Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance)

COMMISSION REGULATION (EC) No 1234/2008

of 24 November 2008

concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products

(Text with EEA relevance)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community,

Having regard to Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products[(1)], and in particular Article 39(1) thereof,

Having regard to 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[(2)], and in particular Article 35(1) thereof,

Having regard to 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[(3)], and in particular of Article 16(4) and Article 41(6) thereof,

Whereas:

(1) The Community legal framework regarding variations to the terms of marketing authorisations is laid down in Commission Regulation (EC) No 1084/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products granted by a competent authority of a Member State[(4)] and Commission Regulation (EC) No 1085/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products falling within the scope of Council Regulation (EEC) No 2309/93[(5)]. In the light of practical experience in the application of those two Regulations, it is appropriate to proceed to their review in order to establish a simpler, clearer and more flexible legal framework, while guaranteeing the same level of public and animal health protection.

(2) The procedures laid down in Regulations (EC) No 1084/2003 and (EC) No 1085/2003 should therefore be adjusted, without departing from the general principles on which those procedures are based. For reasons of proportionality, homeopathic and traditional herbal medicinal products which have not been granted a marketing authorisation but

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are subject to a simplified registration procedure should remain excluded from the scope of the Regulation.

(3) Variations to medicinal products can be classified in different categories, depending on the level of risk to public or animal health and the impact on the quality, safety and efficacy of the medicinal product concerned. Definitions for each of those categories should therefore be laid down. In order to bring further predictability, guidelines on the details of the various categories of variations should be established and regularly updated in the light of scientific and technical progress, taking in particular account of developments regarding international harmonisation. The European Medicines Agency (hereinafter the Agency) and the Member States should also be empowered to give recommendations on the classification of unforeseen variations.

(4) It should be clarified that certain changes which have the highest potential impact on the quality, safety or efficacy of medicinal products require a complete scientific assessment, in the same way as for the evaluation of new marketing authorisation applications.

(5) In order to further reduce the overall number of variations procedures and to enable competent authorities to focus on those variations that have a genuine impact on quality, safety or efficacy, an annual reporting system should be introduced for certain minor variations. Such variations should not require any prior approval and should be notified within 12 months following implementation. However, other types of minor variations whose immediate reporting is necessary for the continuous supervision of the medicinal product concerned should not be subject to the annual reporting system.

(6) Each variation should require a separate submission. Grouping of variations should nevertheless be allowed in certain cases, in order to facilitate the review of the variations and reduce the administrative burden. Grouping of variations to the terms of several marketing authorisations from the same marketing authorisation holder should be allowed only insofar as all concerned marketing authorisations are affected by the exact same group of variations.

(7) In order to avoid duplication of work in the evaluation of variations to the terms of several marketing authorisations, a worksharing procedure should be established under which one authority, chosen amongst the competent authorities of the Member States and the Agency, should examine the variation on behalf of the other concerned authorities.

(8) Provisions should be established reflecting those laid down in Directive 2001/82/EC and Directive 2001/83/EC as regards the role of the coordination groups established under Article 31 of Directive 2001/82/EC and Article 27 of Directive 2001/83/EC, to increase cooperation between Member States and allow for the settlement of disagreements in the evaluation of certain variations.

(9) This Regulation should clarify when the holder of a marketing authorisation is allowed to implement a given variation as such clarification is essential for economic operators.

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(10) A transitional period should be established in order to give all interested parties, in particular Member States authorities and the industry, time to adapt to the new legal framework.

(11) The measures provided for in this Regulation are in accordance with the opinions of the Standing Committee on Medicinal Products for Human Use and the Standing Committee on Veterinary Medicinal Products,

HAS ADOPTED THIS REGULATION:

CHAPTER I

GENERAL PROVISIONS

Article 1

Subject matter and scope

[[F1]1 This Regulation lays down provisions concerning the examination of variations to the terms of all marketing authorisations for medicinal products for human use and veterinary medicinal products granted in accordance with Regulation (EC) No 726/2004, Directive 2001/83/EC, Directive 2001/82/EC, and Council Directive 87/22/EEC[(6)].**]**

2 This Regulation shall not apply to transfers of a marketing authorisation from one marketing authorisation holder (hereinafter holder) to another.

3 Chapter II shall apply only to variations to the terms of marketing authorisations granted in accordance with Directive 87/22/EEC, Chapter 4 of Directive 2001/82/EC or Chapter 4 of Directive 2001/83/EC.

[[F2]3a Chapter IIa shall apply only to variations to the terms of purely national marketing authorisations.**]**

4 Chapter III shall apply only to variations to the terms of marketing authorisations granted in accordance with Regulation (EC) No 726/2004 (hereinafter centralised marketing authorisations).

Textual Amendments

F1 Substituted by Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance).

F2 Inserted by Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance).

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Article 2

Definitions

For the purposes of this Regulation, the following definitions shall apply:

1. **[**F1‘Variation to the terms of a marketing authorisation’ or ‘variation’ means any amendment to:

   (a) the information referred to in Articles 12(3) to 14 of Directive 2001/82/EC and Annex I thereto, Articles 8(3) to 11 of Directive 2001/83/EC and Annex I thereto, Articles 6(2) and 31(2) of Regulation (EC) No 726/2004, or Article 7 of Regulation (EC) No 1394/2007;

   (b) the terms of the decision granting the marketing authorisation for a medicinal product for human use, including the summary of the product characteristics and any conditions, obligations, or restrictions affecting the marketing authorisation, or changes to the labelling or the package leaflet connected with changes to the summary of the product characteristics;

   (c) the terms of the decision granting the marketing authorisation for a veterinary medicinal product, including the summary of the product characteristics and any conditions, obligations, or restrictions affecting the marketing authorisation, or changes to the labelling or the package leaflet.**]**

2. ‘Minor variation of type IA’ means a variation which has only a minimal impact, or no impact at all, on the quality, safety or efficacy of the medicinal product concerned;

3. ‘Major variation of type II’ means a variation which is not an extension and which may have a significant impact on the quality, safety or efficacy of the medicinal product concerned;

4. ‘Extension of a marketing authorisation’ or ‘extension’ means a variation which is listed in Annex I and fulfils the conditions laid down therein;

5. ‘Minor variation of type IB’ means a variation which is neither a minor variation of type IA nor a major variation of type II nor an extension;

6. ‘Member State concerned’ means a Member State whose competent authority has granted a marketing authorisation for the medicinal product in question;

7. ‘Relevant authority’ means:

   (a) the competent authority of each Member State concerned;

   (b) in the case of centralised marketing authorisations, the Agency;

8. **[**F1‘Urgent safety restriction’ means an interim change in the terms of the marketing authorisation due to new information having a bearing on the safe use of the medicinal product;**]**

9. ‘**[**F2Purely national marketing authorisation’ means any marketing authorisation granted by a Member State in accordance with the *acquis* outside the mutual recognition or decentralised procedure and that has not been subject to a complete harmonisation following a referral procedure.**]**

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Article 3

Classification of variations

1 In relation to any variation which is not an extension the classification laid down in Annex II shall apply.

[F1 2 A variation which is not an extension and whose classification is undetermined after application of the rules provided for in this Regulation, taking into account the guidelines referred to in Article 4(1) and, where relevant, any recommendations delivered pursuant to Article 5, shall by default be considered a minor variation of type IB.**]**

3 By way of derogation from paragraph 2, a variation which is not an extension and whose classification is undetermined after application of the rules provided for in this Regulation shall be considered a major variation of type II in the following cases:

a upon request from the holder when submitting the variation;

[F1 b where the competent authority of the reference Member State as referred to in Article 32 of Directive 2001/82/EC and Article 28 of Directive 2001/83/EC (hereinafter 'the reference Member State'), in consultation with the other Member States concerned, or the Agency in the case of a centralised marketing authorisation, or the competent authority in the case of a purely national marketing authorisation, concludes, following the assessment of validity of a notification in accordance with Article 9(1), Article 13b(1), or Article 15(1) and taking into account the recommendations delivered pursuant to Article 5, that the variation may have a significant impact on the quality, safety or efficacy of the medicinal product concerned.**]**

Textual Amendments

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***[**F1 Article 4*

Guidelines

1 The Commission shall, after consulting the Member States and the Agency, draw up guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of this Regulation, and on the documentation to be submitted pursuant to those procedures.