COUNCIL OF THE EUROPEAN UNION

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NOTE

from:	General Secretariat
to:	Working Party on Pharmaceuticals and Medical Devices
Subject:	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 - Need for a corrigendum

1. Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004[1] laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency has been amended a number of times after its publication. The most recent amendments concern pharmacovigilance and are introduced by Regulation (EU) No 1235/2010 of the European parliament and of the Council of 15 December 2010[2] amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004.

[1] OJ L 136. 30.4.2004, p.1.
[2] OJ L 348. 31.12.2010, p.1.

2. Article 16(4) of Regulation (EC) No 726/2004 as it is now in force constitutes the legal basis for the Commission Regulation (EC) No 1234/2008 of 24 November 2008[3] concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products. The corresponding legal basis for veterinary medicinal products is set out in Article 41(6).[4]

3. The "Omnibus" Regulation (EC) No 219/2009 of the European Parliament and of the Council of 11 March 2009[5] amended Article 16(4) and 41(6) of Regulation (EC) No 726/2004 in order to provide that Commission Regulations on variations be adopted through the Regulatory procedure with scrutiny.

4. During the same time period, Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009[6] amending Directive 2001/82/EC and Directive 2001/83/EC, as regards variations to the terms of marketing authorisations for medicinal products, was adopted following a Commission proposal that aimed at creating a harmonised legal basis for variations.

5. In December 2008, the Commission presented its proposal for amending Regulation (EC) No 726/2004 as regards pharmacovigilance. This proposal resulted in Regulation (EU) No 1235/2010, which enters into force on 2 July 2012.

6. Regulation (EU) No 1235/2010 replaces Article 16 as a whole and the new article does no more provide a legal basis for the Commission to adopt a regulation on variations. As a result, Regulation (EC) No 726/2004 will from 2 July 2012 no more contain any provision that sets out the legal basis for the Commission Regulation (EC) No 1234/2008.

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3 OJ L 334. 12.12.2008, p.7.
4 The relevant texts are set out in Annex B to this note.
5 OJ L 87. 31.3.2009, p.109.
6 OJ L 168. 30.6.2009, p.33.

7. In view of the fact that Regulation (EU) No 1235/2010 was prepared in parallel with the negotiations on the "Variations Directive" 2009/53/EC and on the "Omnibus Regulation" No 219/2009, and in view of the fact that no change is done to the legal basis for variations for veterinary medicinal products, it is obvious that this removal of Article 16(4) of Regulation (EC) No 726/2004 is a technical mistake that should be rectified.

Conclusion

The Working Party is invited to examine the case and pronounce its support for the issuing of a corrigendum along the lines set out in Annex A.

ANNEX A

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 (OJ L 348. 31.12.2010, p.1)

Must be amended as follows:

On page 6:

For:

" 7. Article 16 is replaced by the following:

'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.

4. 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 7 days after receipt of the request.';"

Read:

"7. Article 16 is replaced by the following:

'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 7 days after receipt of the request.

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 nonessential elements of this Regulation by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 87(2a).';"

ANNEX B

Various provisions helpful as references to the note

Article 16(4) of Regulation (EC) No 726/2004 original version

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 16(4) of Regulation (EC) No 726/2004 as amended by Regulation (EC) No 219/2009

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 nonessential elements of this Regulation by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 87(2a).

The entire Article 16 of Regulation (EC) No 726/2004 until 2 July 2012

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. 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).

The entire Article 16 of of the Commission proposal from 2008

"Article 16

1. After an 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 Article 8(3)(d) and (h) 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 such variations in accordance with this Regulation.

2. The marketing authorisation holder shall forthwith supply to the Agency, to the Commission and to the member States 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) 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 and the Commission 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. 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 not in accordance with the summary of the product characteristics.

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

4. 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.

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

The entire Article 16 of Regulation (EC) No 726/2004 as from 2 July 2012 if no correction is done

‘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.

4. 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 7 days after receipt of the request.';

The entire Article 16 of Regulation (EC) No 726/2004 as from 2 July 2012 if the proposed corrigendum is agreed

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 7 days after receipt of the request.';

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).

For comparison: Article 41(6) of Regulation (EC) No 726/2004

This paragraph is the legal basis for the Commission to adopt its "variations regulation" for medicinal products for veterinary use

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. 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).