated for that purpose by a Member State;

(c) examine any documents relating to the object of the inspection, subject to the provisions in force in the Member States on 21 May 1975 placing restrictions on these powers with regard to the description of the manufacturing method;

(d) inspect the premises, records and documents of marketing authorisation holders or any firms employed by the marketing authorisation holder to perform the activities described in Title IX, and in particular Articles 103 and 104.

(*) OJ L 158, 25.6.1994, p. 19.';

(b) paragraph 3 shall be replaced by the following:

'3. After every inspection as referred to in paragraph 1, the officials representing the competent authority shall report on whether the manufacturer complies with the principles and guidelines of good manufacturing practice laid down in Article 47 or, where appropriate, with the requirements laid down in Articles 101 to 108. The content of such reports shall be communicated to the manufacturer or marketing authorisation holder who has undergone the inspection.';

(c) the following paragraphs shall be added:

'4. Without prejudice to any arrangements which may have been concluded between the Community and third countries, a Member State, the Commission or the Agency may require a manufacturer established in a third country to submit to an inspection as referred to in paragraph 1.

5. Within 90 days of an inspection as referred to in paragraph 1, a certificate of good manufacturing practice shall be issued to a manufacturer if the outcome of the inspection shows that the manufacturer complies with the principles and guidelines of good manufacturing practice as provided for by Community legislation.

If inspections are performed as part of the certification procedure for the monographs of the European Pharmacopoeia, a certificate shall be drawn up.

6. Member States shall enter the certificates of good manufacturing practice which they issue in a Community database managed by the Agency on behalf of the Community.

7. If the outcome of the inspection as referred to in paragraph 1 is that the manufacturer does not comply with the principles and guidelines of good manufacturing practice as provided for by Community legislation, the information shall be entered in the Community database as referred to in paragraph 6.';

78) in Article 114(1) and (2), the terms 'by a State laboratory or a laboratory designated for that purpose' shall be replaced by the terms 'by an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose';

79) Article 116 shall be replaced by the following:

'*Article 116*

The competent authorities shall suspend, revoke, withdraw or vary a marketing authorisation if the view is taken that the product is harmful under normal conditions of use, or that it lacks therapeutic efficacy, or that the risk-benefit balance is not positive under the normal conditions of use, or that its qualitative and quantitative composition is not as declared. Therapeutic efficacy is lacking when it is concluded that therapeutic results cannot be obtained from the medicinal product.

An authorisation shall also be suspended, revoked, withdrawn or varied where the particulars supporting the application as provided for in Article 8 or Articles 10, 10a, 10b, 10c and 11 are incorrect or have not been amended in accordance with Article 23, or where the controls referred to in Article 112 have not been carried out.';

80) Article 117(1) shall be replaced by the following:

'1. Without prejudice to the measures provided for in Article 116, Member States shall take all appropriate steps to ensure that the supply of the medicinal product is prohibited and the medicinal product withdrawn from the market, if the view is taken that:

(a) the medicinal product is harmful under normal conditions of use; or

(b) it lacks therapeutic efficacy; or

(c) the risk-benefit balance is not favourable under the authorised conditions of use; or

(d) its qualitative and quantitative composition is not as declared; or

(e) the controls on the medicinal product and/or on the ingredients and the controls at an intermediate stage of the manufacturing process have not been carried out or if some other requirement or obligation relating to the grant of the manufacturing authorisation has not been fulfilled.';

81) Article 119 shall be replaced by the following:

'*Article 119*

The provisions of this Title shall apply to homeopathic medicinal products.';

82) Articles 121 and 122 shall be replaced by the following:

'*Article 121*

1. The Commission shall be assisted by the Standing Committee on Medicinal Products for Human Use, hereinafter called "the Standing Committee", in the task of adapting to technical progress the directives on the removal of technical barriers to trade in the medicinal products sector.

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 Standing Committee shall adopt its own rules of procedure which shall be made public.

Article 122

1. Member States shall take all appropriate measures to ensure that the competent authorities concerned communicate to each other such information as is appropriate to guarantee that the requirements placed on the authorisations referred to in Articles 40 and 77, on the certificates referred to in Article 111(5) or on the marketing authorisations are fulfilled.

2. Upon reasoned request, Member States shall forthwith communicate the reports referred to in Article 111(3) to the competent authorities of another Member State.

3. The conclusions reached in accordance with Article 111(1) shall be valid throughout the Community.

However, in exceptional cases, if a Member State is unable, for reasons relating to public health, to accept the conclusions reached following an inspection under Article 111(1), that Member State shall forthwith inform the Commission and the Agency. The Agency shall inform the Member States concerned.

When the Commission is informed of these divergences of opinion, it may, after consulting the Member States concerned, ask the inspector who performed the original inspection to perform a new inspection; the inspector may be accompanied by two other inspectors from Member States which are not parties to the disagreement.';

83) in Article 125, the third subparagraph shall be replaced by the following:

'Decisions to grant or revoke a marketing authorisation shall be made publicly available.';

84) the following Article shall be inserted:

'*Article 126a*

1. In the absence of a marketing authorisation or of a pending application for a medicinal product authorised in another Member State in accordance with this Directive, a Member State may for justified public health reasons authorise the placing on the market of the said medicinal product.

2. When a Member State avails itself of this possibility, it shall adopt the necessary measures in order to ensure that the requirements of this Directive are complied with, in particular those referred to in Titles V, VI, VIII, IX and XI.

3. Before granting such an authorisation a Member State shall:

(a) notify the marketing authorisation holder, in the Member State in which the medicinal product concerned is authorised, of the proposal to grant an authorisation under this Article in respect of the product concerned; and

(b) request the competent authority in that State to furnish a copy of the assessment report referred to in Article 21(4) and of the marketing authorisation in force in respect of the said medicinal product.

4. The Commission shall set up a publicly accessible register of medicinal products authorised under paragraph 1. Member States shall notify the Commission if any medicinal product is authorised, or ceases to be authorised, under paragraph 1, including the name or corporate name and permanent address of the authorisation holder. The Commission shall amend the register of medicinal products accordingly and make this register available on their website.

5. No later than 30 April 2008, the Commission shall present a report to the European Parliament and the Council concerning the application of this provision with a view to proposing any necessary amendments.';

85) the following Article 126b is inserted:

'*Article 126b*

In order to guarantee independence and transparency, the Member States shall ensure that members of staff of the competent authority responsible for granting authorisations, rapporteurs and experts concerned with the authorisation and surveillance of medicinal products have no financial or other interests in the pharmaceutical industry which could affect their impartiality. These persons shall make an annual declaration of their financial interests.

In addition, the Member States shall ensure that the competent authority makes publicly accessible its rules of procedure and those of its committees, agendas for its meetings and records of its meetings, accompanied by decisions taken, details of votes and explanations of votes, including minority opinions.';

86) the following Article shall be inserted:

'*Article 127a*

When a medicinal product is to be authorised in accordance with Regulation (EC) No 726/2004 and the Scientific Committee in its opinion refers to recommended conditions or restrictions with regard to the safe and effective use of the medicinal product as provided for in Article 9(4)(c) of that Regulation, a decision addressed to the Member States shall be adopted in accordance with the procedure provided for in Articles 33 and 34 of this Directive, for the implementation of those conditions or restrictions.';

87) the following Article shall be inserted:

'*Article 127b*

Member States shall ensure that appropriate collection systems are in place for medicinal products that are unused or have expired.'

Article 2

The periods of protection provided for in Article 1, point 8, which amends Article 10(1) of Directive 2001/83/EC, shall not apply to reference medicinal products for which an application for authorisation has been submitted before the date of transposition referred to in Article 3 first paragraph.

Article 3

Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive no later than 30 October 2005. They shall immediately inform the Commission thereof.

When Member States adopt these measures, they shall contain a reference to this Directive or shall be accompanied by such a reference on the occasion of their official publication. The methods of making such reference shall be laid down by the Member States.

Article 4

This Directive shall enter into force on the day of its publication in the *Official Journal of the European Union*.

Article 5

This Directive is addressed to the Member States.

Done at Strasbourg, 31 March 2004.

For the European Parliament	*For the Council*
The President	*The President*
P. COX	D. ROCHE

DIRECTIVE 2004/28/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

amending Directive 2001/82/EC on the Community code relating to veterinary medicinal products

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

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

Having regard to the proposal of the Commission [1],

Having regard to the Opinion of the European Economic and Social Committee [2],

After consulting the Committee of the Regions,

Acting in accordance with the procedure referred to in Article 251 of the Treaty [3],

Whereas:

(1) Directive 2001/82/EC of the European Parliament and of the Council of 23 October 2001 on the Community code relating to veterinary medicinal products [4] codified and consolidated previous Community legislation on veterinary medicinal products in a single text in the interests of clarity and rationalisation.

(2) The Community legislation so far adopted has made a major contribution to the achievement of the objective of free and safe movement of veterinary medicinal products and the elimination of obstacles to trade in such products. However, in the light of the experience gained, it has become clear that new measures are necessary to eliminate the remaining obstacles to free movement.

(3) It is therefore necessary to align national laws, regulations and administrative provisions that contain differences with regard to the basic principles in order to promote the operation of the internal market without adversely affecting public health.

(4) The main purpose of any regulation on the manufacture and distribution of veterinary medicinal products should be to safeguard animal health and welfare as well as public health. The legislation on marketing authorisations for veterinary medicinal products, and the criteria governing the granting of authorisations, are such as to strengthen the protection of public health. That aim should, however, be achieved by means that do not hinder the development of the pharmaceutical industry or trade in veterinary medicinal products within the Community.

(5) 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 [5] provided that, within six years of its entry into force, the Commission was required to publish a general report on the experience acquired as a result of the operation of the marketing authorisation procedures laid down in that Regulation and in other Community legal provisions.

(6) In the light of the Commission's report on the experience acquired, it has proved necessary to improve the operation of the marketing authorisation procedures for veterinary medicinal products in the Community.

(7) Particularly as a result of scientific and technical progress in the field of animal health, the definitions and scope of Directive 2001/82/EC should be clarified in order to achieve high standards for the quality, safety and efficacy of veterinary medicinal products. In order to take account both of the emergence of new therapies and of the growing number of so-called 'borderline' products between the medicinal product sector and other sectors, the definition of 'medicinal product' should be modified so as to avoid any doubt as to the applicable legislation when a product, whilst fully falling within the definition of a medicinal product, may also fall within the definition of other regulated products. Also, in view of the characteristics of pharmaceutical legislation, provision should be made for such legislation to apply. With the same objective of clarifying situations, where a given product comes under the defi-

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[1] OJ C 75 E, 26.3.2002, p. 234.

[2] OJ C 61, 14.3.2003, p. 1.

[3] Opinion of the European Parliament of 23 October 2002 (OJ C 300 E, 11.12.2003, p. 390), Council Common Position of 29 September 2003 (OJ C 297 E, 9.12.2003, p. 72), Position of the European Parliament of 17 December 2003 (not yet published in the Official Journal) and Council Decision of 11 March 2004.

[4] OJ L 311, 28.11.2001, p. 1.

[5] OJ L 214, 24.8.1993, p. 1. Regulation repealed by Regulation (EC) No 726/2004 (see p. 1 of this Official Journal).

nition of a veterinary medicinal product, but could also fall within the definition of other regulated products, it is necessary, in cases of doubt and in order to ensure legal certainty, to state explicitly which provisions have to be complied with. Where a product comes clearly under the definition of other product categories, in particular food, feed, feed additives or biocides, this Directive should not apply. It is also appropriate to improve the consistency of the terminology of pharmaceutical legislation.

(8) The veterinary medicinal products sector has a number of very specific features. Veterinary medicinal products for food-producing animals may be authorised only on conditions that guarantee that the foodstuffs produced will be harmless to consumers as regards any residues of such medicinal products.

(9) The costs of research and development to meet increased requirements as regards the quality, safety and efficacy of veterinary medicinal products are leading to a gradual reduction in the range of products authorised for the species and indications representing smaller market sectors.

(10) The provisions of Directive 2001/82/EC also need, therefore, to be adapted to the specific features of the sector, particularly to meet the health and welfare needs of food-producing animals on terms that guarantee a high level of consumer protection, and in a context that provides adequate economic interest for the veterinary medicinal products industry.

(11) In certain circumstances, particularly where certain types of pets are concerned, the need to obtain a marketing authorisation for a veterinary medicinal product in accordance with Community provisions is clearly disproportionate. Moreover, the absence of authorisation to market an immunological product in the Community should not be an obstacle to international movements of certain live animals for the purpose of which binding health measures have to be taken. The provisions on the authorisation or use of such medicinal products to take account of measures to combat certain infectious animal diseases at Community level also need to be adapted.

(12) Evaluation of the operation of market authorisation procedures has revealed the need to revise, in particular, the mutual-recognition procedure in order to improve the opportunities for cooperation between Member States. This cooperation process should be formalised by setting up a coordination group for this procedure and by defining its operation so as to settle disagreements within the framework of a revised decentralised procedure.

(13) With regard to referrals, the experience acquired reveals the need for an appropriate procedure, particularly in the case of referrals relating to an entire therapeutic class or to all veterinary medicinal products containing the same active substance.

(14) Marketing authorisation for veterinary medicinal products should be limited initially to five years. After this first renewal, the marketing authorisation should normally be valid for an unlimited period. 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 veterinary medicinal product in the Member States concerned during that period, should be considered invalid, in order, in particular, to avoid the administrative burden of maintaining such authorisations. However, exemptions from this rule should be granted when these are justified on public or animal health grounds.

(15) Biological medicinal products similar to a reference medicinal product do not usually meet all the conditions to be considered as a generic medicinal product mainly due to manufacturing process characteristics, raw materials used, molecular characteristics and therapeutic modes of action. When a biological product does not meet all the conditions to be considered as a generic medicinal product, the results of appropriate tests should be provided in order to fulfil the requirements related to safety (pre-clinical tests) or to efficacy (clinical tests) or to both.

(16) The criteria of quality, safety and efficacy should enable the risk-benefit balance of all veterinary medicinal products to be assessed both when they are placed on the market and at any other time the competent authority deems this appropriate. In this connection, it is necessary to harmonise and adapt the criteria for refusal, suspension and revocation of marketing authorisations.

(17) In the veterinary sector, if no medicinal product has been authorised for a given species or a given disorder, the possibility of using other existing products should be made a straightforward matter, but without prejudicing consumer health in the case of medicinal products intended for administration to food-producing animals. In particular, medicinal products should be used only under conditions that guarantee that the foodstuffs produced will be harmless to consumers as regards any residues of medicinal products.

(18) There is also a need to stimulate the interest of the veterinary pharmaceuticals industry in certain market segments in order to encourage the development of new veterinary medicinal products. The period of administrative data-protection vis-a-vis generics should be harmonised.

(19) There is also a need to clarify the obligations of, and division of responsibilities between, the applicant for a marketing authorisation, the holder of a marketing authorisation and the competent authorities in charge of monitoring the quality of foodstuffs, particularly through compliance with the provisions on the use of veterinary medicinal products. In addition, in order to facilitate the testing of new medicinal products while guaranteeing a high level of protection for consumers, sufficiently long withdrawal periods should be laid down for foodstuffs that animals involved in tests might produce.

(20) Without prejudice to the provisions aimed at guaranteeing consumer protection, the specific characteristics of homeopathic veterinary medicinal products, and particularly their use in organic farming, should be taken into account by establishing a simplified procedure for registration on terms defined in advance.

(21) In order to increase the information available to users and to improve consumer protection in the case of food-producing animals, the provisions on the labelling of veterinary medicinal products and the accompanying package leaflet should be strengthened. The requirement that a veterinary medicinal product may only be dispensed after a veterinary prescription has been made out should, as a general principle, be extended to all medicinal products for food-producing animals. However, it should be possible to grant exemptions, where appropriate. The administrative procedures for supplying medicinal products for pets, on the other hand, should be simplified.

(22) The quality of veterinary medicinal products manufactured or available in the Community should be guaranteed by requiring that the active substances used in their composition comply with the principles of good manufacturing practice. It has proved necessary to reinforce the Community provisions on inspections and to compile a Community register of the results of those inspections. The provisions for the official release of batches of immunological medicinal products should be reviewed in order to take account of the improvement of the general system for monitoring the quality of medicinal products and to reflect technical and scientific progress, and also in order to make mutual recognition fully effective.

(23) The environmental impact should be studied and consideration should be given on a case-by-case basis to specific provisions seeking to limit it.

(24) Pharmacovigilance and, more generally, market surveillance and sanctions in the event of failure to comply with the provisions should be stepped up. In the field of pharmacovigilance, account should be taken of the facilities offered by new information technologies to improve exchanges between Member States.

(25) The measures necessary for the implementation of this Directive 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 [1].

(26) Directive 2001/82/EC should be amended accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Directive 2001/82/EC shall be amended as follows:

1) Article 1 shall be amended as follows:

(a) point 1 shall be deleted;

(b) point 2 shall be replaced by the following:

'2. *Veterinary medicinal product:*

(a) any substance or combination of substances presented as having properties for treating or preventing disease in animals; or

(b) any substance or combination of substances which may be used in or administered to animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.';

(c) point 3 shall be deleted;

[1] OJ L 184, 17.7.1999, p. 23.

(d) points 8, 9 and 10 shall be replaced by the following:

'8. *Homeopathic veterinary medicinal product:*

Any veterinary medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in Member States. A homeopathic veterinary medicinal product may contain a number of principles.

9. *Withdrawal period:*

The period necessary between the last administration of the veterinary medicinal product to animals, under normal conditions of use and in accordance with the provisions of this Directive, and the production of foodstuffs from such animals, in order to protect public health by ensuring that such foodstuffs do not contain residues in quantities in excess of the maximum residue limits for active substances laid down pursuant to Regulation (EEC) No 2377/90.

10. *Adverse reaction:*

A reaction to a veterinary medicinal product which is harmful and unintended and which occurs at doses normally used in animals for the prophylaxis, diagnosis or treatment of disease or to restore, correct or modify a physiological function.';

(e) the following point shall be inserted:

'17a. *Representative of the marketing authorisation holder:*

The person, commonly known as local representative, designated by the marketing authorisation holder to represent him in the Member State concerned.';

(f) point 18 shall be replaced by the following:

'18. *Agency:*

The European Medicines Agency established by Regulation (EC) No 726/2004 (*);

(*) OJ L 136, 30.4.2004, p. 1.';

(g) point 19 shall be replaced by the following:

'19. *Risks relating to use of the product:*

— any risk relating to the quality, safety and efficacy of the veterinary medicinal products as regards animal or human health;

— any risk of undesirable effects on the environment.';

(h) the following points shall be added:

'20. *Risk/benefit balance:*

An evaluation of the positive therapeutic effects of the veterinary medicinal product in relation to the risks as defined above.

21. *Veterinary prescription:*

Any prescription for a veterinary medicinal product issued by a professional person qualified to do so in accordance with applicable national law.

22. *Name of veterinary medicinal product:*

The name, which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trademark or the name of the marketing authorisation holder.

23. *Common name:*

The international non-proprietary name recommended by the World Health Organisation, or, if one does not exist, the usual common name.

24. *Strength:*

The content of active substances, expressed quantitatively per dosage unit, per unit of volume or weight according to the dosage form.

25. *Immediate packaging:*

The container or any other form of packaging that is in direct contact with the medicinal product.

26. *Outer packaging:*

The packaging into which is placed the immediate packaging.

27. *Labelling:*

Information on the immediate or outer packaging.

28. *Package leaflet:*

The leaflet containing information for the user that accompanies the medicinal product.';

2) Articles 2 and 3 shall be replaced by the following:

'*Article 2*

1. This Directive shall apply to veterinary medicinal products, including pre-mixes for medicated feedingstuffs, intended to be placed on the market in Member States and prepared industrially or by a method involving an industrial process.

2. In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a "veterinary medicinal product" and within the definition of a product covered by other Community legislation, the provisions of this Directive shall apply.

3. Notwithstanding paragraph 1, this Directive shall also apply to active substances used as starting materials to the extent set out in Articles 50, 50a, 51 and 80 and additionally to certain substances that may be used as veterinary medicinal products that have anabolic, anti-infectious, anti-parasitic, anti-inflammatory, hormonal or psychotropic properties to the extent set out in Article 68.

Article 3

1. This Directive shall not apply to:

(a) medicated feedingstuffs as defined in Council Directive 90/167/EEC of 26 March 1990 laying down the conditions governing the preparation, placing on the market and use of medicated feedingstuffs in the Community (*);

(b) inactivated immunological veterinary medicinal products which are manufactured from pathogens and antigens obtained from an animal or animals from a holding and used for the treatment of that animal or the animals of that holding in the same locality;

(c) veterinary medicinal products based on radio-active isotopes;

(d) any additives covered by Council Directive 70/524/EEC of 23 November 1970 concerning additives in feedingstuffs (**) where they are incorporated in animal feedingstuffs and supplementary animal feedingstuffs in accordance with that Directive; and

(e) without prejudice to Article 95, medicinal products for veterinary use intended for research and development trials.

However, medicated feedingstuffs referred to in subparagraph (a) may be prepared only from pre-mixes that have been authorised under this Directive.

2. Except for the provisions on the possession, prescription, dispensing and administration of veterinary medicinal products, this Directive shall not apply to:

(a) any medicinal product prepared in a pharmacy in accordance with a veterinary prescription for an individual animal or a small group of animals, commonly known as the magistral formula; and

(b) any medicinal product prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and intended to be supplied directly to the end-user, commonly known as the officinal formula.

(*) OJ L 92, 7.4.1990, p. 42.

(**) OJ L 270, 14.12.1970, p. 1. Directive as last amended by Regulation (EC) No 1756/2002 (OJ L 265, 3.10.2002, p. 1).';

3) Article 4(2) shall be replaced by the following:

'2. In the case of veterinary medicinal products intended solely for aquarium fish, cage birds, homing pigeons, terrarium animals, small rodents, and ferrets and rabbits kept exclusively as pets, Member States may permit exemptions, in their territory, from the provisions in Articles 5 to 8, provided that such products do not contain substances the use of which requires veterinary control and that all possible measures are taken to prevent unauthorised use of the products for other animals.';

4) Articles 5 and 6 shall be replaced by the following:

'*Article 5*

1. No veterinary medicinal product may be placed on the market of a Member State unless a marketing authorisation has been granted by the competent authorities of that Member State in accordance with this Directive or a marketing authorisation has been granted in accordance with Regulation (EC) No 726/2004.

When a veterinary medicinal product has been granted an initial authorisation in accordance with the first subparagraph, any additional species, strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions, shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 13(1).

2. The marketing authorisation holder shall be responsible for the marketing of the medicinal product. The designation of a representative shall not relieve the marketing authorisation holder of his legal responsibility.

Article 6

1. A veterinary medicinal product may not be the subject of a marketing authorisation for the purpose of administering it to one or more food-producing species unless the pharmacologically active substances which it contains appear in Annexes I, II or III to Regulation (EEC) No 2377/90.

2. If an amendment to the Annexes to Regulation (EEC) No 2377/90 so warrants, the marketing authorisation holder or, where appropriate, the competent authorities shall take all necessary measures to amend or revoke the marketing authorisation within 60 days of the date on which the amendment to the Annexes to that Regulation was published in the *Official Journal of the European Union*.

3. By way of derogation from paragraph 1, a veterinary medicinal product containing pharmacologically active substances not included in Annexes I, II or III to Regulation (EEC) No 2377/90 may be authorised for particular animals of the equidae family that have been declared, in accordance with Commission Decision 93/623/EEC of 20 October 1993 establishing the identification document (passport) accompanying registered equidae (*) and Commission Decision 2000/68/EC of 22 December 1999 amending Decision 93/623/EEC and establishing the identification of equidae for breeding and production (**), as not being intended for slaughter for human consumption. Such veterinary medicinal products shall neither include active substances that appear in Annex IV to Regulation (EEC) No 2377/90 nor be intended for use in the treatment of conditions, as detailed in the authorised Summary of Product Characteristics, for which a veterinary medicinal product is authorised for animals of the equidae family.

(*) OJ L 298, 3.12.1993, p. 45. Decision as amended by Commission Decision 2000/68/EC (OJ L 23, 28.1.2000, p. 72).

(**) OJ L 23, 28.1.2000, p. 72.';

5) Article 8 shall be replaced by the following:

'*Article 8*

In the event of serious epizootic diseases, Member States may provisionally allow the use of immunological veterinary medicinal products without a marketing authorisation, in the absence of a suitable medicinal product and after informing the Commission of the detailed conditions of use.

The Commission may avail itself of the option set out in the first paragraph when explicit provision is made for that option under Community rules concerning certain serious epizootic diseases.

If an animal is being imported from, or exported to, a third country and is thereby subject to specific binding health rules, a Member State may permit the use, for the animal in question, of an immunological veterinary medicinal product that is not covered by a marketing authorisation in the Member State in question but is authorised under the legislation of the third country. Member States shall take all appropriate measures concerning the supervision of the importation and the use of such immunological products.';

6) Articles 10 to 13 shall be replaced by the following:

'*Article 10*

1. Member States shall take the necessary measures to ensure that, if there is no authorised veterinary medicinal product in a Member State for a condition affecting a non food-producing species, by way of exception, the veterinarian responsible may, under his/her direct personal responsibility and in particular to avoid causing unacceptable suffering, treat the animal concerned with:

(a) a veterinary medicinal product authorised in the Member State concerned under this Directive or under Regulation (EC) No 726/2004 for use with another animal species, or for another condition in the same species; or

(b) if there is no product as referred to in point (a), either:

(i) a medicinal product authorised for human use in the Member State concerned in accordance with Directive 2001/83/EC of the European Parliament and of the Council or under Regulation (EC) No 726/2004, or

(ii) in accordance with specific national measures, a veterinary medicinal product authorised in another Member State in accordance with this Directive for use in the same species or in another species for the condition in question or for another condition; or

(c) if there is no product as referred to in subparagraph (b), and within the limits of the law of the Member State concerned, a veterinary medicinal product prepared extemporaneously by a person authorised to do so under national legislation in accordance with the terms of a veterinary prescription.

The veterinarian may administer the medicinal product personally or allow another person to do so under the veterinarian's responsibility.

2. By way of derogation from Article 11, the provisions of paragraph 1 of this Article shall also apply to the treatment by a veterinarian of an animal belonging to the equidae family provided that it has been declared, in accordance with Commission Decisions 93/623/EEC and 2000/68/EC, as not being intended for slaughter for human consumption.

3. By way of derogation from Article 11, and in accordance with the procedure referred to in Article 89(2), the Commission shall establish a list of substances essential for the treatment of equidae and for which the withdrawal period shall be not less than six months according to the control mechanisms laid down in Commission Decisions 93/623/EEC and 2000/68/EC.

Article 11

1. Member States shall take the necessary measures to ensure that, if there is no authorised veterinary medicinal product in a Member State for a condition affecting a food-producing species, by way of exception, the veterinarian responsible may, under his direct personal responsibility and in particular to avoid causing unacceptable suffering, treat the animals concerned on a particular holding with:

(a) a veterinary medicinal product authorised in the Member State concerned under this Directive or under Regulation (EC) No 726/2004 for use with another animal species, or for another condition in the same species; or

(b) if there is no product as referred to in point (a), either:

(i) a medicinal product for human use authorised in the Member State concerned in accordance with Directive 2001/83/EC or under Regulation (EC) No 726/2004, or

(ii) a veterinary medicinal product authorised in another Member State in accordance with this Directive for use in the same species or in another food-producing species for the condition in question or for another condition; or

(c) if there is no product as referred to in subparagraph (b), and within the limits of the law of the Member State concerned, a veterinary medicinal product prepared extemporaneously by a person authorised to do so under national legislation in accordance with the terms of a veterinary prescription.

The veterinarian may administer the medicinal product personally or allow another person to do so under the veterinarian's responsibility.

2. Paragraph 1 shall apply provided that pharmacologically active substances included in the medicinal product are listed in Annex I, II or III to Regulation (EEC) No 2377/90, and that the veterinarian specifies an appropriate withdrawal period.

Unless the medicinal product used indicates a withdrawal period for the species concerned, the specified withdrawal period shall not be less than:

— 7 days for eggs,

— 7 days for milk,

— 28 days for meat from poultry and mammals including fat and offal,

— 500 degree-days for fish meat.

However, these specific withdrawal periods may be modified in accordance with the procedure referred to in Article 89(2).

3. With regard to homeopathic veterinary medicinal products in which active principles figure in Annex II to Regulation (EEC) No 2377/90, the withdrawal period referred to in the second subparagraph of paragraph 2 shall be reduced to zero.

4. When a veterinarian has recourse to the provisions of paragraphs 1 and 2 of this Article, he shall keep adequate records of the date of examination of the animals, details of the owner, the number of animals treated, the diagnosis, the medicinal products prescribed, the doses administered, the duration of treatment and the withdrawal periods recommended, and shall make these records available for inspection by the competent authorities for a period of at least five years.

5. Without prejudice to the other provisions of this Directive, Member States shall take all necessary measures concerning the import, distribution, dispensing of and information on the medicinal products which they permit for administration to food-producing animals in accordance with paragraph 1(b)(ii).

Article 12

1. For the purposes of obtaining a marketing authorisation in respect of a veterinary medicinal product, otherwise than under the procedure established by Regulation (EC) No 726/2004, an application shall be lodged with the competent authority of the Member State concerned.

In the case of veterinary medicinal products which are intended for one or more food-producing species but whose pharmacologically active substances have not yet been included, for the species in question, in Annexes I, II or III to Regulation (EEC) No 2377/90, a marketing authorisation may not be applied for until after a valid application has been made for the establishment of maximum residue limits in accordance with that Regulation. At least six months shall elapse between a valid application for the establishment of maximum residue limits and an application for a marketing authorisation.

However, in the case of veterinary medicinal products referred to in Article 6(3), a marketing authorisation may be applied for without a valid application in accordance with Regulation (EEC) No 2377/90. All the scientific documentation necessary for the demonstration of the quality, safety and efficacy of the veterinary medicinal product, as provided for in paragraph 3, shall be submitted.

2. A marketing authorisation may only be granted to an applicant established in the Community.

3. The application for marketing authorisation shall include all the administrative information and scientific documentation necessary for demonstrating the quality, safety and efficacy of the veterinary medicinal product in question. The file shall be submitted in accordance with Annex I and shall contain, in particular, the following information:

(a) name or business name and permanent address or registered place of business of the person responsible for placing the product on the market and, if different, of the manufacturer or manufacturers involved and of the sites of manufacture;

(b) name of veterinary medicinal product;

(c) qualitative and quantitative particulars of all the constituents of the veterinary medicinal product, including its international non-proprietary name (INN) recommended by the WHO, where an INN exists, or its chemical name;

(d) description of the method of manufacture;

(e) therapeutic indications, contra-indications and adverse reactions;

(f) dosage for the various species of animal for which the veterinary medicinal product is intended, its pharmaceutical form, method and route of administration and proposed shelf life;

(g) reasons for any precautionary and safety measures to be taken when storing the veterinary medicinal product, administering it to animals and disposing of waste, together with an indication of potential risks that the veterinary medicinal product might pose to the environment, to human and animal health and to plants;

(h) indication of the withdrawal period in the case of medicinal products intended for food-producing species;

(i) description of the testing methods employed by the manufacturer;

(j) results of:

— pharmaceutical (physico-chemical, biological or microbiological) tests,

— safety tests and residue tests,

— pre-clinical and clinical trials;

— tests assessing the potential risks posed by the medicinal product for the environment. This impact shall be studied and consideration shall be given on a case-by-case basis to specific provisions seeking to limit it.

(k) a detailed description of the pharmacovigilance system and, where appropriate, the risk management system that the applicant will put in place;

(l) a summary in accordance with Article 14 of the product characteristics, a mock-up of the immediate packaging and the outer packaging of the veterinary medicinal product, together with the package leaflet, in accordance with Articles 58 to 61;

(m) a document showing that the manufacturer is authorised in his own country to produce veterinary medicinal products;

(n) copies of any marketing authorisation obtained in another Member State or in a third country for the relevant veterinary medicinal product, together with a list of those Member States in which an application for authorisation submitted in accordance with this Directive is under examination. Copies of the summary of the product characteristics proposed by the applicant in accordance with Article 14 or approved by the competent authority of the Member State in accordance with Article 25 and copies of the package insert proposed, details of any decision to refuse authorisation, whether in the Community or a third country and the reasons for that decision. All this information shall be updated on a regular basis;

(o) proof that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country;

(p) in the case of veterinary medicinal products intended for one or more food-producing species and containing one or more pharmacologically active substances not yet included, for the species in question, in Annexes I, II or III to Regulation (EEC) No 2377/90, a document certifying that a valid application for the establishment of maximum residue limits has been submitted to the Agency in accordance with the aforementioned Regulation.

The documents and particulars relating to the results of the tests referred to in point (j) of the first subparagraph shall be accompanied by detailed and critical summaries, drawn up as specified in Article 15.

Article 13

1. By way of derogation from point (j) of the first subparagraph of Article 12(3), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 5 for not less than eight years in a Member State or the Community.

A generic veterinary medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.

The first subparagraph shall also apply when the reference medicinal product was not authorised in the Member State in which the application for the generic medicinal product is submitted. In this case, the applicant shall indicate in the application the Member State in which the reference medicinal product is or has been authorised. At the request of the competent authority of the Member State in which the application is submitted, the competent authority of the other Member State shall transmit, within a period of one month, confirmation that the reference medicinal product is or has been authorised together with the full composition of the reference product and if necessary other relevant documentation.

However, the ten-year period provided for in the second subparagraph shall be extended to 13 years in the case of veterinary medicinal products for fish or bees or other species designated in accordance with the procedure referred to in Article 89(2).

2. For the purposes of this Article:

(a) "reference medicinal product" shall mean a product authorised within the meaning of Article 5 in accordance with the provisions of Article 12;

(b) "generic medicinal product" shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information intended to provide proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required of the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.

3. In cases where the veterinary medicinal product does not fall under the definition of a generic medicinal product set out in paragraph 2(b) or where bio-equivalence cannot be demonstrated through bioavailability studies or in the case of changes to the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration vis-à-vis the reference medicinal product, the results of the appropriate safety and residue tests and pre-clinical tests or clinical trials shall be provided.

4. Where a biological veterinary medicinal product which is similar to a reference biological veterinary medicinal product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or in manufacturing processes of the biological veterinary medicinal product and the reference biological veterinary medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided. The type and quantity of supplementary data to be provided must comply with the relevant criteria stated in Annex I and the related detailed guidelines. The results of other tests and trials from the reference medicinal product's dossier shall not be provided.

5. In the case of veterinary medicinal products intended for one or more food-producing species and containing a new active substance that has not been authorised in the Community by 30 April 2004 the ten-year period provided for in the second subparagraph of paragraph 1 shall be extended by one year for each extension of the marketing authorisation to another food-producing species, if it is authorised within the five years following the granting of the initial marketing authorisation.

This period shall not, however, exceed a total of 13 years, for a marketing authorisation for four or more food-producing species.

The extension of the ten-year period to 11, 12, or 13 years for a veterinary medicinal product intended for food-producing species shall be granted only if the marketing authorisation holder also originally applied for determination of the maximum residue limits established for the species covered by the authorisation.

6. Conducting the necessary studies, tests and trials with a view to the application of paragraphs 1 to 5 and the consequential practical requirements shall not be regarded as contrary to patent-related rights or to supplementary-protection certificates for medicinal products.';

7) the following Articles shall be inserted:

'*Article 13a*

1. By way of derogation from point (j) of the first subparagraph of Article 12(3), and without prejudice to the law on the protection of industrial and commercial property, the applicant shall not be required to provide the results of safety and residue tests or of pre-clinical tests or clinical trials if he can demonstrate that the active substances of the veterinary medicinal product have been in well-established veterinary use within the Community for at least ten years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in Annex I. In that event, the applicant shall provide appropriate scientific literature.

2. The assessment report published by the Agency following the evaluation of an application for the establishment of maximum residue limits in accordance with Regulation (EEC) No 2377/90 may be used in an appropriate manner as literature, particularly for the safety tests.

3. If an applicant makes use of scientific literature to obtain authorisation for a food-producing species, and submits, in respect of the same medicinal product and with a view to obtaining authorisation for another food-producing species, new residue studies in accordance with Regulation (EEC) No 2377/90, together with further clinical trials, it shall not be permissible for a third party to use such studies or such trials pursuant to Article 13, for a period of three years from the grant of the authorisation for which they were carried out.

Article 13b

In the case of veterinary medicinal products containing active substances used in the composition of authorised veterinary medicinal products but not hitherto used in combination for therapeutic purposes, the results of safety and residue tests, if necessary, and new pre-clinical tests or new clinical trials relating to that combination shall be provided in accordance with point (j) of the first subparagraph of Article 12(3), but it shall not be necessary to provide scientific references relating to each individual active substance.

Article 13c

After the marketing authorisation has been granted, the marketing authorisation holder may allow use to be made of the pharmaceutical, safety and residues, pre-clinical and clinical documentation contained in the file for the veterinary medicinal product with a view to examining a subsequent application for a veterinary medicinal product having the same qualitative and quantitative composition in active substances and the same pharmaceutical form.

Article 13d

By way of derogation from point (j) of the first subparagraph of Article 12(3), and in exceptional circumstances with respect to immunological veterinary medicinal products, the applicant shall not be required to provide the results of certain field trials on the target species if these trials cannot be carried out for duly substantiated reasons, in particular on account of other Community provisions.';

8) Articles 14 to 16 shall be replaced by the following:

'*Article 14*

The summary of the product characteristics shall contain, in the order indicated below, the following information:

1) name of the veterinary medicinal product followed by the strength and the pharmaceutical form;

2) qualitative and quantitative composition in terms of the active substances and constituents of the excipient, knowledge of which is essential for proper administration of the medicinal product. The usual common name or chemical description shall be used;

3) pharmaceutical form;

4) clinical particulars:

4.1. target species,

4.2. indications for use, specifying the target species,

4.3. contra-indications,

4.4. special warnings for each target species,

4.5. special precautions for use, including special precautions to be taken by the person administering the medicinal product to the animals,

4.6. adverse reactions (frequency and seriousness),

4.7. use during pregnancy, lactation or lay,

4.8. interaction with other medicinal products and other forms of interaction,

4.9. amounts to be administered and administration route,

4.10. overdose (symptoms, emergency procedures, antidotes), if necessary,

4.11. withdrawal periods for the various foodstuffs, including those for which the withdrawal period is zero;

5) pharmacological properties:

5.1. pharmacodynamic properties,

5.2. pharmacokinetic particulars;

6) pharmaceutical particulars:

6.1. list of excipients,

6.2. major incompatibilities,

6.3. shelf life, when necessary after reconstitution of the medicinal product or when the immediate packaging is opened for the first time,

6.4. special precautions for storage,

6.5. nature and composition of immediate packaging,

6.6. special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products, if appropriate;

7) marketing authorisation holder;

8) marketing authorisation number(s);

9) date of the first authorisation or date of renewal of the authorisation;

10) date of revision of the text.

For authorisation under Article 13, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed need not be included.

Article 15

1. Applicants shall ensure that the detailed and critical summaries referred to in the second subparagraph of Article 12(3) are drafted and signed by persons with the requisite technical or professional qualifications, set out in a brief curriculum vitae, before being submitted to the competent authorities.

2. Persons with the technical or professional qualifications referred to in paragraph 1 shall justify any use made of the scientific literature referred to in Article 13a(1) in accordance with the conditions set out in Annex I.

3. A brief curriculum vitae of the persons referred to in paragraph 1 shall be appended to the detailed critical summaries.

Article 16

1. Member States shall ensure that homeopathic veterinary medicinal products manufactured and placed on the market within the Community are registered or authorised in accordance with Articles 17, 18 and 19, except where such veterinary medicinal products are covered by a registration or authorisation granted in accordance with national legislation on or before 31 December 1993. In the case of homeopathic medicinal products registered in accordance with Article 17, Article 32 and Article 33(1) to (3) shall apply.

2. Member States shall establish a simplified registration procedure for the homeopathic veterinary medicinal products referred to in Article 17.

3. By way of derogation from Article 10, homeopathic veterinary medicinal products may be administered to non-food producing animals under the responsibility of a veterinarian.

4. By way of derogation from Article 11(1) and (2), Member States shall permit the administration of homeopathic veterinary medicinal products intended for food-producing species the active constituents of which appear in Annex II to Regulation (EEC) No 2377/90 under the responsibility of a veterinarian. Member States shall take appropriate measures to control the use of veterinary homeopathic medicinal products registered or authorised in another Member State in accordance with this Directive for use in the same species.';

9) Article 17 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. Without prejudice to the provisions of Regulation (EEC) No 2377/90 on the establishment of maximum residue limits of pharmacologically active substances intended for food-producing animals, only homeopathic veterinary medicinal products which satisfy all of the following conditions may be subject to a special, simplified registration procedure:

(a) they are administered by a route described in the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in Member States;

(b) no specific therapeutic indication appears on the labelling of the veterinary medicinal product or in any information relating thereto;

(c) there is a sufficient degree of dilution to guarantee the safety of the medicinal product. In particular, the medicinal product shall not contain more than one part per 10 000 of the mother tincture.

If it appears justified in the light of new scientific evidence, points (b) and (c) of the first subparagraph may be adapted in accordance with the procedure referred to in Article 89(2).

At the time of registration, Member States shall determine the classification for the dispensing of the medicinal product.';

(b) paragraph 3 shall be deleted;

10) Article 18 shall be amended as follows:

(a) the third indent shall be replaced by the following:

'— manufacturing and control file for each pharmaceutical form and a description of the method of dilution and potentisation,';

(b) the sixth indent shall be replaced by the following:

'— one or more mock-ups of the outer packaging and immediate packaging of the medicinal products to be registered,';

(c) the following eighth indent shall be added:

'— proposed withdrawal period together with all requisite justification.';

11) Article 19 shall be replaced by the following:

'*Article 19*

1. Homeopathic veterinary medicinal products other than those referred to in Article 17(1) shall be authorised in accordance with Articles 12, 13a, 13b, 13c, 13d and 14.

2. A Member State may introduce or retain on its territory specific rules for the safety tests and pre-clinical and clinical trials of homeopathic veterinary medicinal products intended for pet species and non-food-producing exotic species other than those referred to in Article 17(1), in accordance with the principles and characteristics of homeopathy as practised in that Member State. In this case, the Member State concerned shall notify the Commission of the specific rules in force.';

12) Articles 21, 22 and 23 shall be replaced by the following:

'*Article 21*

1. Member States shall take all appropriate measures to ensure that the procedure for granting a marketing authorisation for a veterinary medicinal product is completed within a maximum of 210 days after the submission of a valid application.

Applications for marketing authorisations for the same veterinary medicinal product in two or more Member States, shall be submitted in accordance with Articles 31 to 43.

2. Where a Member State notes that another marketing authorisation application for the same medicinal product is being examined in another Member State, the Member State concerned shall decline to assess the application and shall advise the applicant that Articles 31 to 43 apply.

Article 22

Where a Member State is informed, in accordance with point (n) of Article 12(3), that another Member State has authorised a veterinary medicinal product which is the subject of an application for authorisation in the Member State concerned, that Member State shall reject the application unless it was submitted in compliance with Articles 31 to 43.

Article 23

In order to examine the application submitted pursuant to Articles 12 to 13d, Member States' competent authorities:

1) shall check that the documentation submitted in support of the application complies with Articles 12 to 13d and ascertain whether the conditions for the issue of the marketing authorisation have been fulfilled;

2) may submit the medicinal product, its starting materials and if necessary intermediate products or other constituent materials for testing by an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose, in order to ensure that the testing methods employed by the manufacturer and described in the application documents, in accordance with point (i) of the first subparagraph of Article 12(3), are satisfactory;

3) may similarly check, in particular through consultation of a national or Community reference laboratory, that the analytical method used for detecting residues presented by the applicant for the purposes of Article 12(3)(j), second indent is satisfactory;

4) may, where appropriate, require the applicant to provide further information as regards the items listed in Articles 12, 13a, 13b, 13c and 13d. Where the competent authorities take this course of action, the time-limits specified in Article 21 shall be suspended until the further data required have been provided. Similarly, these time-limits shall be suspended for any period which the applicant may be given to provide oral or written explanations.';

13) Article 25 shall be replaced by the following:

'*Article 25*

1. When granting a marketing authorisation, the competent authority shall inform the holder of the summary of product characteristics that it has approved.

2. The competent authority shall take all necessary measures to ensure that information concerning the veterinary medicinal product, and in particular the labelling and package leaflet, is in conformity with the summary of product characteristics approved when the marketing authorisation was granted or subsequently.

3. The competent authority shall make the marketing authorisation publicly available without delay, together with the summary of product characteristics for each veterinary medicinal product that it has authorised.

4. The competent authority shall draw up an assessment report and comments on the file as regards the results of the pharmaceutical, safety and residue tests and the pre-clinical and clinical trials of the veterinary medicinal product concerned. The assessment report shall be updated whenever new information becomes available which is of importance for the evaluation of the quality, safety or efficacy of the veterinary medicinal product concerned.

The competent authority shall make the assessment report and its reasons for the opinion publicly available without delay, after deleting any information of a commercially confidential nature.';

14) Article 26 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. The marketing authorisation may require the holder to indicate on the immediate packaging and/or the outer wrapping and the package leaflet, where the latter is required, other particulars essential for safety or health protection, including any special precautions relating to use and any other warnings resulting from the clinical and pharmacological trials prescribed in Article 12(3)(j) and in Articles 13 to 13d or from experience gained during the use of the veterinary medicinal product once it has been marketed.'.

(b) paragraph 2 shall be deleted;

(c) paragraph 3 shall be replaced by the following:

'3. 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 veterinary medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. Such authorisations may be granted only for objective, verifiable reasons. Continuation of the authorisation shall be linked to the annual reassessment of these conditions.';

15) Article 27 shall be amended as follows:

(a) paragraphs 2 and 3 shall be replaced by the following:

'2. The competent authority may require the applicant or the marketing authorisation holder to provide sufficient quantities of the substances to enable controls to be made on the identification of the presence of residues of the veterinary medicinal products in question.

At the competent authority's request, the marketing authorisation holder shall provide his technical expertise to facilitate the implementation of the analytical method for detecting residues of the veterinary medicinal products in the national reference laboratory designated under Council Directive 96/23/EC of 29 April 1996 on measures to monitor certain substances and residues thereof in live animals and animal products (*).

3. The authorisation holder shall immediately supply the competent authority with any new information that might entail the amendment of the particulars or documents referred to in Articles 12(3), 13, 13a, 13b and 14 or Annex I.

In particular, he shall immediately inform the competent authority of any prohibition or restriction imposed by the competent authorities of any country in which the veterinary medicinal product is placed on the market and of any other new information which might influence the assessment of the benefits and risks of the veterinary medicinal product concerned.

In order to permit continuous assessment of the risk-benefit balance, the competent authority may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance remains favourable.

(*) 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).';

(b) paragraph 4 shall be deleted;

(c) paragraph 5 shall be replaced by the following:

'5. The marketing authorisation holder shall immediately inform the competent authorities, with a view to authorisation, of any alteration which he proposes to make to the particulars or documents referred to in Articles 12 to 13d.';

16) the following Article shall be inserted:

'*Article 27a*

After a marketing authorisation has been granted, the holder of the authorisation shall inform the competent authority of the authorising Member State of the date of the actual placing on the market of the veterinary medicinal product in that Member State, taking into account the various presentations authorised.

The holder shall also notify the competent authority if the product ceases to be placed on the market of the Member State, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product.

Upon request by the competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the volume of sales of the veterinary medicinal product, and any data in his possession relating to the volume of prescriptions.';

17) Article 28 shall be replaced by the following:

'*Article 28*

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

2. The authorisation may be renewed after five years on the basis of a re-evaluation 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 competent authority 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 competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal in accordance with paragraph 2.

4. Any authorisation that is not followed within three years of its granting by the actual placing on the market of the authorised veterinary medicinal product in the authorising Member State shall cease to be valid.

5. When an authorised veterinary medicinal product previously placed on the market in the authorising Member State is no longer actually present on the market in that Member State for a period of three consecutive years, the authorisation granted for that veterinary medicinal product shall cease to be valid.

6. The competent authority may, in exceptional circumstances, and on human or animal health grounds, grant exemptions from paragraphs 4 and 5. Such exemptions shall be duly justified.';

18) Article 30 shall be replaced by the following:

'*Article 30*

The marketing authorisation shall be refused if the file submitted to the competent authorities does not comply with Articles 12 to 13d and Article 15.

The authorisation shall also be refused if, after examination of the documents and particulars listed in Articles 12 and 13(1), it is clear that:

(a) the risk-benefit balance of the veterinary medicinal product is, under the authorised conditions of use, unfavourable; when the application concerns a veterinary medicinal product for zootechnical use, particular regard shall be had to the benefits for animal health and welfare and to consumer safety; or

(b) the product has no therapeutic effect or the applicant has not provided sufficient proof of such effect as regards the species of animal which is to be treated; or

(c) its qualitative or quantitative composition is not as stated; or

(d) the withdrawal period recommended by the applicant is not long enough to ensure that foodstuffs obtained from the treated animal do not contain residues which might constitute a health hazard to the consumer, or is insufficiently substantiated; or

(e) the labelling or the package leaflet proposed by the applicant does not comply with this Directive; or

(f) the veterinary medicinal product is offered for sale for a use prohibited under other Community provisions.

However, when a Community legislative framework is in the course of being adopted, the competent authority may refuse authorisation for a veterinary medicinal product where such action is necessary for the protection of public health, consumer or animal health.

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

19) the title of Chapter 4 shall be replaced by the following:

'*CHAPTER 4*

Mutual recognition procedure and decentralised procedure';

20) Articles 31 to 37 shall be replaced by the following:

'*Article 31*

1. A coordination group shall be set up for the examination of any question relating to marketing authorisation of a veterinary medicinal product in two or more Member States in accordance with the procedures laid down in this Chapter. The Agency shall provide the secretariat of this coordination group.

2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of three years. Members of the group may arrange to be accompanied by experts.

3. The coordination group shall draw up its own rules of procedure, which shall enter into force after a favourable opinion has been given by the Commission. These rules of procedure shall be made public.

Article 32

1. With a view to the granting of a marketing authorisation for a veterinary medicinal product in more than one Member State, the applicant shall submit an application based on an identical dossier in those Member States. The dossier shall contain all the administrative information and scientific and technical documentation described in Articles 12 to 14. The documents submitted shall include a list of Member States concerned by the application.

The applicant shall request one Member State to act as reference Member State and to prepare an assessment report in respect of the veterinary medicinal product in accordance with paragraphs 2 or 3.

Where appropriate, the assessment report shall contain an evaluation for the purposes of Article 13(5) or Article 13a(3).

2. If the veterinary medicinal product has already received a marketing authorisation at the time of application, the concerned Member States shall recognise the marketing authorisation granted by the reference Member State. To this end, the marketing authorisation holder shall request the reference Member State either to prepare an assessment report in respect of the veterinary medicinal product or, if necessary, to update any existing assessment report. The reference Member State shall prepare or update the assessment report within 90 days of receipt of a valid application. The assessment report together with the approved summary of product characteristics, labelling and package leaflet shall be forwarded to the concerned Member States and the applicant.

3. If the veterinary medicinal product has not received authorisation by the time of application, the applicant shall request the reference Member State to prepare a draft assessment report and drafts of the summary of product characteristics, labelling and package leaflet. The reference Member State shall prepare these drafts within 120 days of the receipt of a valid application and shall send them to the concerned Member States and the applicant.

4. Within 90 days after receipt of the documents referred to in paragraphs 2 and 3, the Member States concerned shall approve the assessment report, the summary of product characteristics, the labelling and the package leaflet and inform the reference Member State accordingly. The reference Member State shall record the agreement of all parties, close the procedure and inform the applicant accordingly.

5. Each Member State in which an application following paragraph 1 has been submitted shall adopt a decision in conformity with the approved assessment report, summary of product characteristics, labelling and package leaflet within 30 days after acknowledgement of the agreement.

Article 33

1. If a Member State cannot, within the period allowed in Article 32(4), agree with the assessment report, summary of product characteristics, labelling and package leaflet on grounds of a potential serious risk to human or animal health or to the environment, a detailed statement of the reasons shall be provided to the reference Member State, the other Member States concerned and the applicant. The points of disagreement shall be referred without delay to the coordination group.

If a Member State to which an application has been submitted invokes the reasons referred to in Article 71(1), it shall no longer be regarded as a Member State concerned by this Chapter.

2. The Commission shall adopt guidelines defining a potential serious risk for human or animal health or for the environment.

3. Within the coordination group, all Member States referred to in paragraph 1 shall use their best endeavours to reach agreement on the action to be taken. They shall provide the applicant with the opportunity to make his point of view known orally or in writing. If, within 60 days of the communication of the reasons for disagreement to the coordination group the Member States reach an agreement, the reference Member State shall record the agreement, close the procedure and inform the applicant accordingly. Article 32(5) shall apply.

4. If within the period of 60 days the Member States fail to reach an agreement, the Agency shall be immediately informed with a view to application of the procedure laid down in Articles 36, 37 and 38. The Agency shall be provided with a detailed description of the matters on which agreement could not be reached and the reasons for the disagreement. The applicant shall be provided with a copy of this information.

5. As soon as the applicant has been informed that the matter has been referred to the Agency, he shall forthwith forward to the Agency a copy of the information and documents referred to in the first subparagraph of Article 32(1).

6. In the case referred to in paragraph 4, the Member States that have approved the assessment report, summary of product characteristics, labelling and package leaflet of the reference Member State may, on request by the applicant, grant a marketing authorisation for the veterinary medicinal product without waiting for the outcome of the procedure laid down in Article 36. In that case, the authorisation granted shall be without prejudice to the outcome of that procedure.

Article 34

1. If two or more applications submitted in accordance with Articles 12 to 14 have been made for marketing authorisation for a particular veterinary medicinal product and Member States have adopted divergent decisions concerning the authorisation of that veterinary medicinal product, or suspension or revocation of authorisation, a Member State, or the Commission, or the marketing-authorisation holder may refer the matter to the Committee for Medicinal Products for Veterinary Use, hereinafter referred to as "the Committee", for the application of the procedure laid down in Articles 36, 37 and 38.

2. With a view to promoting the harmonisation of veterinary medicinal products authorised in the Community, and to strengthening the efficiency of the provisions of Articles 10 and 11, Member States shall send to the coordination group, no later than 30 April 2005, a list of veterinary medicinal products for which a harmonised summary of product characteristics should be prepared.

The coordination group shall agree on a list of medicinal products, on the basis of proposals sent by Member States, and shall forward the list to the Commission.

The medicinal products on the list shall be subject to the provisions in paragraph 1 in accordance with a timetable established in cooperation with the Agency.

The Commission, acting in collaboration with the Agency, and taking into consideration the views of the interested parties, shall agree the final list and timetable.

Article 35

1. Member States or the Commission or the applicant or marketing authorisation holder shall, in specific cases where the interests of the Community are involved, refer the matter to the Committee for the application of the procedure laid down in Articles 36, 37 and 38 before a decision is reached on a request for a marketing authorisation or on the suspension or withdrawal of an authorisation, or on any other variations to the terms of a marketing authorisation which appear necessary, so as to take account in particular of the information collected in accordance with Title VII.

The Member State concerned or the Commission shall clearly identify the question which is referred to the Committee for consideration and shall inform the applicant or the marketing authorisation holder.

The Member State and the applicant or the marketing authorisation holder shall forward to the Committee all available information relating to the matter in question.

2. Where the referral to the Committee concerns a range of medicinal products or a therapeutic class, the Agency may limit the procedure to specific parts of the authorisation.

In that case, Article 39 shall apply to those medicinal products only if they are covered by the marketing authorisation procedure referred to in this Chapter.

Article 36

1. When reference is made to the procedure laid down in this Article, the Committee shall consider the matter concerned and shall issue a reasoned opinion within 60 days of the date on which the matter was referred to it.

However, in cases submitted to the Committee in accordance with Articles 34 and 35, this period may be extended by the Committee for a further period of up to 90 days, taking into account the views of the marketing authorisation holders concerned.

In an emergency, and on a proposal from its Chairman, the Committee may agree to a shorter deadline.

2. In order to consider the matter, the Committee shall appoint one of its members to act as rapporteur. The Committee may also appoint independent experts to advise it on specific questions. When appointing such experts, the Committee shall define their tasks and specify the time limit for the completion of these tasks.

3. Before issuing its opinion, the Committee shall provide the applicant or the marketing authorisation holder with an opportunity to present written or oral explanations within a time limit that it will specify.

The opinion of the Committee shall include the draft summary of product characteristics and the drafts of the labelling and package leaflet.

If it considers appropriate, the Committee may invite any other person to provide information relating to the matter before it.

The Committee may suspend the time limit referred to in paragraph 1 to allow the applicant or the marketing authorisation holder to prepare the explanations.

4. The Agency shall forthwith inform the applicant or the marketing authorisation holder when the opinion of the Committee is that:

— the application does not satisfy the criteria for authorisation, or

— the summary of product characteristics proposed by the applicant or the marketing authorisation holder in accordance with Article 14 should be amended, or

— the authorisation should be granted subject to conditions, with regard to conditions considered essential for the safe and effective use of the veterinary medicinal product including pharmacovigilance, or

— a marketing authorisation should be suspended, varied or revoked.

Within 15 days after receipt of the opinion, the applicant or the marketing authorisation holder may notify the Agency in writing of his intention to request a re-examination of the opinion. In that case, he 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 Committee shall re-examine its opinion in accordance with the fourth subparagraph of Article 62(1) of Regulation (EC) No 726/2004. The reasons for the conclusion reached shall be annexed to the assessment report referred to in paragraph 5 of this Article.

5. Within 15 days after its adoption, the Agency shall forward the final opinion of the Committee to Member States, the Commission and the applicant or the marketing authorisation holder, together with a report describing the assessment of the veterinary medicinal product and the reasons for its conclusions.

In the event of an opinion in favour of granting or maintaining a marketing authorisation, the following documents shall be annexed to the opinion:

(a) a draft summary of the product characteristics, as referred to in Article 14; where necessary this will reflect the differences in the veterinary conditions in Member States;

(b) any conditions affecting the authorisation within the meaning of paragraph 4;

(c) details of any recommended conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product; and

(d) drafts of the labelling and package leaflet.

Article 37

Within 15 days after receipt of the opinion, the Commission shall prepare a draft of the decision to be taken in respect of the application, taking into account Community law.

In the event of a draft decision that envisages the granting of a marketing authorisation, the documents referred to in the second subparagraph of Article 36(5) shall be annexed.

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

The draft decision shall be forwarded to Member States and the applicant or marketing authorisation holder.';

21) Article 38 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. The Commission shall take a final decision in accordance with, and within 15 days after the end of, the procedure referred to in Article 89(3).';

(b) In paragraph 2, the second and third indents shall be replaced by the following:

'— 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,

— Member States shall have the option of submitting a written request that the draft decision be discussed in a plenary meeting of the Standing Committee.';

(c) paragraph 3 shall be replaced by the following:

'3. A decision as referred to in paragraph 1 shall be addressed to all Member States and communicated to the marketing authorisation holder or the applicant for information. The concerned Member States and the reference Member State shall either grant or withdraw marketing authorisation, or vary the terms of a marketing authorisation as necessary to comply with the decision within 30 days of its notification and shall refer to it. They shall inform the Commission and the Agency accordingly.';

22) in Article 39, the third subparagraph of paragraph 1 shall be deleted;

23) in Article 42, paragraph 2 shall be replaced by the following:

'2. At least every ten years the Commission shall publish a report on experience gained on the basis of the procedures provided for in this chapter and shall propose any amendments necessary to improve the procedures. The Commission shall submit this report to the European Parliament and the Council.';

24) Article 43 shall be replaced by the following:

'*Article 43*

Articles 33(4), (5) and (6) and 34 to 38 shall not apply to the homeopathic veterinary medicinal products referred to in Article 17.

Articles 32 to 38 shall not apply to the homeopathic veterinary medicinal products referred to in Article 19(2).';

25) in Article 44, the following paragraph shall be added:

'4. The Member State shall forward to the Agency a copy of the manufacturing authorisations referred to in paragraph 1. The Agency shall enter that information in the Community database referred to in Article 80(6).';

26) in Article 50, point (f) shall be replaced by the following:

'(f) comply with the principles and the guidelines on good manufacturing practice for medicinal products and use as starting materials only active substances which have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials.';

27) the following Article shall be inserted:

'*Article 50a*

1. For the purposes of this Directive, manufacturing active substances for use as starting materials shall include the complete or partial manufacture or the import of an active substance used as a starting material, as defined in Part 2, Section C of Annex I, and the various processes of dividing up, packaging or presentation prior to its incorporation in a veterinary medicinal product, including repackaging or re-labelling, such as carried out by a starting material distributor.

2. Any amendments which may be necessary to adapt the provisions of this Article to scientific and technical progress shall be adopted in accordance with the procedure referred to in Article 89(2).';

28) in Article 51, the following paragraphs shall be added:

'The principles of good manufacturing practice as regards the manufacturing of active substances for use as starting materials as referred to in Article 50(f) shall be adopted in the form of detailed guidelines.

The Commission shall also publish guidelines on the form and content of the authorisation referred to in Article 44(1), the reports referred to in Article 80(3) and the form and content of the certificate of good manufacturing practice referred to in Article 80(5).';

29) in Article 53, paragraph 1 shall be replaced by the following:

'1. Member States shall ensure that the qualified person referred to in Article 52(1) fulfils the conditions of qualification referred to in paragraphs 2 and 3.';

30) in Article 54, paragraph 1 shall be replaced by the following:

'1. A person engaging, in a Member State, in the activities of the person referred to in Article 52(1) on the date on which Directive 81/851/EEC became applicable, without complying with the provisions of Article 53, shall be eligible to continue to engage in those activities within the Community.';

31) in Article 55, paragraph 1(b) shall be replaced by the following:

'(b) in the case of veterinary medicinal products coming from third countries, even if manufactured in the Community, each production batch imported has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances, and all the other tests or controls necessary to ensure the quality of veterinary medicinal products in accordance with the requirements of the marketing authorisation.';

32) Article 58 shall be amended as follows:

(a) paragraph 1 shall be amended as follows:

(i) The introductory wording shall be replaced by the following:

'Except in the case of the medicinal products referred to in Article 17(1), the competent authority shall approve the immediate packaging and outer packaging of veterinary medicinal products. Packaging shall bear the following information, which shall conform with the particulars and documents provided pursuant to Articles 12 to 13d and the summary of product characteristics, and shall appear in legible characters:';

(ii) Points (a) and (b) shall be replaced by the following:

'(a) the name of the medicinal product, followed by its strength and pharmaceutical form. The common name shall appear if the medicinal product contains only one active substance and its name is an invented name;

(b) a statement of the active substances expressed qualitatively and quantitatively per unit or according to the form of administration for a particular volume or weight, using the common names;';

(iii) Point (e) shall be replaced by the following:

'(e) name or corporate name and permanent address or registered place of business of the marketing authorisation holder and, where appropriate, of the representative designated by the marketing authorisation holder;';

(iv) Point (f) shall be replaced by the following:

'(f) the species of animal for which the veterinary medicinal product is intended; the method and, if necessary, the route of administration. Space shall be provided for the prescribed dose to be indicated;';

(v) Point (g) shall be replaced by the following:

'(g) the withdrawal period for veterinary medicinal products to be administered to food-producing species, for all the species concerned and for the various foodstuffs concerned (meat and offal, eggs, milk, honey), including those for which the withdrawal period is zero;';

(vi) Point (j) shall be replaced by the following:

'(j) specific precautions relating to the disposal of unused medicinal products or waste derived from veterinary medicinal products, where appropriate, as well as a reference to any appropriate collection system in place;';

(vii) Point (l) shall be replaced by the following:

'(l) the words "For animal treatment only" or, in the case of the medicinal products referred to in Article 67, the words "For animal treatment only — to be supplied only on veterinary prescription".';

(b) the following paragraph shall be added:

'5. In the case of medicinal products that have been granted a marketing authorisation under Regulation (EC) No 726/2004, Member States may permit or require that the outer packaging bear additional information concerning distribution, possession, sale or any necessary precautions, provided that such information is not in infringement of Community law or the terms of the marketing authorisation, and is not promotional.

This additional information shall appear in a box with a blue border to separate it clearly from the information referred to in paragraph 1.';

33) Article 59 shall be amended as follows:

(a) the introductory wording of paragraph 1 shall be replaced by the following:

'1. As regards ampoules, the particulars listed in the first paragraph of Article 58(1) shall be given on the outer package. On the immediate packaging, however, only the following particulars shall be necessary:';

(b) paragraphs 2 and 3 shall be replaced by the following:

'2. As regards small immediate packaging containing a single dose, other than ampoules, on which it is impossible to give the particulars mentioned in paragraph 1, the requirements of Article 58(1), (2) and (3) shall apply only to the outer package.

3. The particulars mentioned in the third and sixth indents of paragraph 1 shall appear on the outer package and on the immediate packaging of the medicinal products in the language or languages of the country in which they are placed on the market.';

34) Article 60 shall be replaced by the following:

'*Article 60*

Where there is no outer package, all the particulars which should feature on such a package pursuant to Articles 58 and 59 shall be shown on the immediate packaging.';

35) Article 61 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. The inclusion of a package leaflet in the packaging of veterinary medicinal products shall be obligatory unless all the information required by this Article can be conveyed on the immediate packaging and the outer packaging. Member States shall take all appropriate measures to ensure that the package leaflet relates solely to the veterinary medicinal product with which it is included. The package leaflet shall be written in terms that are comprehensible to the general public and in the official language or languages of the Member State in which the medicinal product is marketed.

The first subparagraph shall not prevent the package leaflet from being written in several languages, provided that the information given is identical in all the languages.

Competent authorities may exempt labels and package leaflets for specific veterinary medicinal products from the obligation for certain particulars to appear and for the leaflet to be in the official language or languages of the Member State in which the product is placed on the market, when the product is intended to be administered only by a veterinarian.';

(b) paragraph 2 shall be amended as follows:

(i) The introductory wording shall be replaced by the following:

'2. The competent authorities shall approve package leaflets. Leaflets shall contain at least the following information, in the order indicated, which shall conform to the particulars and documents provided pursuant to Articles 12 to 13d and the approved summary of product characteristics:';

(ii) Points (a) and (b) shall be replaced by the following:

'(a) name or corporate name and permanent address or registered place of business of the marketing authorisation holder and of the manufacturer and, where appropriate, of the representative of the marketing authorisation holder;

(b) name of the veterinary medicinal product followed by its strength and pharmaceutical form. The common name shall appear if the product contains only one active substance and its name is an invented name. Where the medicinal product is authorised according to the procedure provided for in Articles 31 to 43 under different names in the Member States concerned, a list of the names authorised in each Member State;';

(c) paragraph 3 shall be deleted;

36) Article 62 shall be replaced by the following:

'*Article 62*

Where the provisions of this Title are not observed and a formal notice addressed to the person concerned has been ineffectual, Member States' competent authorities may suspend or revoke the marketing authorisation.';

37) Article 64(2) shall be amended as follows:

(a) the introductory wording shall be replaced by the following:

'2. In addition to the clear mention of the words "homeopathic veterinary medicinal product without approved therapeutic indications", the labelling and, where appropriate, package leaflet for the homeopathic veterinary medicinal products referred to in Article 17(1) shall bear the following information and no other information:';

(b) the first indent shall be replaced by the following:

'— the scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the pharmacopoeia used in accordance with point (8) of Article 1. If the homeopathic veterinary medicinal product is composed of more than one stock, the labelling may mention an invented name in addition to the scientific names of the stocks,';

38) the title of Title VI shall be replaced by the following:

'TITLE VI

POSSESSION, DISTRIBUTION AND DISPENSING OF VETERINARY MEDICINAL PRODUCTS';

39) Article 65 shall be amended as follows:

(a) the following paragraph shall be inserted:

'3a. The holder of a distribution authorisation shall have an emergency plan guaranteeing the effective implementation of any recall operation ordered by the competent authorities or undertaken in cooperation with the manufacturer of the medicinal product in question or the holder of the marketing authorisation.';

(b) the following paragraph shall be inserted:

'5. Any distributor, not being the marketing authorisation holder, who imports a product from another Member State shall notify the marketing authorisation holder and the competent authority in the Member State to which the product will be imported of his intention to import it. In the case of products which have not been granted an authorisation pursuant to Regulation (EC) No 726/2004, the notification to the competent authority shall be without prejudice to additional procedures provided for in the legislation of that Member State.';

40) Article 66 shall be amended as follows:

(a) paragraph 2 shall be amended as follows:

(i) The introductory wording shall be replaced by the following:

'Any person permitted under paragraph 1 to supply veterinary medicinal products shall be required to keep detailed records for veterinary medicinal products that may be supplied only on prescription, the following information being recorded in respect of each incoming or outgoing transaction:';

(ii) The third subparagraph shall be replaced by the following:

'These records shall be available for inspection by the competent authorities for a period of five years.';

(b) paragraph 3 shall be replaced by the following:

'3. Member States may permit the supply on their territory of veterinary medicinal products for food-producing animals for which a veterinary prescription is required by or under the supervision of a person registered for this purpose who provides guarantees with respect to qualifications, record-keeping and reporting in accordance with national law. Member States shall notify the Commission of relevant provisions of national law. This provision shall not apply to the supply of veterinary medicinal products for the oral or parenteral treatment of bacterial infections.';

(c) paragraph 4 shall be deleted;

41) Article 67 shall be amended as follows:

(a) the first paragraph shall be amended as follows:

(i) The introductory wording shall be replaced by the following:

'Without prejudice to stricter Community or national rules relating to dispensing veterinary medicinal products and serving to protect human and animal health, a veterinary prescription shall be required for dispensing to the public the following veterinary medicinal products:';

(ii) The following point shall be inserted:

'(aa) veterinary medicinal products for food-producing animals.

However, Member States may grant exemptions from this requirement according to criteria established in accordance with the procedure referred to in Article 89(2).

Member States may continue to apply national provisions until either:

(i) the date of application of the decision adopted in accordance with the first subparagraph; or

(ii) 1 January 2007, if no such decision has been adopted by 31 December 2006;';

(iii) The third indent of point (b) shall be deleted;

(iv) Point (d) shall be replaced by the following:

'(d) official formula, within the meaning of Article 3(2)(b), intended for food-producing animals.';

(b) the second paragraph shall be replaced by the following:

'Member States shall take all necessary measures to ensure that, in the case of medicinal products supplied only on prescription, the quantity prescribed and supplied shall be restricted to the minimum amount required for the treatment or therapy concerned.

In addition, a prescription shall be required for new veterinary medicinal products containing an active substance that has been authorised for use in a veterinary medicinal product for fewer than five years.';

42) the first paragraph of Article 69 shall be replaced by the following:

'Member States shall ensure that the owners or keepers of food-producing animals can provide proof of purchase, possession and administration of veterinary medicinal products to such animals for five years after their administration, including when the animal is slaughtered during the five-year period.';

43) the introductory wording of Article 70 shall be replaced by the following:

'By way of derogation from Article 9 and without prejudice to Article 67, Member States shall ensure that veterinarians providing services in another Member State can take with them and administer to animals small quantities of veterinary medicinal products not exceeding daily requirements other than immunological veterinary medicinal products which are not authorised for use in the Member State in which the services are provided (hereinafter: "host Member State"), provided that the following conditions are satisfied:';

44) the following subparagraph shall be added to Article 71(1):

'The Member State may also invoke the provisions of the first subparagraph in order to withhold marketing authorisation in accordance with a decentralised procedure as provided for in Articles 31 to 43.';

45) in Article 72, paragraph 2 shall be replaced by the following:

'2. Member States may impose specific requirements on veterinary practitioners and other health-care professionals in respect of the reporting of suspected serious or unexpected adverse reactions and human adverse reactions.';

46) Article 73 shall be amended as follows:

(a) the first paragraph shall be replaced by the following:

'In order to ensure the adoption of appropriate and harmonised regulatory decisions concerning the veterinary medicinal products authorised within the Community, having regard to information obtained about suspected adverse reactions to veterinary medicinal products under normal conditions of use, Member States shall administer a veterinary pharmacovigilance system. This system shall be used to collect information useful in the surveillance of veterinary medicinal products, with particular reference to adverse reactions in animals and in human beings relating to the use of veterinary medicinal products, and to evaluate such information scientifically.';

(b) after the second paragraph, the following paragraph shall be inserted:

'Member States shall ensure that suitable information collected within this system is communicated to other Member States and the Agency. This information shall be recorded in the database referred to in point (k) of the second subparagraph of Article 57(1) of Regulation (EC) No 726/2004 and shall be permanently accessible to all Member States and without delay to the public.';

47) The following article shall be inserted:

'*Article 73a*

The management of funds intended for activities connected with pharmacovigilance, the operation of communication networks and market surveillance shall be under the permanent control of the competent authorities in order to guarantee their independence.'

48) The introductory wording of the second paragraph of Article 74 shall be replaced by the following:

'That qualified person shall reside in the Community and shall be responsible for the following:';

49) Article 75 shall be replaced by the following:

'*Article 75*

1. The marketing authorisation holder shall maintain detailed records of all suspected adverse reactions occurring within the Community or in a third country.

Save in exceptional circumstances, these reactions shall be communicated electronically in the form of a report in accordance with the guidelines referred to in Article 77(1).

2. The marketing authorisation holder shall record all suspected serious adverse reactions and human adverse reactions relating to the use of veterinary medicinal products that are brought to his attention, and report them promptly to the competent authority of the Member State on whose territory the incident occurred, and no later than 15 days following receipt of the information.

The marketing authorisation holder shall also record all suspected serious adverse reactions and human adverse reactions related to the use of veterinary medicinal products of which he can reasonably be expected to have knowledge, and report them promptly to the competent authority of Member State on whose territory the incident occurred, and no later than 15 days following receipt of the information.

3. The marketing authorisation holder shall ensure that all suspected serious unexpected adverse reactions, human adverse reactions and any suspected transmission via a veterinary medicinal product of any infectious agent occurring on the territory of a third country are reported promptly in accordance with the guidelines referred to in Article 77(1), so that they are available to the Agency and the competent authorities of the Member States in which the veterinary medicinal product is authorised, and no later than 15 days following the receipt of the information.

4. By way of derogation from paragraphs 2 and 3, in the case of veterinary medicinal products which are covered by Directive 87/22/EEC, have benefited from the authorisation procedures under Articles 31 and 32 of this Directive or have been the subject of the procedures provided for in Articles 36, 37 and 38 of this Directive, the marketing authorisation holder shall additionally ensure that all suspected serious adverse reactions and human adverse reactions occurring in the Community are reported in such a way so as to be accessible to the reference Member State or a competent authority designated as reference Member State. The reference Member State shall assume responsibility for the analysis and follow-up of any such adverse reactions.

5. Unless other requirements have been laid down as a condition for the granting of the marketing authorisation or subsequently as indicated in the guidelines referred to in Article 77(1), reports of all adverse reactions shall be submitted to the competent authorities in the form of a periodic safety update report, 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 market and once a year for the following two years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request.

The periodic safety update reports shall include a scientific evaluation of the risk-benefit balance of the veterinary medicinal product.

6. Amendments to paragraph 5 may be adopted in accordance with the procedure referred to in Article 89(2) in the light of the experience gained from its operation.

7. Following the granting of a marketing authorisation, the holder of such authorisation may request the amendment of the periods referred to in paragraph 5 of this Article in accordance with the procedure laid down by Commission Regulation (EC) No 1084/2003 (*).

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

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.

(*) OJ L 159, 27.6.2003, p. 1.';

50) Article 76(1) shall be replaced by the following:

'1. The Agency, in collaboration with Member States and the Commission, shall set up a data-processing network to facilitate the exchange of pharmacovigilance information regarding veterinary medicinal products marketed in the Community in order to allow the competent authorities to share the information at the same time.';

51) in Article 77(1), the second subparagraph shall be replaced by the following:

'In accordance with those guidelines, the marketing authorisation holder shall use internationally agreed veterinary medical terminology for the transmission of reports on adverse reactions.

The Commission shall publish the guidelines, which shall take account of international harmonisation work achieved in the field of pharmacovigilance.';

52) Article 78 shall be amended as follows:

(a) paragraph 2 shall be replaced by the following:

'2. If urgent action is necessary for protecting human or animal health, the Member State concerned may suspend the marketing authorisation of a veterinary medicinal product, provided that the Agency, the Commission and the other Member States are informed on the following working day at the latest.';

(b) the following paragraph shall be added:

'3. When the Agency is informed in accordance with paragraphs 1 or 2, it shall give its opinion as soon as possible, according to the urgency of the matter.

On the basis of this opinion, the Commission may request all Member States in which the veterinary medicinal is marketed to take temporary measures immediately.

Final measures shall be adopted in accordance with the procedure referred to in Article 89(3).';

53) Article 80 shall be amended as follows:

(a) paragraph 1 shall be replaced by the following:

'1. The competent authority of the Member State concerned shall ensure, by means of repeated inspections and, if necessary, unannounced inspections, and where appropriate, by asking an Official Medicines Control Laboratory or a laboratory designated for that purpose to conduct tests on samples, that the legal requirements relating to veterinary medicinal products are complied with.

The competent authority may also carry out unannounced inspections at the premises of manufacturers of active substances used as starting materials for veterinary medicinal products, and of the premises of the marketing authorisation holder whenever it considers that there are grounds for suspecting non-compliance with the provisions of Article 51. Such inspections may also be carried out at the request of another Member State, the Commission or the Agency.

In order to verify whether the data submitted in order to obtain a conformity certificate comply with the monographs of the European Pharmacopoeia, the standardisation body for nomenclatures and quality norms within the meaning of the Convention relating to the elaboration of a European Pharmacopoeia (*) (European Directorate for the Quality of Medicines) may ask the Commission or the Agency to request such an inspection when the starting material concerned is the subject of a European Pharmacopoeia monograph.

The competent authority of the Member State concerned may carry out inspections of starting material manufacturers at the manufacturer's own request.

Such inspections shall be carried out by authorised representatives of the competent authority who shall be empowered to:

(a) inspect manufacturing or trading establishments and any laboratories entrusted by the holder of the manufacturing authorisation with the task of carrying out control tests pursuant to Article 24;

(b) take samples including with a view to an independent analysis by an Official Medicines Control Laboratory or by a laboratory designated for that purpose by a Member State;

(c) examine any documents relating to the object of the inspection, subject to the provisions in force in the Member States on 9 October 1981 placing restrictions on these powers with regard to the description of the manufacturing method;

(d) inspect the premises, records and documents of marketing authorisation holders or any firms performing the activities described in Title VII, and in particular Articles 74 and 75 thereof, on behalf of a marketing authorisation holder.

(*) OJ L 158, 25.6.1994, p. 19.';

(b) paragraph 3 shall be replaced by the following:

'3. The authorised representatives of the competent authority shall report after each of the inspections mentioned in paragraph 1 on whether the principles and guidelines on good manufacturing practice referred to in Article 51 or, where appropriate, the requirements set out in Title VII, are being complied with. The inspected manufacturer or market authorisation holder shall be informed of the content of such reports.';

(c) the following paragraphs shall be added:

'4. Without prejudice to any arrangements which may have been concluded between the Community and a third country, a Member State, the Commission or the Agency may require a manufacturer established in a third country to undergo an inspection as referred to in paragraph 1.

5. Within 90 days after an inspection as referred to in paragraph 1, a certificate of good manufacturing practice shall be issued to the manufacturer if the inspection established that the manufacturer in question is complying with the principles and guidelines on good manufacturing practice as provided for by Community law.

In the event of an inspection carried out at the request of the European Pharmacopoeia, a certificate of compliance with the monograph shall be issued, if appropriate.

6. Member States shall enter the certificates of good manufacturing practice which they issue in a Community database managed by the Agency on behalf of the Community.

7. If the outcome of the inspection as referred to in paragraph 1 is that the manufacturer does not comply with the principles and guidelines of good manufacturing practice as provided for by Community legislation, the information shall be entered in the Community database as referred to in paragraph 6.';

54) Article 82 shall be replaced by the following:

'*Article 82*

1. Where it considers it necessary for reasons of human or animal health, a Member State may require the marketing authorisation holder for an immunological veterinary medicinal product to submit samples of batches of the bulk product and/or veterinary medicinal product for control by an Official Medicines Control Laboratory before the product is put into circulation.

2. On request by the competent authorities, the marketing authorisation holder shall promptly supply the samples referred to in paragraph 1, together with the reports of the control referred to in Article 81(2).

The competent authority shall inform all the other Member States in which the veterinary medicinal product is authorised as well as the European Directorate for the Quality of Medicines of its intention to control batches or the batch in question.

In such cases, the competent authorities of another Member State shall not apply the provisions of paragraph 1.

3. After studying the control reports referred to in Article 81(2), the laboratory responsible for the control shall repeat, on the samples provided, all the tests carried out by the manufacturer on the finished product, in accordance with the relevant provisions shown in the dossier for marketing authorisation.

The list of tests to be repeated by the laboratory responsible for the control shall be restricted to justified tests, provided that all Member States concerned, and if appropriate the European Directorate for the Quality of Medicines, agree to this.

For immunological veterinary medicinal products authorised under Regulation (EC) No 726/2004, the list of tests to be repeated by the control laboratory may be reduced only after agreement by the Agency.

4. All Member States concerned shall recognise the results of the tests.

5. Unless the Commission is informed that a longer period is necessary to conduct the tests, Member States shall ensure that this control is completed within 60 days of receipt of the samples.

The competent authority shall notify the other Member States concerned, the European Directorate for the Quality of Medicines, the marketing authorisation holder and, if appropriate, the manufacturer, of the results of the tests within the same period of time.

If a competent authority concludes that a batch of a veterinary medicinal product is not in conformity with the control report of the manufacturer or the specifications provided for in the marketing authorisation, it shall take all the necessary measures vis-a-vis the marketing authorisation holder and the manufacturer, where appropriate, and shall inform accordingly the other Member States in which the veterinary medicinal product is authorised.';

55) Article 83 shall be amended as follows:

(a) paragraph 1 shall be amended as follows:

(i) The introductory words shall be replaced by the following:

'Member States' competent authorities shall suspend, revoke, withdraw or vary marketing authorisations when it is clear that:';

(ii) Point (a) shall be replaced by the following:

'(a) the risk-benefit assessment of the veterinary medicinal product is, under the authorised conditions of use, unfavourable, particular regard being had to the benefits for animal health and welfare and to consumer safety, when the authorisation concerns a veterinary medicinal product for zootechnical use;';

(iii) The second subparagraph of point (e) shall be deleted;

(iv) Point (f) shall be replaced by the following:

'(f) information given in the application documents pursuant to Articles 12 to 13d and 27 is incorrect;';

(v) Point (h) shall be deleted;

(vi) The following second subparagraph shall be added:

'However, when a Community legislative framework is in the course of being adopted, the competent authority may refuse authorisation for a veterinary medicinal product where such action is necessary for the protection of public health, consumer and animal health.';

(b) paragraph 2 shall be amended as follows:

(i) The introductory words shall be replaced by the following:

'Marketing authorisations may be suspended, revoked, withdrawn or varied when it is established that:';

(ii) Point (a) shall be replaced by the following:

'(a) the particulars supporting the application, as provided for in Articles 12 to 13d, have not been amended in accordance with Article 27(1) and (5);';

56) in Article 84, point (a) of paragraph 1 shall be replaced by the following:

'(a) it is clear that the risk-benefit assessment of the veterinary medicinal product is, under the authorised conditions of use, unfavourable, particular regard being had to the benefits for animal health and welfare and to the safety and health benefits for the consumer, when the authorisation concerns a veterinary medicinal product for zootechnical use.';

57) in Article 85, the following paragraph shall be added:

'3. Member States shall prohibit the advertising to the general public of veterinary medicinal products that:

(a) in accordance with Article 67, are available on veterinary prescription only; or

(b) contain psychotropic drugs or narcotics, such as those covered by the United Nations Conventions of 1961 and 1971.';

58) in Article 89, paragraphs 2 and 3 shall be replaced by the following:

'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 Standing Committee shall adopt its rules of procedure. These rules of procedure shall be made public.';

59) Article 90 shall be replaced by the following:

'*Article 90*

Member States shall take all necessary measures to ensure that the competent authorities concerned communicate the appropriate information to each other, particularly regarding compliance with the requirements adopted for the authorisations referred to in Article 44, for the certificates referred to in Article 80(5) or for authorisation to place products on the market.

Upon reasoned request, Member States shall forthwith communicate the reports referred to in Article 80(3) to the competent authorities of another Member State.

The conclusions reached following an inspection as referred to in Article 80(1) carried out by the inspectors of the Member State concerned shall be valid for the Community.

However, by way of exception, if a Member State has not been able, for serious reasons of human or animal health, to accept the conclusions of an inspection as referred to in Article 80(1), that Member State shall forthwith inform the Commission and the Agency. The Agency shall inform the Member States concerned.

When the Commission is informed of such serious reasons, it may, after consulting the Member States concerned, ask the inspector of the competent supervisory authority to carry out a new inspection; the inspector may be accompanied by two other inspectors from Member States that are not parties to the disagreement.';

60) in Article 94, the third subparagraph shall be replaced by the following:

'Decisions to grant or revoke a marketing authorisation shall be made publicly available.';

61) Article 95 shall be replaced by the following:

'*Article 95*

Member States shall not permit foodstuffs for human consumption to be taken from test animals unless the competent authorities have established an appropriate withdrawal period. The withdrawal period shall either:

(a) be at least as laid down in Article 11(2), including, where appropriate, a safety factor reflecting the nature of the substance being tested; or

(b) if maximum residue limits have been established by the Community in accordance with Regulation (EEC) No 2377/90, ensure that this maximum limit will not be exceeded in foodstuffs.';

62) the following articles shall be inserted:

'*Article 95a*

Member States shall ensure that appropriate collection systems are in place for veterinary medicinal products that are unused or expired.

Article 95b

When a veterinary medicinal product is to be authorised in accordance with Regulation (EC) No 726/2004 and the Scientific Committee in its opinion refers to recommended conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product as provided for in Article 34(4)(d) of that Regulation, a decision addressed to Member States shall be adopted in accordance with the procedure laid down in Articles 37 and 38 of this Directive, for the implementation of those conditions or restrictions.'

Article 2

The periods of protection provided for in Article 1, point 6, which amends Article 13 of Directive 2001/82/EC, shall not apply to reference medicinal products for which an application for authorisation has been submitted before the date of transposition referred to in Article 3 first paragraph.

Article 3

Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 30 October 2005 at the latest. They shall immediately inform the Commission thereof.

When Member States adopt these measures, they shall contain a reference to this Directive or shall be accompanied by such reference on the occasion of their official publication. The methods of making such reference shall be laid down by the Member States.

Article 4

This Directive shall enter into force on the day of its publication in the *Official Journal of the European Union*.

Article 5

This Directive is addressed to the Member States.

Done at Strasbourg, 31 March 2004.

For the European Parliament	*For the Council*
The President	*The President*
P. COX	D. ROCHE

DIRECTIVE 2004/24/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission [1],

Having regard to the opinion of the European Economic and Social Committee [2],

Acting in accordance with the procedure laid down in Article 251 of the Treaty [3],

Whereas:

(1) Directive 2001/83/EC [4] requires that applications for authorisation to place a medicinal product on the market have to be accompanied by a dossier containing particulars and documents relating in particular to the results of physico-chemical, biological or microbiological tests as well as pharmacological and toxicological tests and clinical trials carried out on the product and thus proving its quality, safety and efficacy.

(2) Where the applicant can demonstrate by detailed references to published scientific literature that the constituent or the constituents of the medicinal product has or have a well-established medicinal use with recognised efficacy and an acceptable level of safety within the meaning of Directive 2001/83/EC, he/she should not be required to provide the results of pre-clinical tests or the results of clinical trials.

(3) A significant number of medicinal products, despite their long tradition, do not fulfil the requirements of a well-established medicinal use with recognised efficacy and an acceptable level of safety and are not eligible for a marketing authorisation. To maintain these products on the market, the Member States have enacted differing procedures and provisions. The differences that currently exist between the provisions laid down in the Member States may hinder trade in traditional medicinal products within the Community and lead to discrimination and distortion of competition between manufacturers of these products. They may also have an impact on the protection of public health since the necessary guarantees of quality, safety and efficacy are not always provided at present.

(4) Having regard to the particular characteristics of these medicinal products, especially their long tradition, it is desirable to provide a special, simplified registration procedure for certain traditional medicinal products. However, this simplified procedure should be used only where no marketing authorisation can be obtained pursuant to Directive 2001/83/EC, in particular because of a lack of sufficient scientific literature demonstrating a well-established medicinal use with recognised efficacy and an acceptable level of safety. It should likewise not apply to homeopathic medicinal products eligible for marketing authorisation or for registration under Directive 2001/83/EC.

(5) The long tradition of the medicinal product makes it possible to reduce the need for clinical trials, in so far as the efficacy of the medicinal product is plausible on the basis of long-standing use and experience. Pre-clinical tests do not seem necessary, where the medicinal product on the basis of the information on its traditional use proves not to be harmful in specified conditions of use. However, even a long tradition does not exclude the possibility that there may be concerns with regard to the product's safety, and therefore the competent authorities should be entitled to ask for all data necessary for assessing the safety. The quality aspect of the medicinal product is independent of its traditional use so that no derogation should be made with regard to the necessary physico-chemical, biological and microbiological tests. Products should comply with quality standards in relevant European Pharmacopoeia monographs or those in the pharmacopoeia of a Member State.

(6) The vast majority of medicinal products with a sufficiently long and coherent tradition are based on herbal substances. It therefore seems appropriate to limit the scope of the simplified registration in a first step to traditional herbal medicinal products.

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[1] OJ C 126 E, 28.5.2002, p. 263.

[2] OJ C 61, 14.3.2003, p. 9.

[3] Opinion of the European Parliament of 21 November 2002 (OJ C 25 E, 29.1.2004, p. 222), Council Common Position of 4 November 2003 (OJ C 305 E, 16.12.2003, p. 52), Position of the European Parliament of 17 December 2003 (not yet published in the Official Journal) and Council Decision of 11 March 2004.

[4] OJ L 311, 28.11.2001, p. 67; Directive as last amended by Commission Directive 2003/63/EC (OJ L 159, 27.6.2003, p. 46).

(7) The simplified registration should be acceptable only where the herbal medicinal product may rely on a sufficiently long medicinal use in the Community. Medicinal use outside the Community should be taken into account only if the medicinal product has been used within the Community for a certain time. Where there is limited evidence of use within the Community, it is necessary to assess carefully the validity and relevance of use outside the Community.

(8) With the objective of further facilitating the registration of certain traditional herbal medicinal products and of further enhancing harmonisation, there should be the possibility of establishing a Community list of herbal substances that fulfil certain criteria, such as having been in medicinal use for a sufficiently long time, and hence are considered not to be harmful under normal conditions of use.

(9) Having regard to the particularities of herbal medicinal products, a Committee for Herbal Medicinal Products should be established within the European Agency for the Evaluation of Medicinal Products (hereinafter 'the Agency') set up by Council Regulation (EEC) No 2309/93 [1]. The Committee should carry out tasks concerning the simplified registration and authorisation of medicinal products as provided for in this Directive. Its tasks should relate in particular to establishing Community herbal monographs relevant for the registration as well as the authorisation of herbal medicinal products. It should be composed of experts in the field of herbal medicinal products.

(10) It is important to ensure full consistency between the new Committee and the Committee for Human Medicinal Products already existing within the Agency.

(11) In order to promote harmonisation, Member States should recognise registrations of traditional herbal medicinal products granted by another Member State based on Community herbal monographs or consisting of substances, preparations or combinations thereof contained in a list to be established. For other products, Member States should take due account of such registrations.

(12) This Directive allows non-medicinal herbal products, fulfilling the criteria of food legislation, to be regulated under food legislation in the Community.

(13) The Commission should present a report on the application of the chapter on traditional herbal medicinal products to the European Parliament and to the Council including an assessment on the possible extension of traditional-use registration to other categories of medicinal products.

(14) It is therefore appropriate to amend Directive 2001/83/EC accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Directive 2001/83/EC is hereby amended as follows:

1. in Article 1 the following is added:

'29. *Traditional herbal medicinal product:*

a herbal medicinal product that fulfils the conditions laid down in Article 16a(1);

30. *Herbal medicinal product:*

any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations;

31. *Herbal substances:*

All mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author);

32. *Herbal preparations:*

preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.'

[1] 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).

2. The following chapter is inserted in Title III:

'*CHAPTER 2a*

Specific provisions applicable to traditional herbal medicinal products

Article 16a

1. A simplified registration procedure (hereinafter "traditional-use registration") is hereby established for herbal medicinal products which fulfil all of the following criteria:

(a) they have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment;

(b) they are exclusively for administration in accordance with a specified strength and posology;

(c) they are an oral, external and/or inhalation preparation;

(d) the period of traditional use as laid down in Article 16c(1)(c) has elapsed;

(e) the data on the traditional use of the medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience.

2. Notwithstanding Article 1(30), the presence in the herbal medicinal product of vitamins or minerals for the safety of which there is well-documented evidence shall not prevent the product from being eligible for registration in accordance with paragraph 1, provided that the action of the vitamins or minerals is ancillary to that of the herbal active ingredients regarding the specified claimed indication(s).

3. However, in cases where the competent authorities judge that a traditional herbal medicinal product fulfils the criteria for authorisation in accordance with Article 6 or registration pursuant to Article 14, the provisions of this chapter shall not apply.

Article 16b

1. The applicant and registration holder shall be established in the Community.

2. In order to obtain traditional-use registration, the applicant shall submit an application to the competent authority of the Member State concerned.

Article 16c

1. The application shall be accompanied by:

(a) the particulars and documents:

(i) referred to in Article 8(3)(a) to (h), (j) and (k);

(ii) the results of the pharmaceutical tests referred to in the second indent of Article 8(3)(i);

(iii) the summary of product characteristics, without the data specified in Article 11(4);

(iv) in case of combinations, as referred to in Article 1(30) or Article 16a(2), the information referred to in Article 16a(1)(e) relating to the combination as such; if the individual active ingredients are not sufficiently known, the data shall also relate to the individual active ingredients;

(b) any authorisation or registration obtained by the applicant in another Member State, or in a third country, to place the medicinal product on the market, and details of any decision to refuse to grant an authorisation or registration, whether in the Community or a third country, and the reasons for any such decision;

(c) bibliographical or expert evidence to the effect that the medicinal product in question, or a corresponding product has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the Community. At the request of the Member State where the application for traditional-use registration has been submitted, the Committee for Herbal Medicinal Products shall draw up an opinion on the adequacy of the evidence of the long-standing use of the product, or of the corresponding product. The Member State shall submit relevant documentation supporting the referral;

(d) a bibliographic review of safety data together with an expert report, and where required by the competent authority, upon additional request, data necessary for assessing the safety of the medicinal product.

Annex I shall apply by analogy to the particulars and documents specified in point (a).

2. A corresponding product, as referred to in paragraph 1(c), is characterised by having the same active ingredients, irrespective of the excipients used, the same or similar intended purpose, equivalent strength and posology and the same or similar route of administration as the medicinal product applied for.

3. The requirement to show medicinal use throughout the period of 30 years, referred to in paragraph 1(c), is satisfied even where the marketing of the product has not been based on a specific authorisation. It is likewise satisfied if the number or quantity of ingredients of the medicinal product has been reduced during that period.

4. Where the product has been used in the Community for less than 15 years, but is otherwise eligible for simplified registration, the Member State where the application for traditional-use registration has been submitted shall refer the product to the Committee for Herbal Medicinal Products. The Member State shall submit relevant documentation supporting the referral.

The Committee shall consider whether the other criteria for a simplified registration as referred to in Article 16a are fully complied with. If the Committee considers it possible, it shall establish a Community herbal monograph as referred to in Article 16h(3) which shall be taken into account by the Member State when taking its final decision.

Article 16d

1. Without prejudice to Article 16h(1), Chapter 4 of Title III shall apply by analogy to registrations granted in accordance with Article 16a, provided that:

(a) a Community herbal monograph has been established in accordance with Article 16h(3), or

(b) the herbal medicinal product consists of herbal substances, preparations or combinations thereof contained in the list referred to in Article 16f.

2. For other herbal medicinal products as referred to in Article 16a, each Member State shall, when evaluating an application for traditional-use registration, take due account of registrations granted by another Member State in accordance with this chapter.

Article 16e

1. Traditional-use registration shall be refused if the application does not comply with Articles 16a, 16b or 16c or if at least one of the following conditions is fulfilled:

(a) the qualitative and/or quantitative composition is not as declared;

(b) the indications do not comply with the conditions laid down in Article 16a;

(c) the product could be harmful under normal conditions of use;

(d) the data on traditional use are insufficient, especially if pharmacological effects or efficacy are not plausible on the basis of long-standing use and experience;

(e) the pharmaceutical quality is not satisfactorily demonstrated.

2. The competent authorities of the Member States shall notify the applicant, the Commission and any competent authority that requests it, of any decision they take to refuse traditional-use registration and the reasons for the refusal.

Article 16f

1. A list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products shall be established in accordance with the procedure referred to in Article 121(2). The list shall contain, with regard to each herbal substance, the indication, the specified strength and the posology, the route of administration and any other information necessary for the safe use of the herbal substance as a traditional medicinal product.

2. If an application for traditional-use registration relates to a herbal substance, preparation or a combination thereof contained in the list referred to in paragraph 1, the data specified in Article 16c(1)(b)(c) and (d) do not need to be provided. Article 16e(1)(c) and (d) shall not apply.

3. If a herbal substance, preparation or a combination thereof ceases to be included in the list referred to in paragraph 1, registrations pursuant to paragraph 2 for herbal medicinal products containing this substance shall be revoked unless the particulars and documents referred to in Article 16c(1) are submitted within three months.

Article 16g

1. Articles 3(1) and (2), 4(4), 6(1), 12, 17(1), 19, 20, 23, 24, 25, 40 to 52, 70 to 85, 101 to 108, 111(1) and (3), 112, 116 to 118, 122, 123, 125, 126, second subparagraph, and 127 of this Directive as well as Commission Directive 91/356/EEC (*) shall apply, by analogy, to traditional-use registration granted under this chapter.

2. In addition to the requirements of Articles 54 to 65, any labelling and user package leaflet shall contain a statement to the effect that:

(a) the product is a traditional herbal medicinal product for use in specified indication(s) exclusively based upon long-standing use; and

(b) the user should consult a doctor or a qualified health care practitioner if the symptoms persist during the use of the medicinal product or if adverse effects not mentioned in the package leaflet occur.

A Member State may require that the labelling and the user package leaflet shall also state the nature of the tradition in question.

3. In addition to the requirements of Articles 86 to 99, any advertisement for a medicinal product registered under this chapter shall contain the following statement: Traditional herbal medicinal product for use in specified indication(s) exclusively based upon long-standing use.

Article 16h

1. A Committee for Herbal Medicinal Products is hereby established. That Committee shall be part of the Agency and shall have the following competence:

(a) as regards simplified registrations, to:

— perform the tasks arising from Article 16c(1) and (4),

— perform the tasks arising from Article 16d,

— prepare a draft list of herbal substances, preparations and combinations thereof, as referred to in Article 16f(1), and

— establish Community monographs for traditional herbal medicinal products, as referred to in paragraph 3 of this Article;

(b) as regards authorisations of herbal medicinal products, to establish Community herbal monographs for herbal medicinal products, as referred to in paragraph 3 of this Article;

(c) as regards referrals to the Agency under Chapter 4 of Title III, in relation to herbal medicinal products as referred to in Article 16a, to perform the tasks set out in Article 32;

(d) where other medicinal products containing herbal substances are referred to the Agency under Chapter 4 of Title III, to give an opinion on the herbal substance where appropriate.

Finally, the Committee for Herbal Medicinal Products shall perform any other task conferred upon it by Community law.

The appropriate coordination with the Committee for Human Medicinal Products shall be ensured by a procedure to be determined by the Executive Director of the Agency in accordance with Article 57(2) of Regulation (EEC) No 2309/93.

2. Each Member State shall appoint, for a three-year term which may be renewed, one member and one alternate to the Committee for Herbal Medicinal Products.

The alternates shall represent and vote for the members in their absence. Members and alternates shall be chosen for their role and experience in the evaluation of herbal medicinal products and shall represent the competent national authorities.

The said Committee may coopt a maximum of five additional members chosen on the basis of their specific scientific competence. These members shall be appointed for a term of three years, which may be renewed, and shall not have alternates.

With a view to the coopting of such members, the said Committee shall identify the specific complementary scientific competence of the additional member(s). Coopted members shall be chosen among experts nominated by Member States or the Agency.

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

3. The Committee for Herbal Medicinal Products shall establish Community herbal monographs for herbal medicinal products with regard to the application of Article 10(1)(a)(ii) as well as traditional herbal medicinal products. The said Committee shall fulfil further responsibilities conferred upon it by provisions of this chapter and other Community law.

When Community herbal monographs within the meaning of this paragraph have been established, they shall be taken into account by the Member States when examining an application. Where no such Community herbal monograph has yet been established, other appropriate monographs, publications or data may be referred to.

When new Community herbal monographs are established, the registration holder shall consider whether it is necessary to modify the registration dossier accordingly. The registration holder shall notify any such modification to the competent authority of the Member State concerned.

The herbal monographs shall be published.

4. The general provisions of Regulation (EEC) No 2309/93 relating to the Committee for Human Medicinal Products shall apply by analogy to the Committee for Herbal Medicinal Products.

Article 16i

Before 30 April 2007, the Commission shall submit a report to the European Parliament and to the Council concerning the application of the provisions of this chapter.

The report shall include an assessment on the possible extension of traditional-use registration to other categories of medicinal products.

(*) OJ L 193, 17.7.1991, p. 30.'

Article 2

1. The Member States shall take the necessary measures to comply with this Directive by 30 October 2005. They shall forthwith inform the Commission thereof.

When Member States adopt these measures, they shall contain a reference to this Directive or shall be accompanied by such a reference on the occasion of their official publication. The methods of making such reference shall be laid down by the Member States.

2. For the traditional herbal medicinal products as referred to in Article 1, which are already on the market on the entry into force of this Directive, the competent authorities shall apply the provisions of this Directive within seven years after its entry into force.

Article 3

This Directive shall enter into force on the day of its publication in the *Official Journal of the European Union*.

Article 4

This Directive is addressed to the Member States.

Done at Strasbourg, 31 March 2004.

For the European Parliament	*For the Council*
The President	*The President*
P. COX	D. ROCHE