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)

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. **[**F1For the fulfilment of its pharmacovigilance tasks, including the approval of risk management systems and monitoring their effectiveness provided for under this Regulation, the Committee for Medicinal Products for Human Use shall rely on the scientific assessment and recommendations of the Pharmacovigilance Risk Assessment Committee referred to in Article 56(1)(aa).**]**

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.

Textual Amendments

F1 Inserted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

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)];

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;

[F1aa a recommendation on the frequency of submission of periodic safety update reports;**]**

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;

[F1ca details of any recommended measures for ensuring the safe use of the medicinal product to be included in the risk management system;

cb if appropriate, details of any recommended obligation to conduct post-authorisation safety studies or to comply with obligations on the recording or reporting of suspected adverse reactions which are stricter than those referred to in Chapter 3;

cc if appropriate, details of any recommended obligation to conduct post-authorisation efficacy studies where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed. Such an obligation to conduct such studies shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC;**]**

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;

[F2e the assessment report as regards the results of the pharmaceutical and pre-clinical tests and of the clinical trials, and as regards the risk management system and the pharmacovigilance system for the medicinal product concerned.**]**

Textual Amendments

F1 Inserted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

F2 Substituted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European

Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

Article 10

[[F2]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 points (a) to (d) of Article 9(4).

Where a draft decision envisages the granting of a marketing authorisation subject to the conditions referred to in points (c), (ca), (cb), or (cc) of Article 9(4), it shall lay down deadlines for the fulfilment of the conditions, where necessary.

Where the draft decision differs from the opinion of the Agency, the Commission shall attach 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).

[[F2]6 The Agency shall disseminate the documents referred to in points (a) to (d) of Article 9(4), together with any deadlines laid down pursuant to the third subparagraph of paragraph 1 of this Article.**]**

Textual Amendments

F2 Substituted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation

and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

[F1 Article 10a

1 After the granting of a marketing authorisation, the Agency may impose an obligation on the marketing authorisation holder:

a to conduct a post-authorisation safety study if there are concerns about the risks of an authorised medicinal product. If the same concerns apply to more than one medicinal product, the Agency shall, following consultation with the Pharmacovigilance Risk Assessment Committee, encourage the marketing authorisation holders concerned to conduct a joint post-authorisation safety study;

b to conduct a post-authorisation efficacy study when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly. The obligation to conduct the post-authorisation efficacy study shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC.

The imposition of such an obligation shall be duly justified, notified in writing, and shall include the objectives and timeframe for submission and conduct of the study.

2 The Agency shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation within a time limit which it shall specify, if the marketing authorisation holder so requests within 30 days of receipt of the written notification of the obligation.

3 On the basis of the written observations submitted by the marketing authorisation holder, and of the opinion of the Agency, the Commission shall withdraw or confirm the obligation. Where the Commission confirms the obligation, the marketing authorisation shall be varied to include the obligation as a condition of the marketing authorisation and the risk management system shall be updated accordingly.

Textual Amendments

F1 Inserted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

Article 10b

1 In order to determine the situations in which post-authorisation efficacy studies may be required under point (cc) of Article 9(4) and point (b) of Article 10a(1) of this Regulation, the Commission may adopt, by means of delegated acts in accordance with Article 87b, and subject to the conditions of Articles 87c and 87d, measures supplementing the provisions in point (cc) of Article 9(4) and point (b) of Article 10a(1).

2 When adopting such delegated acts, the Commission shall act in accordance with the provisions of this Regulation.**]**

Textual Amendments

F1 Inserted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

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 **[**[F3]Without prejudice to Article 4(4) and (5) 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.

Textual Amendments

F3 Substituted by Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 (Text with EEA relevance).

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.

[[F2]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 the evaluation of data contained in suspected adverse reactions reports and periodic safety update reports submitted in accordance with Chapter 3, and information on all variations introduced since the marketing authorisation was granted, at least 9 months before the marketing authorisation ceases to be valid in accordance with paragraph 1.**]**

[[F2]3 Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, including exposure of an insufficient number of patients to the medicinal product concerned, 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.

[[F4]The Commission shall adopt a Regulation laying down provisions for granting such authorisation. That measure, designed to amend non-essential elements of this Regulation by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 87(2a).**]**

[[F2]8 In exceptional circumstances and following consultation with the applicant, the marketing authorisation may be granted subject to certain conditions, in particular relating to the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. The marketing authorisation may be granted only when the applicant can show that he is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, 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 marketing 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.

Textual Amendments

F2 Substituted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

F4 Substituted by Regulation (EC) No 219/2009 of the European Parliament and of the Council of 11 March 2009 adapting a number of instruments subject to the procedure referred to in Article 251 of the Treaty to Council Decision 1999/468/EC with regard to the regulatory procedure with scrutiny Adaptation to the regulatory procedure with scrutiny — Part Two.

[F1 Article 14a

The marketing authorisation holder shall incorporate any conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4) or in Article 10a, or in Article 14(7) and (8) in his risk management system.**]**

Textual Amendments

F1 Inserted by Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance).

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.

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

Status:
Point in time view as at 02/07/2012.

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EC) No 726/2004 of the European Parliament and of the Council, Chapter 1.