# 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 2

### Supervision and penalties

*[F1[X1 Article 16*

1 After a marketing authorisation has been granted in accordance with this Regulation, the marketing authorisation holder shall, in respect of the methods of manufacture and control provided for in points (d) and (h) of Article 8(3) of Directive 2001/83/EC, take account of scientific and technical progress and introduce any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods. He shall apply for approval of corresponding variations in accordance with this Regulation.

2 The marketing authorisation holder shall forthwith provide the Agency, the Commission and the Member States with any new information which might entail the amendment of the particulars or documents referred to in Article 8(3), Article 10, 10a, 10b and 11, or Article 32(5) of Directive 2001/83/EC, in Annex I thereto, or in Article 9(4) of this Regulation.

In particular, the marketing authorisation holder shall forthwith inform the Agency and the Commission of any prohibition or restriction imposed by the competent authorities of any country in which the medicinal product is marketed and of any other new information which might influence the evaluation of the benefits and risks of the medicinal product concerned. The information shall include both positive and negative results of clinical trials or other studies in all indications and populations, whether or not included in the marketing authorisation, as well as data on the use of the medicinal product where such use is outside the terms of the marketing authorisation.

3 The marketing authorisation holder shall ensure that the product information is kept up to date with the current scientific knowledge including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal established in accordance with Article 26.

3a In order to be able to continuously assess the risk-benefit balance, the Agency may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance remains favourable. The marketing authorisation holder shall answer fully and promptly any such request.

The Agency may at any time ask the marketing authorisation holder to submit a copy of the pharmacovigilance system master file. The marketing authorisation holder shall submit the copy at the latest seven days after receipt of the request.**]]**

**[**[F2]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. Those measures, 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).**]**

**Editorial Information**

**X1** Substituted by Corrigendum to 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 (Official Journal of the European Union L 348 of 31 December 2010).

**Textual Amendments**

**F1** 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).

**F2** 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.

*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*

**[**[F1]1 In the case of medicinal products manufactured within the Union, the supervisory authorities for manufacturing 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 **[**[F1]In the case of medicinal products imported from third countries, the supervisory authorities for imports 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 Union 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 Union.**]**

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

**[**[F3]3 The supervisory authority for pharmacovigilance shall be the competent authority of the Member State in which the pharmacovigilance system master file is located.**]**

**Textual Amendments**

**F1** 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).

**F3** 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 19*

**[**[F1]1 The supervisory authorities for manufacturing and imports shall be responsible for verifying on behalf of the Union that the marketing authorisation holder for the medicinal product or the manufacturer or importer established within the Union satisfies the requirements concerning manufacturing and imports laid down in Titles IV and XI of Directive 2001/83/EC.

The supervisory authorities for pharmacovigilance shall be responsible for verifying on behalf of the Union that the marketing authorisation holder for the medicinal product satisfies the pharmacovigilance requirements laid down in Titles IX and XI of Directive 2001/83/EC. They may, if this is considered necessary, conduct pre-authorisation inspections to verify the accuracy and successful implementation of the pharmacovigilance system as it has been described by the applicant in support of his application.**]**

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.

**[**[F1]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 Committee referred to in paragraph 2. The report of the inspectors shall be made available electronically to the Commission, the Member States and the Agency.**]**

**Textual Amendments**

**F1** 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 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.

**[**[F1]3 Following an opinion by the Agency, the Commission shall adopt the necessary provisional measures, which shall be applied immediately.

A final decision in respect of the medicinal product concerned shall be adopted within 6 months, in accordance with the regulatory procedure referred to in Article 87(2).

The Commission may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.**]**

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.

**[**[F3]8 Notwithstanding paragraphs 1 to 7 of this Article, the Union procedures laid down in Article 31 and Article 107i of Directive 2001/83/EC shall apply, as appropriate, where the reason for the Member State or the Commission to consider taking decisions or measures referred to in this Article is based on the evaluation of data resulting from pharmacovigilance activities.

9 By way of derogation from paragraphs 1 to 7 of this Article, where a procedure under Article 31 or Articles 107i to 107k of Directive 2001/83/EC concerns a range of medicinal products or a therapeutic class, medicinal products that are authorised in accordance with this Regulation and that belong to that range or class shall only be included in the procedure under Article 31, or Articles 107i to 107k of that Directive.**]**

**Textual Amendments**

**F1** 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).

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**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 2.