►B 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)

(OJ L 348, 31.12.2010, p. 1)

Corrected by:

►C1 Corrigendum, OJ L 201, 27.7.2012, p. 138 (1235/2010)

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REGULATION (EU) No 1235/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

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(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee ([1]),

Having regard to the opinion of the Committee of the Regions ([2]),

Having regard to the opinion of the European Data Protection Supervisor ([3]),

Acting in accordance with the ordinary legislative procedure ([4]),

Whereas:

(1) Regulation (EC) No 726/2004 ([5]) creates a Union-wide marketing authorisation procedure for certain categories of medicinal products (the 'centralised procedure'), lays down rules for the pharmacovigilance of those products and establishes the European Medicines Agency (the 'Agency').

(2) Pharmacovigilance rules are necessary for the protection of public health in order to prevent, detect and assess adverse reactions to medicinal products for human use placed on the Union market, as the full safety profile of medicinal products for human use can be known only after they have been placed on the market.

([1]) OJ C 306, 16.12.2009, p. 22.
([2]) OJ C 79, 27.3.2010, p. 50.
([3]) OJ C 229, 23.9.2009, p. 19.
([4]) Position of the European Parliament of 22 September 2010 (not yet published in the Official Journal) and Council Decision of 29 November 2010.
([5]) OJ L 136, 30.4.2004, p. 1.

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(3) The pollution of waters and soils with pharmaceutical residues is an emerging environmental problem. Member States should consider measures to monitor and evaluate the risk of environmental effects of such medicinal products for human use, including those which may have an impact on public health. The Commission should, based, inter alia, on data received from the Agency, the European Environment Agency, and Member States, produce a report on the scale of the problem, along with an assessment on whether amendments to Union legislation on medicinal products for human use or other relevant Union legislation are required.

(4) In the light of the experience acquired and following an assessment by the Commission of the Union system of pharmacovigilance, it has become clear that it is necessary to take measures in order to improve the operation of Union law on the pharmacovigilance of medicinal products for human use.

(5) The main tasks of the Agency in the area of pharmacovigilance laid down in Regulation (EC) No 726/2004 should be maintained and further developed, in particular as regards the management of the Union pharmacovigilance database and data-processing network (the 'Eudravigilance database'), the coordination of safety announcements by the Member States and the provision to the public of information regarding safety issues.

(6) In order to allow all competent authorities to receive, access simultaneously and share pharmacovigilance information for medicinal products for human use authorised in the Union, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose any additional reporting requirements on marketing authorisation holders. The database should be fully and permanently accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.

(7) In order to increase transparency as regards pharmacovigilance issues, a European medicines web-portal should be created and maintained by the Agency.

(8) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Union level, it is appropriate to create a new scientific committee within the Agency: the Pharmacovigilance Risk Assessment Committee. That committee should be composed of members appointed by Member States who are competent in the safety of medicines including the detection, assessment, minimisation and communication of risk, and in the design of post-authorisation safety studies and pharmacovigilance audits, and of members appointed by the Commission, who are independent scientific experts, or representatives of healthcare professionals and patients.

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(9) The rules on Scientific Committees of the Agency laid down in Regulation (EC) No 726/2004 should apply to the Pharmacovigilance Risk Assessment Committee.

(10) In order to ensure harmonised responses across the Union to safety concerns regarding medicinal products for human use, the Committee for Medicinal Products for Human Use and the coordination group established by 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 [1] should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee with regard to any question relating to the pharmacovigilance of medicinal products for human use. However, for the sake of consistency and continuity of the safety assessments, the final responsibility for issuing an opinion on the risk-benefit assessment of medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004 should remain with the Committee for Medicinal Products for Human Use and with the authorities competent for the granting of marketing authorisations.

(11) It is appropriate that the Pharmacovigilance Risk Assessment Committee should give a recommendation as part of any Union-wide post-authorisation assessment based on pharmacovigilance data relating to medicinal products for human use and it should be responsible for making recommendations on risk management systems and monitoring their effectiveness. Such Union-wide assessments should follow the procedures laid down in Directive 2001/83/EC also for medicinal products for human use that were authorised through the centralised procedure.

(12) In accordance with Directive 2001/83/EC the Agency provides the secretariat to the coordination group. In view of the enlarged mandate of the coordination group in the area of pharmacovigilance, the technical and administrative support by the secretariat of the Agency to the coordination group should be reinforced. Provision should be made for the Agency to ensure appropriate coordination between the coordination group and the Agency's Scientific Committees.

(13) In order to protect public health, the pharmacovigilance activities of the Agency should be adequately funded. It should be ensured that adequate funding is possible for pharmacovigilance activities by empowering the Agency to charge fees to marketing authorisation holders. However, the management of those collected funds should be under the permanent control of the Management Board in order to guarantee the independence of the Agency.

(14) To ensure the highest levels of expertise and the functioning of the Pharmacovigilance Risk Assessment Committee, rapporteurs providing assessments for Union pharmacovigilance procedures, periodic safety update reports, post-authorisation safety study protocols and risk management systems should receive payment through the Agency.

[1] OJ L 311, 28.11.2001, p. 67.

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(15) Therefore, the Agency should be empowered to charge fees in return for performing the activities of the coordination group within the Union system of pharmacovigilance, as provided for in Directive 2001/83/EC, and the rapporteurs within the coordination group should, in turn, be paid by the Agency.

(16) It is necessary, from a public health perspective, to complement the data available at the time of authorisation with additional data about the safety and, in certain cases, also about the efficacy of medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004. The Commission should therefore be empowered to impose on the marketing authorisation holder the obligation to conduct post-authorisation studies on safety and on efficacy. It should be possible to impose that obligation at the time of granting the marketing authorisation or later, and it should be a condition of the marketing authorisation. Such studies may be aimed at collecting data to enable the assessment of safety or efficacy of medicinal products for human use in everyday medical practice.

(17) It is essential that a strengthened system of pharmacovigilance not lead to the premature granting of marketing authorisations. However, some medicinal products for human use are authorised subject to additional monitoring. This includes all medicinal products for human use with a new active substance and biological medicinal products, including biosimilars, which are priorities for pharmacovigilance. Competent authorities may also require additional monitoring for specific medicinal products for human use that are subject to the obligation to conduct a post-authorisation safety study or to conditions or restrictions with regard to the safe and effective use of the medicinal product that will be specified in the risk management plan. Risk management plans are normally required for new active substances, biosimilars, medicinal products for paediatric use and for medicinal products for human use involving a significant change in the marketing authorisation, including a new manufacturing process of a biotechnologically-derived medicinal product. Medicinal products for human use subject to additional monitoring should be identified as such by a black symbol, which will be selected by the Commission on the basis of a recommendation by the Pharmacovigilance Risk Assessment Committee, and an appropriate standardised explanatory sentence in the summary of product characteristics and in the package leaflet. The Agency should keep an up-to-date, publicly available list of such medicinal products.

(18) Experience has shown that the responsibilities of marketing authorisation holders with regard to pharmacovigilance of authorised medicinal products for human use should be clarified. The marketing authorisation holder should be responsible for continuously monitoring the safety of its medicinal products for human use, for informing the authorities of any changes that might have an impact on the marketing authorisation, and for ensuring that the product information is kept up to date. As medicinal products for human use could be used outside the

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terms of the marketing authorisation, the marketing authorisation holder's responsibilities should include providing all available information, including the results of clinical trials or other studies, as well as reporting any use of the medicinal product which is outside the terms of the marketing authorisation. It is also appropriate to ensure that all relevant information collected on the safety of the medicinal product for human use is taken into account when the marketing authorisation is being renewed.

(19) Scientific and medical literature is an important source of information on suspected adverse reaction case reports. Currently, for active substances included in more than one medicinal product for human use, literature cases are reported in adverse reaction case reports in a duplicative way. In order to enhance the efficiency of reporting, the Agency should monitor a defined list of literature for a defined list of active substances used in medicinal products for which there are several marketing authorisations.

(20) As a result of the submission of all suspected adverse reaction data for medicinal products for human use authorised by the Member States directly to the Eudravigilance database, it is not necessary to provide for different reporting rules for medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004. The rules on suspected adverse reaction recording and reporting laid down in Directive 2001/83/EC should therefore apply to medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004.

(21) It is necessary to increase the shared use of resources between competent authorities for the assessment of periodic safety update reports. The assessment procedures provided for in Directive 2001/83/EC should therefore apply for the single assessment of periodic safety update reports for different medicinal products for human use containing the same active substance or the same combination of active substances, including joint assessments of medicinal products for human use authorised both nationally and through the centralised procedure.

(22) It is appropriate to strengthen the supervisory role for medicinal products for human use authorised through the centralised procedure by providing that the supervisory authority for pharmacovigilance should be the competent authority of the Member State in which the pharmacovigilance system master file of the marketing authorisation holder is located.

(23) This Regulation shall apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data [1] and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data [2]. In order to detect, assess, understand and prevent adverse reactions, and to identify and take actions to reduce the risks of, and increase the benefits

[1] OJ L 281, 23.11.1995, p. 31.
[2] OJ L 8, 12.1.2001, p. 1.

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from, medicinal products for human use for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while respecting the Union legislation relating to data protection. The purpose of safeguarding public health constitutes a substantial public interest and consequently the processing of personal data can be justified if identifiable health data are processed only when necessary and only when the parties involved assess this necessity at every stage of the pharmacovigilance process.

(24) This Regulation and Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use [1] widen the tasks of the Agency with regard to pharmacovigilance, including the monitoring of literature cases, the improved use of information technology tools and the provision of more information to the general public. The Agency should be enabled to fund these activities from fees charged to marketing authorisation holders. These fees should not cover tasks carried out by national competent authorities for which such authorities charge fees in accordance with Directive 2001/83/EC.

(25) The pharmacovigilance activities provided for in this Regulation require that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well as the minimum requirements for the quality system for the performance of pharmacovigilance activities by the Agency, the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities, and the minimum requirements for the monitoring of the data contained in the Eudravigilance database to determine whether there are new risks or whether risks have changed. The format and content of the electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders, the format and content of electronic periodic safety update reports and risk management plans as well as the format of protocols, abstracts and final study reports for the post-authorisation safety studies should also be established. In accordance with Article 291 of the Treaty on the Functioning of the European Union (TFEU), rules and general principles concerning mechanisms for the control by Member States of the Commission's exercise of implementing powers are to be laid down in advance by a regulation adopted in accordance with the ordinary legislative procedure. Pending the adoption of that new regulation, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission [2] continues to apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.

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[1] See page 74 of this Official Journal.
[2] OJ L 184, 17.7.1999, p. 23.

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(26) The Commission should be empowered to adopt delegated acts in accordance with Article 290 TFEU in order to supplement the provisions in point (cc) of Article 9(4) and in point (b) of Article 10a(1) of Regulation (EC) No 726/2004. The Commission should be empowered to adopt supplementary measures laying down the situations in which post-authorisation efficacy studies may be required. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level.

(27) The provisions on the monitoring of medicinal products for human use in Regulation (EC) No 726/2004 constitute specific provisions in the meaning of Article 15(2) of Regulation (EC) No 765/2008 of the European Parliament and of the Council of 9 July 2008 setting out the requirements for accreditation and market surveillance relating to the marketing of products ([1]).

(28) Proper coordination between the newly established Pharmacovigilance Risk Assessment Committee and the other Committees of the Agency, in particular the Committee for Medicinal Products for Human Use, the Committee for Orphan Medicinal Products and the Committee for Advanced Therapies established under Regulation (EC) No 1394/2007 ([2]) should be ensured.

(29) Regulations (EC) No 726/2004 and (EC) No 1394/2007 should therefore be amended accordingly,

HAVE ADOPTED THIS REGULATION:

Article 1

Amendments to Regulation (EC) No 726/2004

Regulation (EC) No 726/2004 is hereby amended as follows:

1. in Article 5(2) the following sentence is added:

   ‘For 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).’;

2. Article 9(4) is amended as follows:

   (a) the following point is inserted:

   ‘(aa) a recommendation on the frequency of submission of periodic safety update reports;’;

   (b) the following points are inserted:

   ‘(ca) 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;

([1]) OJ L 218, 13.8.2008, p. 30.
([2]) OJ L 324, 10.12.2007, p. 121.

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(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;';

(c) point (e) is replaced by the following:

'(e) 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.';

3. Article 10 is amended as follows:

(a) paragraph 1 is replaced by the following:

'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.';

(b) paragraph 6 is replaced by the following:

'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.';

4. the following Articles are inserted:

'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;

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(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.

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.';

5. Article 14 is amended as follows:

(a) the second subparagraph of paragraph 2 is replaced by the following:

'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.';

(b) paragraph 3 is replaced by the following:

'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.';

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(c) paragraph 8 is replaced by the following:

'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.';

6. the following Article is inserted:

'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.';

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7. In Article 16, paragraphs 1, 2 and 3 are 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.

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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.';

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8. Article 18 is amended as follows:

(a) paragraph 1 is replaced by the following:

'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.';

(b) in paragraph 2, the first subparagraph is replaced by the following:

'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.';

(c) the following paragraph is added:

'3. The supervisory authority for pharmacovigilance shall be the competent authority of the Member State in which the pharmacovigilance system master file is located.';

9. Article 19 is amended as follows:

(a) paragraph 1 is replaced by the following:

'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.

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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.';

(b) in paragraph 3, the second subparagraph is replaced by the following:

'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.';

10. Article 20 is amended as follows:

(a) paragraph 3 is replaced by the following:

'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.';

(b) the following paragraphs are added:

'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.';

11. Chapter 3 of Title II is replaced by the following:

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‘CHAPTER 3

PHARMACOVIGILANCE

Article 21

1. The obligations of marketing authorisation holders laid down in Article 104 of Directive 2001/83/EC shall apply to marketing authorisation holders for medicinal products for human use authorised in accordance with this Regulation.

Without prejudice to paragraphs 2, 3 and 4 of this Article, holders of marketing authorisations granted before 2 July 2012 shall, by way of derogation from Article 104(3)(c) of Directive 2001/83/EC not be required to operate a risk management system for each medicinal product.

2. The Agency may impose an obligation on a marketing authorisation holder to operate a risk management system, as referred to in point (c) of Article 104(3) of Directive 2001/83/EC, if there are concerns about the risks affecting the risk-benefit balance of an authorised medicinal product. In that context, the Agency shall also oblige the marketing authorisation holder to submit a detailed description of the risk-management system which he intends to introduce for the medicinal product concerned.

The imposition of such obligations shall be duly justified, notified in writing, and shall include the timeframe for submission of the detailed description of the risk-management system.

3. 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.

4. 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 accordingly, to include the measures to be taken as part of the risk management system as conditions of the marketing authorisation referred to in point (ca) of Article 9(4).

Article 22

The obligations of marketing authorisation holders laid down in Article 106a(1) of Directive 2001/83/EC, and the obligations of the Member States, the Agency and the Commission laid down in paragraphs 2, 3 and 4 of that Article shall apply to the safety announcements referred to in point (e) of Article 57(1) of this Regulation concerning medicinal products for human use authorised in accordance with this Regulation.

Article 23

1. The Agency shall, in collaboration with the Member States, set up, maintain and make public a list of medicinal products that are subject to additional monitoring.

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That list shall include the names and active substances of:

(a) medicinal products authorised in the Union that contain a new active substance which, on 1 January 2011, was not contained in any medicinal product authorised in the Union;

(b) any biological medicinal product not covered by point (a) that was authorised after 1 January 2011.

2. At the request of the Commission, following consultation with the Pharmacovigilance Risk Assessment Committee, medicinal products that are authorised pursuant to this Regulation subject to conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4), or in Articles 10a, Article 14(7) and (8) and in Article 21(2), may also be included in the list.

At the request of a national competent authority, following consultation with the Pharmacovigilance Risk Assessment Committee, medicinal products that are authorised pursuant to Directive 2001/83/EC, subject to the conditions referred to in Articles 21a, 22, 22a and 104a of that Directive, may also be included in the list.

3. The list shall include an electronic link to the product information and to the summary of the risk management plan.

4. The Agency shall remove a medicinal product from the list 5 years after the Union reference date referred to in Article 107c(5) of Directive 2001/83/EC.

However, the Commission or the national competent authority, as appropriate, may, following a recommendation of the Pharmacovigilance Risk Assessment Committee, extend that period until such time as they conclude that the conditions referred to in Article 14a and Article 21(2) of this Regulation or referred to in Articles 22b and 104a of Directive 2001/83/EC have been fulfilled.

5. For medicinal products included in that list, the summary of product characteristics and the package leaflet shall include the statement "This medicinal product is subject to additional monitoring". That statement shall be preceded by a black symbol which shall be selected by the Commission following a recommendation of the Pharmacovigilance Risk Assessment Committee by 2 January 2012, and shall be followed by an appropriate standardised explanatory sentence.

Article 24

1. The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a database and data processing network (hereinafter the "Eudravigilance database") to collate pharmacovigilance information regarding medicinal products authorised in the Union and to allow competent authorities to access that information simultaneously and to share it.

The Eudravigilance database shall contain information on suspected adverse reactions in human beings arising from use of the medicinal product within the terms of the marketing authorisation as well as from uses outside the terms of the marketing authorisation, and on those occurring in the course of post-authorisation studies with the medicinal product or associated with occupational exposure.

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2. The Agency shall, in collaboration with the Member States and the Commission, draw up the functional specifications for the Eudravigilance database, together with a timeframe for their implementation.

The Agency shall prepare an annual report on the Eudravigilance database and send it to the European Parliament, the Council and the Commission. The first annual report shall be prepared by 2 January 2013.

The Management Board of the Agency shall on the basis of an independent audit report that takes into account the recommendation of the Pharmacovigilance Risk Assessment Committee confirm and announce when the Eudravigilance database has achieved full functionality and the system meets the functional specifications drawn up pursuant to the first subparagraph.

Any substantial change to the Eudravigilance database and the functional specifications shall take into account the recommendations of the Pharmacovigilance Risk Assessment Committee.

The Eudravigilance database shall be fully accessible to the competent authorities of the Member States and to the Agency and the Commission. It shall also be accessible to marketing authorisation holders to the extent necessary for them to comply with their pharmacovigilance obligations.

The Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the Eudravigilance database, while guaranteeing personal data protection. The Agency shall work together with all stakeholders, including research institutions, healthcare professionals, and patient and consumer organisations, in order to define the "appropriate level of access" for healthcare professionals and the public to the Eudravigilance database.

The data held on the Eudravigilance database shall be made publicly accessible in an aggregated format together with an explanation of how to interpret the data.

3. The Agency shall, in collaboration either with the marketing authorisation holder or with the Member State that submitted an individual suspected adverse reaction report to the Eudravigilance database, be responsible for operating procedures that ensure the quality and integrity of the information collected in the Eudravigilance database.

4. Individual suspected adverse reaction reports and follow-ups submitted to the Eudravigilance database by marketing authorisation holders shall be transmitted electronically upon receipt to the competent authority of the Member State where the reaction occurred.

Article 25

The Agency shall, in collaboration with the Member States, develop standard web-based structured forms for the reporting of suspected adverse reactions by healthcare professionals and patients in accordance with the provisions referred to in Article 107a of Directive 2001/83/EC.

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Article 25a

The Agency shall, in collaboration with the national competent authorities and the Commission, set up and maintain a repository for periodic safety update reports (hereinafter the "repository") and the corresponding assessment reports so that they are fully and permanently accessible to the Commission, the national competent authorities, the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use and the coordination group referred to in Article 27 of Directive 2001/83/EC (hereinafter the "coordination group").

The Agency shall, in collaboration with the national competent authorities and the Commission, and after consultation with the Pharmacovigilance Risk Assessment Committee, draw up the functional specifications for the repository.

The Management Board of the Agency shall, on the basis of an independent audit report that takes into account the recommendations of the Pharmacovigilance Risk Assessment Committee, confirm and announce when the repository has achieved full functionality and meets the functional specifications drawn up pursuant to the second paragraph.

Any substantial change to the repository and the functional specifications shall always take into account the recommendations of the Pharmacovigilance Risk Assessment Committee.

Article 26

1. The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a European medicines web-portal for the dissemination of information on medicinal products authorised in the Union. By means of that portal, the Agency shall make public at least the following:

(a) the names of members of the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the members of the coordination group, together with their professional qualifications and with the declarations referred to in Article 63(2) of this Regulation;

(b) agendas and minutes from each meeting of the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and of the coordination group as regards pharmacovigilance activities;

(c) a summary of the risk management plans for medicinal products authorised in accordance with this Regulation;

(d) the list of medicinal products referred to in Article 23 of this Regulation;

(e) a list of the locations in the Union where pharmacovigilance system master files are kept and contact information for pharmacovigilance enquiries, for all medicinal products authorised in the Union;

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(f) information about how to report to national competent authorities suspected adverse reactions to medicinal products and the standard structured forms referred to in Article 25 for their web-based reporting by patients and healthcare professionals, including links to national websites;

(g) Union reference dates and frequency of submission of periodic safety update reports established in accordance with Article 107c of Directive 2001/83/EC;

(h) protocols and public abstracts of results of the post-authorisation safety studies referred to in Articles 107n and 107p of Directive 2001/83/EC;

(i) the initiation of the procedure provided for in Articles 107i to 107k of Directive 2001/83/EC, the active substances or medicinal products concerned and the issue being addressed, any public hearings pursuant to that procedure and information on how to submit information and to participate in public hearings;

(j) conclusions of assessments, recommendations, opinions, approvals and decisions taken by the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and by the coordination group, the national competent authorities and the Commission in the framework of the procedures of Articles 28, 28a and 28b of this Regulation and of sections 2 and 3 of Chapter 3 and Chapter 4 of Title IX of Directive 2001/83/EC.

2. Before the launch of this portal, and during subsequent reviews, the Agency shall consult relevant stakeholders, including patient and consumer groups, healthcare professionals and industry representatives.

Article 27

1. The Agency shall monitor selected medical literature for reports of suspected adverse reactions to medicinal products containing certain active substances. It shall publish the list of active substances being monitored and the medical literature subject to this monitoring.

2. The Agency shall enter into the Eudravigilance database relevant information from the selected medical literature.

3. The Agency shall, in consultation with the Commission, Member States and interested parties, draw up a detailed guide regarding the monitoring of medical literature and the entry of relevant information into the Eudravigilance database.

Article 28

1. The obligations of marketing authorisation holders and of Member States laid down in Articles 107 and 107a of Directive 2001/83/EC shall apply to the recording and reporting of suspected adverse reactions for medicinal products for human use authorised in accordance with this Regulation.

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2. The obligations of marketing authorisation holders laid down in Article 107b of Directive 2001/83/EC and the procedures under Article 107b and Article 107c of that Directive shall apply to the submission of periodic safety update reports, the establishment of Union reference dates and changes to the frequency of submission of periodic safety update reports for medicinal products for human use authorised in accordance with this Regulation.

The provisions applicable to the submission of periodic safety update reports laid down in the second subparagraph of Article 107c(2) of that Directive shall apply to holders of marketing authorisations which were granted before 2 July 2012 and for which the frequency and dates of submission of the periodic safety update reports are not laid down as a condition to the marketing authorisation until such time as another frequency or other dates of submission of the reports are laid down in the marketing authorisation or are determined in accordance with Article 107c of that Directive.

3. The assessment of the periodic safety update reports shall be conducted by a rapporteur appointed by the Pharmacovigilance Risk Assessment Committee. The rapporteur shall closely collaborate with the rapporteur appointed by the Committee for Medicinal Products for Human Use or the Reference Member State for the medicinal products concerned.

The rapporteur shall prepare an assessment report within 60 days of receipt of the periodic safety update report and send it to the Agency and to the members of the Pharmacovigilance Risk Assessment Committee. The Agency shall send the report to the marketing authorisation holder.

Within 30 days of receipt of the assessment report, the marketing authorisation holder and the members of the Pharmacovigilance Risk Assessment Committee may submit comments to the Agency and to the rapporteur.

Following the receipt of the comments referred to in the third subparagraph, the rapporteur shall within 15 days update the assessment report taking into account any comments submitted, and forward it to the Pharmacovigilance Risk Assessment Committee. The Pharmacovigilance Risk Assessment Committee shall adopt the assessment report with or without further changes at its next meeting and issue a recommendation. The recommendation shall mention the divergent positions with the grounds on which they are based. The Agency shall include the adopted assessment report and the recommendation in the repository set up under Article 25a, and forward both to the marketing authorisation holder.

4. In the case of an assessment report that recommends any action concerning the marketing authorisation, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the report by the Pharmacovigilance Risk Assessment Committee, consider the report and adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned, including a timetable for the implementation of the opinion. Where this opinion of the Committee for Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

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Where the opinion states that regulatory action concerning the marketing authorisation is necessary, the Commission shall adopt a decision to vary, suspend or revoke the marketing authorisation. Article 10 of this Regulation shall apply to the adoption of that decision. Where the Commission adopts such a decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.

5. In the case of a single assessment of periodic safety update reports concerning more than one marketing authorisation in accordance with Article 107e(1) of Directive 2001/83/EC which includes at least one marketing authorisation granted in accordance with this Regulation, the procedure laid down in Articles 107e and 107g of that Directive shall apply.

6. The final recommendations, opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines web-portal referred to in Article 26.

Article 28a

1. Regarding medicinal products for human use authorised in accordance with this Regulation, the Agency shall, in collaboration with the Member States, take the following measures:

(a) monitor the outcome of risk minimisation measures contained in risk management plans and of conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4) or in points (a) and (b) of Article 10a(1), and in Article 14(7) and (8);

(b) assess updates to the risk management system;

(c) monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk-benefit balance.

2. The Pharmacovigilance Risk Assessment Committee shall perform the initial analysis and prioritisation of signals of new risks or risks that have changed or changes to the risk-benefit balance. Where it considers that follow-up action may be necessary, the assessment of those signals and agreement on any subsequent action concerning the marketing authorisation shall be conducted in a timescale commensurate with the extent and seriousness of the issue.

3. The Agency and national competent authorities and the marketing authorisation holder shall inform each other in the event of new risks or risks that have changed or changes to the risk-benefit balance being detected.

Article 28b

1. For non-interventional post-authorisation safety studies concerning medicinal products for human use authorised in accordance with this Regulation which fulfil one of the requirements referred to in Articles 10 and 10a of this Regulation, the procedure provided for in paragraphs 3 to 7 of Article 107m, Articles 107n to 107p and Article 107q(1) of Directive 2001/83/EC shall apply.

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2. Where, in accordance with the procedure referred to in paragraph 1 of this Article, the Pharmacovigilance Risk Assessment Committee issues recommendations for the variation, suspension or revocation of the marketing authorisation, the Committee on Medicinal Products for Human Use shall adopt an opinion taking into account the recommendation, and the Commission shall adopt a decision in accordance with Article 10.

Where the opinion of the Committee on Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee on Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences, together with the recommendation.

Article 28c

1. The Agency shall collaborate with the World Health Organisation in matters of pharmacovigilance and shall take the necessary steps to submit to it, promptly, appropriate and adequate information regarding the measures taken in the Union which may have a bearing on public health protection in third countries.

The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the World Health Organisation.

2. The Agency and the European Monitoring Centre for Drugs and Drug Addiction shall exchange information that they receive on the abuse of medicinal products including information related to illicit drugs.

Article 28d

At the request of the Commission, the Agency shall participate in collaboration with the Member States in international harmonisation and standardisation of technical measures in relation to pharmacovigilance.

Article 28e

The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the Union.

Article 28f

The Agency shall perform regular independent audits of its pharmacovigilance tasks and report the results to its Management Board on a 2-yearly basis.

Article 29

The Commission shall make public a report on the performance of pharmacovigilance tasks by the Agency on 2 January 2014 at the latest and subsequently every 3 years thereafter.';

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12. Article 56(1) is amended as follows:

(a) the following point is inserted:

‘(aa) the Pharmacovigilance Risk Assessment Committee, which shall be responsible for providing recommendations to the Committee for Medicinal Products for Human Use and the coordination group on any question relating to pharmacovigilance activities in respect of medicinal products for human use and on risk management systems and it shall be responsible for monitoring the effectiveness of those risk management systems;’;

(b) point (f) is replaced by the following:

‘(f) a Secretariat, which shall provide technical, scientific and administrative support for the Committees and ensure appropriate coordination between them, and which shall provide technical and administrative support for the coordination group and ensure appropriate coordination between it and the Committees.’;

13. Article 57 is amended as follows:

(a) in paragraph 1, points (c) to (f) are replaced by the following:

‘(c) coordinating the monitoring of medicinal products for human use which have been authorised within the Union and providing advice on the measures necessary to ensure the safe and effective use of these medicinal products for human use, in particular by coordinating the evaluation and implementation of pharmacovigilance obligations and systems and the monitoring of such implementation;

(d) ensuring the collation and dissemination of information on suspected adverse reactions to medicinal products for human use authorised in the Union by means of a database permanently accessible to all Member States;

(e) assisting Member States with the rapid communication of information on pharmacovigilance concerns to healthcare professionals and coordinating the safety announcements of the national competent authorities;

(f) distributing appropriate information on pharmacovigilance concerns to the general public, in particular by setting up and maintaining a European medicines web-portal;’;

(b) in paragraph 2, the following subparagraph is inserted after the first subparagraph:

‘For the purposes of the database, the Agency shall set up and maintain a list of all medicinal products for human use authorised in the Union. To this effect the following measures shall be taken:

(a) the Agency shall, by 2 July 2011 at the latest, make public a format for the electronic submission of information on medicinal products for human use;

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(b) marketing authorisation holders shall, by 2 July 2012 at the latest, electronically submit to the Agency information on all medicinal products for human use authorised or registered in the Union, using the format referred to in point (a);

(c) from the date set out in point (b), marketing authorisation holders shall inform the Agency of any new or varied marketing authorisations granted in the Union, using the format referred to in point (a).';

14. the following Article is inserted:

'Article 61a

1. The Pharmacovigilance Risk Assessment Committee shall be composed of the following:

(a) one member and one alternate member appointed by each Member State, in accordance with paragraph 3 of this Article;

(b) six members appointed by the Commission, with a view to ensuring that the relevant expertise is available within the Committee, including clinical pharmacology and pharmacoepidemiology, on the basis of a public call for expressions of interest;

(c) one member and one alternate member appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent healthcare professionals;

(d) one member and one alternate member appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent patient organisations.

The alternate members shall represent and vote for the members in their absence. The alternate members referred to in point (a) may be appointed to act as rapporteurs in accordance with Article 62.

2. A Member State may delegate its tasks in the Pharmacovigilance Risk Assessment Committee to another Member State. Each Member State may represent no more than one other Member State.

3. The members and alternate members of the Pharmacovigilance Risk Assessment Committee shall be appointed on the basis of their relevant expertise in pharmacovigilance matters and risk assessment of medicinal products for human use, in order to guarantee the highest levels of specialist qualifications and a broad spectrum of relevant expertise. For this purpose, Member States shall liaise with the Management Board and the Commission in order to ensure that the final composition of the Committee covers the scientific areas relevant to its tasks.

4. The members and alternate members of the Pharmacovigilance Risk Assessment Committee shall be appointed for a term of 3 years, which may be prolonged once and thereafter renewed following the procedures referred to in paragraph 1. The Committee shall elect its Chairman from among its members for a term of 3 years, which may be prolonged once.

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5. Paragraphs 3, 4, 6, 7 and 8 of Article 61 shall apply to the Pharmacovigilance Risk Assessment Committee.

6. The mandate of the Pharmacovigilance Risk Assessment Committee shall cover all aspects of the risk management of the use of medicinal products for human use including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product for human use, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit.';

15. Article 62 is amended as follows:

(a) paragraph 1 is amended as follows:

(i) the first subparagraph is replaced by the following:

'Where, in accordance with this Regulation, any of the Committees referred to in Article 56(1) is required to evaluate a medicinal product for human use, it shall appoint one of its members to act as rapporteur, taking into account existing expertise in the Member State. The Committee concerned may appoint a second member to act as co-rapporteur.

A rapporteur appointed for this purpose by the Pharmacovigilance Risk Assessment Committee shall closely collaborate with the rapporteur appointed by the Committee for Medicinal Products for Human Use or the Reference Member State for the medicinal product for human use concerned.';

(ii) the fourth subparagraph is replaced by the following:

'If there is a request for re-examination of one of its opinions where this possibility is provided for in Union law, 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.';

(b) in paragraph 2, the first subparagraph is replaced by the following:

'Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products for human use who, taking into account Article 63(2), would be available to serve on working parties or scientific advisory groups of any of the Committees referred to in Article 56(1), together with an indication of their qualifications and specific areas of expertise.';

(c) in paragraph 3, the following subparagraph is added:

'The first and second subparagraphs shall also apply to the work of rapporteurs in the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.';

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16. Article 64(2) is amended as follows:

(a) point (b) is replaced by the following:

‘(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 to those Committees, and for making available appropriate technical support to the coordination group;’;

(b) point (d) is replaced by the following:

‘(d) for ensuring appropriate coordination between the Committees referred to in Article 56(1) and, where necessary, between the Committees and the coordination group;’;

17. in Article 66(g), the words ‘Article 67’ are replaced by the words ‘Article 68’;

18. Article 67 is amended as follows:

(a) in paragraph 3, the first subparagraph is replaced by the following:

‘The Agency’s revenue shall consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.’;

(b) paragraph 4 is replaced by the following:

‘4. Activities relating to pharmacovigilance, to the operation of communications networks and to market surveillance shall be under the permanent control of the Management Board in order to guarantee the independence of the Agency. This shall not preclude the Agency from charging fees to marketing authorisation holders for performing these activities by the Agency on the condition that its independence is strictly guaranteed.’;

19. Article 82(3) is replaced by the following:

‘3. Without prejudice to the unique, Union nature of the content of the documents referred to in points (a) to (d) of Article 9(4) and in points (a) to (e) of Article 34(4), this Regulation shall not prohibit the use of two or more commercial designs for a given medicinal product for human use covered by a single marketing authorisation.’;

20. in Article 83(6), the second sentence is replaced by the following:

‘Article 28(1) and (2) shall apply *mutatis mutandis*.’;

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21. the following Articles are inserted:

'Article 87a

In order to harmonise the performance of the pharmacovigilance activities provided for in this Regulation, the Commission shall adopt implementing measures as provided for in Article 108 of Directive 2001/83/EC covering the following areas:

(a) the content and maintenance of the pharmacovigilance system master file kept by the marketing authorisation holder;

(b) the minimum requirements for the quality system for the performance of pharmacovigilance activities by the Agency;

(c) the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities;

(d) the minimum requirements for the monitoring of data included in the Eudravigilance database to determine whether there are new risks or whether risks have changed;

(e) the format and content of electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders;

(f) the format and content of electronic periodic safety update reports and risk management plans;

(g) the format of protocols, abstracts and final study reports of the post-authorisation safety studies.

Those measures shall take account of the work on international harmonisation carried out in the area of pharmacovigilance and shall, where necessary, be revised to take account of technical and scientific progress. Those measures shall be adopted in accordance with the regulatory procedure referred to in Article 87(2).

Article 87b

1. The power to adopt the delegated acts referred to in Article 10b shall be conferred on the Commission for a period of 5 years from 1 January 2011. The Commission shall draw up a report in respect of the delegated powers not later than 6 months before the end of the 5 year period. The delegation of powers shall be automatically extended for periods of an identical duration, unless the European Parliament or the Council revokes it in accordance with Article 87c.

2. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

3. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in Articles 87c and 87d.

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Article 87c

1. The delegation of powers referred to in Article 10b may be revoked at any time by the European Parliament or by the Council.

2. The institution which has commenced an internal procedure for deciding whether to revoke the delegation of powers shall endeavour to inform the other institution and the Commission within a reasonable time before the final decision is taken, indicating the delegated powers which could be subject to revocation and possible reasons for a revocation.

3. The decision of revocation shall put an end to the delegation of the powers specified in that decision. It shall take effect immediately or at a later date specified therein. It shall not affect the validity of the delegated acts already in force. It shall be published in the *Official Journal of the European Union*.

Article 87d

1. The European Parliament or the Council may object to a delegated act within a period of 2 months from the date of notification.

At the initiative of the European Parliament or the Council that period shall be extended by 2 months.

2. If, on expiry of the period referred to in paragraph 1, neither the European Parliament nor the Council has objected to the delegated act, it shall be published in the *Official Journal of the European Union* and shall enter into force on the date stated therein.

The delegated act may be published in the *Official Journal of the European Union* and enter into force before the expiry of that period if the European Parliament and the Council have both informed the Commission of their intention not to raise objections.

3. If either the European Parliament or the Council objects to the delegated act within the period referred to in paragraph 1, it shall not enter into force. The institution which objects shall state the reasons for objecting to the delegated act.'.

Article 2

Amendments to Regulation (EC) No 1394/2007

Article 20(3) of Regulation (EC) No 1394/2007 is replaced by the following:

'3. The Executive Director of the Agency shall ensure appropriate coordination between the Committee for Advanced Therapies and the other Committees of the Agency, in particular the Committee for Medicinal Products for Human Use, the Pharmacovigilance Risk Assessment Committee and the Committee for Orphan Medicinal Products, their working parties and any other scientific advisory groups.'.

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Article 3

Transitional provisions

1. The obligation on the part of the marketing authorisation holder to maintain and make available on request a pharmacovigilance system master file in respect of one or more medicinal products for human use provided for in Article 104(3)(b) of Directive 2001/83/EC as amended by Directive 2010/84/EU, which applies to medicinal products for human use authorised pursuant to Regulation (EC) No 726/2004 by virtue of Article 21 of Regulation (EC) No 726/2004 as amended by this Regulation, shall apply to marketing authorisations granted before 2 July 2012 as from either:

(a) the date on which those marketing authorisations are renewed; or

(b) the expiry of a period of 3 years starting from 2 July 2012,

whichever is the earlier.

2. The procedure provided for in Articles 107m to 107q of Directive 2001/83/EC as amended by Directive 2010/84/EU, which apply by virtue of Article 28b of Regulation (EC) No 726/2004 as amended by this Regulation, shall apply only to studies which have commenced after 2 July 2012.

3. The obligation of the Agency under the second subparagraph of Article 28c(1) of Regulation (EC) No 726/2004 as amended by this Regulation shall apply once the full functionality of Eudravigilance has been announced by the Management Board.

Article 4

Entry into force and application

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

It shall apply from 2 July 2012.