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►B ►M8 REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency ◀

(Text with EEA relevance)

(OJ L 136, 30.4.2004, p. 1)

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►M2	Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007	L 324	121	10.12.2007
►M3	Regulation (EC) No 219/2009 of the European Parliament and of the Council of 11 March 2009	L 87	109	31.3.2009
►M4	Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009	L 152	11	16.6.2009
►M5	Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010	L 348	1	31.12.2010
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**REGULATION (EC) No 726/2004 OF THE EUROPEAN
PARLIAMENT AND OF THE COUNCIL
of 31 March 2004**

**laying down Union procedures for the authorisation and
supervision of medicinal products for human use and establishing
a European Medicines Agency**

▼B

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TITLE I

DEFINITIONS AND SCOPE

Article 1

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The purpose of this Regulation is to lay down Union procedures for the authorisation, supervision and pharmacovigilance of medicinal products for human use and to establish a European Medicines Agency ('the Agency') which shall carry out the tasks relating to medicinal products for human use and veterinary medicinal products that are laid down in this Regulation and other relevant Union legislation.

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The provisions of this Regulation shall not affect the powers of Member States' authorities as regards setting the prices of medicinal products or their inclusion in the scope of the national health system or social security schemes on the basis of health, economic and social conditions. In particular, Member States shall be free to choose from the particulars shown in the marketing authorisation those therapeutic indications and pack sizes which will be covered by their social security bodies.

Article 2

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The definitions laid down in Article 1 of Directive 2001/83/EC shall apply for the purposes of this Regulation.

As a consequence, in this Regulation, the terms, 'medicinal product' and 'medicinal product for human use' mean a medicinal product as defined in point (2) of Article 1 of Directive 2001/83/EC.

In addition, the following definitions shall apply for the purposes of this Regulation:

- (1) 'veterinary medicinal product' means a medicinal product as defined in point (1) of Article 4 of Regulation (EU) 2019/6 of the European Parliament and of the Council (¹);
- (2) 'antimicrobial' means an antimicrobial as defined in point (12) of Article 4 of Regulation (EU) 2019/6.

(¹) Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7.1.2019, p. 43).

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The holder of a marketing authorisation for medicinal products covered by this Regulation must be established in the ►M8 Union ◀. The holder shall be responsible for the placing on the market of those medicinal products, whether he does it himself or via one or more persons designated to that effect.

Article 3

1. No medicinal product appearing in the Annex may be placed on the market within the ►M8 Union ◀ unless a marketing authorisation has been granted by the ►M8 Union ◀ in accordance with the provisions of this Regulation.

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2. Any medicinal product not appearing in Annex I may be granted a marketing authorisation by the Union in accordance with this Regulation, if:

- (a) the medicinal product contains an active substance which, on 20 May 2004, was not authorised in the Union; or
- (b) the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorisation in accordance with this Regulation is in the interest of patients' health at Union level.

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3. ►M8 A generic medicinal product of a reference medicinal product authorised by the Union may be authorised by the competent authorities of the Member States in accordance with Directive 2001/83/EC under the following conditions:

- (a) the application for authorisation is submitted in accordance with Article 10 of Directive 2001/83/EC; ◀
- (b) the summary of the product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the ►M8 Union ◀ except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed; and
- (c) the generic medicinal product is authorised under the same name in all the Member States where the application has been made. For the purposes of this provision, all the linguistic versions of the INN (international non-proprietary name) shall be considered to be the same name.

▼M8**▼B***Article 4*

1. Applications for the marketing authorisations referred to in Article 3 shall be submitted to the Agency.

2. The ►M8 Union ◀ shall grant and supervise marketing authorisations for medicinal products for human use in accordance with Title II.

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TITLE II

AUTHORISATION AND SUPERVISION OF MEDICINAL PRODUCTS FOR HUMAN USE

Chapter 1

Submission and examination of applications — Authorisations

Article 5

1. A Committee for Medicinal Products for Human Use is hereby established. The Committee shall be part of the Agency.

2. Without prejudice to Article 56 or to other tasks which ▶M8 Union ◀ law may confer on it, the Committee for Medicinal Products for Human Use shall be responsible for drawing up the opinion of the Agency on any matter concerning the admissibility of the files submitted in accordance with the centralised procedure, the granting, variation, suspension or revocation of an authorisation to place a medicinal product for human use on the market in accordance with the provisions of this Title, and pharmacovigilance. ▶M5 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). ◀

3. At the request of the Executive Director of the Agency or the Commission representative, the Committee for Medicinal Products for Human Use shall also draw up an opinion on any scientific matter concerning the evaluation of medicinal products for human use. The Committee shall take due account of any requests by Member States for an opinion. The Committee shall also formulate an opinion whenever there is disagreement in the evaluation of medicinal products through the mutual recognition procedure. The opinion of the Committee shall be made publicly accessible.

Article 6

1. Each application for the authorisation of a medicinal product for human use shall specifically and completely include the particulars and documents as referred to in Articles 8(3), 10, 10a, 10b or 11 of, and Annex I to, Directive 2001/83/EC. The documents must include a statement to the effect that clinical trials carried out outside the European Union meet the ethical requirements of Directive 2001/20/EC. These particulars and documents shall take account of the unique, ▶M8 Union ◀ nature of the authorisation requested and, otherwise than in exceptional cases relating to the application of the law on trade marks, shall include the use of a single name for the medicinal product.

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The application shall be accompanied by the fee payable to the Agency for the examination of the application.

2. In the case of a medicinal product for human use containing or consisting of genetically modified organisms within the meaning of Article 2 of Directive 2001/18/EC, the application shall be accompanied by:

- (a) a copy of the competent authorities' written consent to the deliberate release into the environment of the genetically modified organisms for research and development purposes where provided for in Part B of Directive 2001/18/EC or in Part B of Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms ⁽¹⁾;
- (b) the complete technical dossier supplying the information required by Annexes III and IV to Directive 2001/18/EC;
- (c) the environmental risk assessment in accordance with the principles set out in Annex II to Directive 2001/18/EC; and
- (d) the results of any investigations performed for the purposes of research or development.

Articles 13 to 24 of Directive 2001/18/EC shall not apply to medicinal products for human use containing or consisting of genetically modified organisms.

3. The Agency shall ensure that the opinion of the Committee for Medicinal Products for Human Use is given within 210 days after receipt of a valid application.

The duration of the analysis of the scientific data in the file concerning the application for marketing authorisation must be at least 80 days, except in cases where the rapporteur and co-rapporteur declare that they have completed their assessment before that time.

On the basis of a duly reasoned request, the said Committee may call for the duration of the analysis of the scientific data in the file concerning the application for marketing authorisation to be extended.

In the case of a medicinal product for human use containing or consisting of genetically modified organisms, the opinion of the said Committee shall respect the environmental safety requirements laid down by Directive 2001/18/EC. During the process of evaluating applications for marketing authorisations for medicinal products for human use containing or consisting of genetically modified organisms, the rapporteur shall carry out necessary consultations of bodies that the ►M8 Union ◀ or Member States have set up in accordance with Directive 2001/18/EC.

4. The Commission shall, in consultation with the Agency, Member States and interested parties, draw up a detailed guide regarding the form in which applications for authorisation are to be presented.

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

▼B*Article 7*

In order to prepare its opinion, the Committee for Medicinal Products for Human Use:

- (a) shall verify that the particulars and documents submitted in accordance with Article 6 comply with the requirements of Directive 2001/83/EC, and shall examine whether the conditions specified in this Regulation for granting a marketing authorisation are satisfied;
- (b) may request that an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose test the medicinal product for human use, its starting materials and, if need be, its intermediate products or other constituent materials in order to ensure that the control methods employed by the manufacturer and described in the application documents are satisfactory;
- (c) may request that the applicant supplement the particulars accompanying the application within a specific time period. Where the said Committee avails itself of this option, the time-limit laid down in Article 6(3), first subparagraph, shall be suspended until such time as the supplementary information requested has been provided. Likewise, this time-limit shall be suspended for the time allowed for the applicant to prepare oral or written explanations.

Article 8

1. Upon receipt of a written request from the Committee for Medicinal Products for Human Use, a Member State shall forward the information showing that the manufacturer of a medicinal product or the importer from a third country is able to manufacture the medicinal product concerned and/or carry out the necessary control tests in accordance with the particulars and documents supplied pursuant to Article 6.

2. Where it considers it necessary in order to complete its examination of an application, the said Committee may require the applicant to undergo a specific inspection of the manufacturing site of the medicinal product concerned. Such inspections may be made unannounced.

The inspection shall be carried out within the time-limit laid down in the first subparagraph of Article 6(3) by inspectors from the Member State holding the appropriate qualifications; they may be accompanied by a rapporteur or an expert appointed by the Committee.

Article 9

1. The Agency shall forthwith inform the applicant if the opinion of the Committee for Medicinal Products for Human Use is that:

- (a) the application does not satisfy the criteria for authorisation set out in this Regulation;

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- (b) the summary of the product characteristics proposed by the applicant needs to be amended;
- (c) the labelling or package leaflet of the product is not in compliance with Title V of Directive 2001/83/EC;

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- (d) the authorisation needs to be granted subject to the conditions provided for in Article 14(8) and Article 14-a.

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2. Within 15 days after receipt of the opinion referred to in paragraph 1, the applicant may give written notice to the Agency that he wishes to request a re-examination of the opinion. In that case, the applicant shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

Within 60 days following receipt of the grounds for the request, the said Committee shall re-examine its opinion in accordance with the conditions laid down in the fourth subparagraph of Article 62(1). The reasons for the conclusion reached shall be annexed to the final opinion.

3. Within 15 days after its adoption, the Agency shall send the final opinion of the said Committee to the Commission, to the Member States and to the applicant, together with a report describing the assessment of the medicinal product by the Committee and stating the reasons for its conclusions.

4. If an opinion is favourable to the granting of the relevant authorisation to place the medicinal product concerned on the market, the following documents shall be annexed to the opinion:

- (a) a draft summary of the product characteristics, as referred to in Article 11 of Directive 2001/83/EC;

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

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- (b) details of any conditions or restrictions which should be imposed on the supply or use of the medicinal product concerned, including the conditions under which the medicinal product may be made available to patients, in accordance with the criteria laid down in Title VI of Directive 2001/83/EC;
- (c) details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product;

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- (ca) details of any recommended measures for ensuring the safe use of the medicinal product to be included in the risk management system;

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- (cb) if appropriate, details of any recommended obligation to conduct post-authorisation safety studies or to comply with obligations on the recording or reporting of suspected adverse reactions which are stricter than those referred to in Chapter 3;
- (cc) if appropriate, details of any recommended obligation to conduct post-authorisation efficacy studies where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed. Such an obligation to conduct such studies shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC;

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- (d) the draft text of the labelling and package leaflet proposed by the applicant, presented in accordance with Title V of Directive 2001/83/EC;

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- (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.

▼B*Article 10***▼M5**

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.

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2. The Commission shall, by means of implementing acts, take a final decision within 15 days after obtaining the opinion of the Standing Committee on Medicinal Products for Human Use. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 87(2).

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3. The Standing Committee on Medicinal Products for Human Use referred to in Article 87(1) shall adjust its rules of procedure so as to take account of the tasks incumbent upon it under this Regulation.

The adjustments shall provide that:

- (a) the opinion of the said Standing Committee is to be given in writing;
- (b) Member States shall have 22 days to forward their written observations on the draft decision to the Commission. However, if a decision has to be taken urgently, a shorter time-limit may be set by the Chairman according to the degree of urgency involved. This time-limit shall not, otherwise than in exceptional circumstances, be shorter than 5 days;
- (c) Member States may request in writing that the draft decision referred to in paragraph 1 be discussed by a plenary meeting of the said Standing Committee, stating their reasons in detail.

4. Where, in the opinion of the Commission, a Member State's written observations raise important new questions of a scientific or technical nature which the opinion delivered by the Agency has not addressed, the Chairman shall suspend the procedure and refer the application back to the Agency for further consideration.

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5. The Commission shall, by means of implementing acts, adopt detailed rules for the implementation of paragraph 4 which specify the applicable time limits and procedures. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 87(2).

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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.

Article 10a

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

- (a) to conduct a post-authorisation safety study if there are concerns about the risks of an authorised medicinal product. If the same concerns apply to more than one medicinal product, the Agency shall, following consultation with the Pharmacovigilance Risk Assessment Committee, encourage the marketing authorisation holders concerned to conduct a joint post-authorisation safety study;
- (b) to conduct a post-authorisation efficacy study when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly. The obligation to conduct the post-authorisation efficacy study shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC.

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

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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***▼M8**

1. The Commission is empowered to adopt delegated acts in accordance with Article 87b, in order to supplement this Regulation by determining 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).

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

▼B*Article 11*

If an applicant withdraws an application for a marketing authorisation submitted to the Agency before an opinion has been given on the application, the applicant shall communicate its reasons for doing so to the Agency. The Agency shall make this information publicly accessible and shall publish the assessment report, if available, after deletion of all information of a commercially confidential nature.

Article 12

1. The marketing authorisation shall be refused if, after verification of the particulars and documents submitted in accordance with Article 6, it appears that the applicant has not properly or sufficiently demonstrated the quality, safety or efficacy of the medicinal product.

Authorisation shall likewise be refused if particulars or documents provided by the applicant in accordance with Article 6 are incorrect or if the labelling and package leaflet proposed by the applicant are not in accordance with Title V of Directive 2001/83/EC.

2. The refusal of a ►M8 Union ◀ marketing authorisation shall constitute a prohibition on the placing on the market of the medicinal product concerned throughout the ►M8 Union ◀.

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3. Information about all refusals and the reasons for them shall be made publicly accessible.

Article 13

1. ►M2 Without prejudice to Article 4(4) and (5) of Directive 2001/83/EC, a marketing authorisation which has been granted in accordance with this Regulation shall be valid throughout the ►M8 Union. It shall confer the same rights and obligations in each of the Member States as a marketing authorisation granted by that Member State in accordance with Article 6 of Directive 2001/83/EC.

Authorised medicinal products for human use shall be entered in the ►M8 Union Register of Medicinal Products and shall be given a number, which shall appear on the packaging.

2. Notification of marketing authorisation shall be published in the *Official Journal of the European Union*, quoting in particular the date of authorisation and the registration number in the ►M8 Union Register, any International Non-proprietary Name (INN) of the active substance of the medicinal product, its pharmaceutical form, and any Anatomical Therapeutic Chemical Code (ATC).

3. The Agency shall immediately publish the assessment report on the medicinal product for human use drawn up by the Committee for Medicinal Products for Human Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

The European Public Assessment Report (EPAR) shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

4. After a marketing authorisation has been granted, the holder of the authorisation shall inform the Agency of the dates of actual marketing of the medicinal product for human use in the Member States, taking into account the various presentations authorised.

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The marketing authorisation holder shall notify the Agency if the product ceases to be placed on the market of a Member State, either temporarily or permanently. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the Agency of the reasons for such action in accordance with Article 14b.

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Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the Agency with all data relating to the volume of sales of the medicinal product at ►M8 Union level, broken down by Member State, and any data in the holder's possession relating to the volume of prescriptions.

▼B*Article 14***▼M8**

1. Without prejudice to paragraphs 4 and 5 of this Article and to Article 14-a, a marketing authorisation shall be valid for five years.

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2. The marketing authorisation may be renewed after five years on the basis of a re-evaluation by the Agency of the risk-benefit balance.

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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.

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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4. Any authorisation which is not followed by the actual placing of the medicinal product for human use on the ►M8 Union ◀ market within three years after authorisation shall cease to be valid.

5. When an authorised medicinal product previously placed on the market is no longer actually present on the market for three consecutive years, the authorisation shall cease to be valid.

6. In exceptional circumstances and on public health grounds the Commission may grant exemptions from paragraphs 4 and 5. Such exemptions must be duly justified.

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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.

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9. When an application is submitted for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. The request shall be duly substantiated.

If the Committee for Medicinal Products for Human Use accepts the request, the time-limit laid down in Article 6(3), first subparagraph, shall be reduced to 150 days.

10. When adopting its opinion, the Committee for Medicinal Products for Human Use shall include a proposal concerning the criteria for the prescription or use of the medicinal products in accordance with Article 70(1) of Directive 2001/83/EC.

11. Without prejudice to the law on the protection of industrial and commercial property, medicinal products for human use which have been authorised in accordance with the provisions of this Regulation shall benefit from an eight-year period of data protection and a ten-year period of marketing protection, in which connection the latter period shall be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies.

▼M8*Article 14-a*

1. In duly justified cases, to meet unmet medical needs of patients, a marketing authorisation may, for medicinal products intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases, be granted prior to the submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. In emergency situations, a marketing authorisation for such medicinal products may be granted also where comprehensive pre-clinical or pharmaceutical data have not been supplied.

2. For the purposes of this Article, 'unmet medical needs' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Union or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

3. Marketing authorisations may be granted pursuant to this Article only if the risk-benefit balance of the medicinal product is favourable and the applicant is likely to be able to provide comprehensive data.

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4. Marketing authorisations granted pursuant to this Article shall be subject to specific obligations. Those specific obligations and, where appropriate, the time limit for compliance shall be specified in the conditions to the marketing authorisation. Those specific obligations shall be reviewed annually by the Agency.

5. As part of the specific obligations referred to in paragraph 4, the holder of a marketing authorisation granted pursuant to this Article shall be required to complete ongoing studies, or to conduct new studies, with a view to confirming that the risk-benefit balance is favourable.

6. The summary of product characteristics and the package leaflet shall clearly mention that the marketing authorisation for the medicinal product has been granted subject to specific obligations as referred to in paragraph 4.

7. By way of derogation from Article 14(1), a marketing authorisation granted pursuant to this Article shall be valid for one year, on a renewable basis.

8. When the specific obligations referred to in paragraph 4 of this Article have been fulfilled, the Commission may, following an application by the marketing authorisation holder, and after receiving a favourable opinion from the Agency, grant a marketing authorisation valid for five years and renewable pursuant to Article 14(2) and (3).

9. The Commission is empowered to adopt delegated acts in accordance with Article 87b in order to supplement this Regulation by specifying:

(a) the categories of medicinal products to which paragraph 1 of this Article applies; and

(b) the procedures and requirements for granting a marketing authorisation pursuant to this Article and for its renewal.

▼M5*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.

▼M6*Article 14b*

1. The marketing authorisation holder shall notify the Agency forthwith of any action the holder takes to suspend the marketing of a medicinal product, to withdraw a medicinal product from the market, to request the withdrawal of a marketing authorisation or not to apply for the renewal of a marketing authorisation, together with the reasons for such action. The marketing authorisation holder shall in particular declare if such action is based on any of the grounds set out in Article 116 or Article 117(1) of Directive 2001/83/EC.

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2. The marketing authorisation holder shall also make the notification pursuant to paragraph 1 of this Article if the action is taken in a third country and such action is based on any of the grounds set out in Article 116 or Article 117(1) of Directive 2001/83/EC.

3. In the cases referred to in paragraphs 1 and 2, the Agency shall forward the information to the competent authorities of the Member States without undue delay.

▼B*Article 15*

The granting of authorisation shall not affect the civil or criminal liability of the manufacturer or of the holder of the marketing authorisation pursuant to the applicable national law in Member States.

Chapter 2**Supervision and penalties****▼M5****▼C1***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.

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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.

▼M8*Article 16a*

1. Variations shall be classified in different categories depending on the level of risk to public health and the potential impact on the quality, safety and efficacy of the medicinal product concerned. Those categories shall range from changes to the terms of the marketing authorisation that have the highest potential impact on the quality, safety or efficacy of the medicinal product, to changes that have no or minimal impact thereon.

2. The procedures for examination of applications for variations shall be proportionate to the risk and impact involved. Those procedures shall range from procedures that allow implementation only after approval based on a complete scientific assessment to procedures that allow immediate implementation and subsequent notification by the marketing authorisation holder to the Agency.

3. The Commission is empowered to adopt delegated acts in accordance with Article 87b in order to supplement this Regulation by:

- (a) specifying the categories in which variations shall be classified; and
- (b) establishing procedures for the examination of applications for variations to the terms of marketing authorisations.

Article 16b

A marketing authorisation may be transferred to a new marketing authorisation holder. Such a transfer shall not be considered to be a variation. The transfer shall be subject to prior approval by the Commission, following the submission of an application for the transfer to the Agency.

The Commission is empowered to adopt delegated acts in accordance with Article 87b in order to supplement this Regulation by establishing procedures for the examination of applications to the Agency for the transfer of marketing authorisations.

▼B*Article 17*

The applicant or the holder of a marketing authorisation shall be responsible for the accuracy of the documents and of the data submitted.

*Article 18***▼MS**

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.

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2. ►M5 In the case of medicinal products imported from third countries, the supervisory authorities for imports shall be the competent authorities of the Member State or Member States that granted the authorisation provided for in Article 40(3) of Directive 2001/83/EC to the importer, unless appropriate agreements have been made between the Union and the exporting country to ensure that those controls are carried out in the exporting country and that the manufacturer applies standards of good manufacturing practice at least equivalent to those laid down by the Union. ◀

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

▼MS

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

▼B*Article 19***▼MS**

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

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

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2. Where, in accordance with Article 122 of Directive 2001/83/EC, the Commission is informed of serious differences of opinion between Member States as to whether the holder of the marketing authorisation for the medicinal product for human use or a manufacturer or importer established within the ►M8 Union ◀ satisfies the requirements referred to

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in paragraph 1, the Commission may, after consultation with the Member States concerned, request an inspector from the supervisory authority to undertake a new inspection of the marketing authorisation holder, the manufacturer or the importer; the inspector in question shall be accompanied by two inspectors from Member States which are not party to the dispute or by two experts nominated by the Committee for Medicinal Products for Human Use.

3. Subject to any agreements which may have been concluded between the ►M8 Union ◀ and third countries in accordance with Article 18(2), the Commission may, following a reasoned request from a Member State or from the said Committee, or on its own initiative, require a manufacturer established in a third country to submit to an inspection.

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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.

▼B*Article 20*

1. Where the supervisory authorities or the competent authorities of any other Member State are of the opinion that the manufacturer or importer established within the ►M8 Union ◀ territory is no longer fulfilling the obligations laid down in Title IV of Directive 2001/83/EC, they shall forthwith inform the Committee for Medicinal Products for Human Use and the Commission, stating their reasons in detail and indicating the course of action proposed.

The same shall apply where a Member State or the Commission considers that one of the measures envisaged in Titles IX and XI of Directive 2001/83/EC should be applied in respect of the medicinal product concerned or where the said Committee has delivered an opinion to that effect in accordance with Article 5 of this Regulation.

2. The Commission shall request the opinion of the Agency within a time-limit which it shall determine in the light of the urgency of the matter, in order to examine the reasons advanced. Whenever practicable, the holder of the authorisation for placing the medicinal product for human use on the market shall be invited to provide oral or written explanations.

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3. At any stage of the procedure laid down in this Article, following appropriate consultation of the Agency, the Commission may take temporary measures. Those temporary measures shall be applied immediately.

Without undue delay, the Commission shall, by means of implementing acts, adopt a final decision concerning the measures to be taken in respect of the medicinal product concerned. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 87(2) of this Regulation.

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

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4. Where urgent action is essential to protect human health or the environment, a Member State may, on its own initiative or at the Commission's request, suspend the use in its territory of a medicinal product for human use which has been authorised in accordance with this Regulation.

When it does so on its own initiative, it shall inform the Commission and the Agency of the reasons for its action at the latest on the next working day following the suspension. The Agency shall inform the other Member States without delay. The Commission shall immediately initiate the procedure provided for in paragraphs 2 and 3.

5. In this case, the Member State shall ensure that health-care professionals are rapidly informed of its action and the reasons for the action. Networks set up by professional associations may be used to this effect. The Member States shall inform the Commission and the Agency of actions taken for this purpose.

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6. The suspensive measures referred to in paragraph 4 may be maintained in force until such time as a final decision has been adopted in accordance with paragraph 3.

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7. The Agency shall, upon request, inform any person concerned of the final decision and make the decision publicly accessible immediately after it has been taken.

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8. Where the procedure is initiated as a result of the evaluation of data relating to pharmacovigilance, the opinion of the Agency, in accordance with paragraph 2 of this Article, shall be adopted by the Committee for Medicinal Products for Human Use on the basis of a recommendation from the Pharmacovigilance Risk Assessment Committee and Article 107j(2) of Directive 2001/83/EC shall apply.

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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.

▼M8*Article 20a*

Where the Agency concludes that a holder of a marketing authorisation granted pursuant to Article 14-a failed to comply with the obligations laid down in the marketing authorisation, the Agency shall inform the Commission accordingly. The Commission shall adopt a decision to vary, suspend or revoke that marketing authorisation in accordance with the procedure set out in Article 10.

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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.

▼M6*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.

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;
- (c) medicinal products that are authorised pursuant to this Regulation, subject to the conditions referred to in point (cb) of Article 9(4), point (a) of the first subparagraph of Article 10a(1) or Article 14(7) or (8);
- (d) medicinal products that are authorised pursuant to Directive 2001/83/EC, subject to the conditions referred to in points (b) and (c) of the first paragraph of Article 21a, Article 22, or point (a) of the first subparagraph of Article 22a(1) thereof.

1a. 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 the conditions referred to in points (c), (ca) or (cc) of Article 9(4), point (b) of the first subparagraph of Article 10a(1) or Article 21(2), may also be included in the list referred to in paragraph 1 of this Article.

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 points (a), (d), (e) or (f) of the first paragraph of Article 21a, point (b) of the first subparagraph of Article 22a(1) or Article 104a(2) thereof, may also be included in the list referred to in paragraph 1 of this Article.

2. The list referred to in paragraph 1 shall include an electronic link to the product information and to the summary of the risk management plan.

3. In the cases referred to in points (a) and (b) of paragraph 1 of this Article, the Agency shall remove a medicinal product from the list five years after the Union reference date referred to in Article 107c(5) of Directive 2001/83/EC.

In the cases referred to in points (c) and (d) of paragraph 1 and in paragraph 1a of this Article, the Agency shall remove a medicinal product from the list once the conditions have been fulfilled.

4. For medicinal products included in the list referred to in paragraph 1, 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 by 2 July 2013, following a recommendation of the Pharmacovigilance Risk Assessment Committee, and shall be followed by an appropriate standardised explanatory sentence.

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4a. By 5 June 2018, the Commission shall present to the European Parliament and the Council a report on the use of the list referred to in paragraph 1 based on the experience and data provided by the Member States and the Agency.

The Commission shall, if appropriate, on the basis of that report, and after consultation with the Member States and other appropriate stakeholders, present a proposal in order to adjust the provisions relating to the list referred to in paragraph 1.

▼M5*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.

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.

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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.

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.

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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;
- (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;

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(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.

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

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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.

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.

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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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TITLE III

AUTHORISATION AND SUPERVISION OF VETERINARY MEDICINAL PRODUCTS

Chapter 1

Submission and examination of applications — Authorisations

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▼B

TITLE IV

THE EUROPEAN MEDICINES AGENCY — RESPONSIBILITIES AND ADMINISTRATIVE STRUCTURE

Chapter 1

Tasks of the Agency

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Article 55

A European Medicines Agency is hereby established.

The Agency shall be responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products for human use and of veterinary medicinal products.

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Article 56

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1. The Agency shall comprise:

(a) the Committee for Medicinal Products for Human Use, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for human use;

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(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;

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(b) the Committee for Veterinary Medicinal Products set up pursuant to Article 139(1) of Regulation (EU) 2019/6;

▼M1

(c) the Committee on Orphan Medicinal Products;
(d) the Committee on Herbal Medicinal Products;

▼M2

- (da) the Committee for Advanced Therapies;

▼M1

- (e) the Paediatric Committee;

▼M5

- (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;

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- (g) an Executive Director, who shall exercise the responsibilities set out in Article 64;
- (h) a Management Board, which shall exercise the responsibilities set out in Articles 65, 66 and 67.

▼M8

2. The committees referred to in points (a), (aa), (c), (d), (da) and (e) of paragraph 1 of this Article may each establish standing and temporary working parties. The committee referred to in point (a) of paragraph 1 of this Article may establish scientific advisory groups in connection with the evaluation of specific types of medicinal products or treatments, to which it may delegate certain tasks associated with drawing up the scientific opinions referred to in Article 5.

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When establishing working parties and scientific advisory groups, the committees shall in their rules of procedures referred to in Article 61(8) provide for:

- (a) the appointment of members of these working parties and scientific advisory groups on the basis of the lists of experts referred to in the second subparagraph of Article 62(2); and
- (b) consultation of these working parties and scientific advisory groups.

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3. The Executive Director, in consultation with the Committee for Medicinal Products for Human Use and the Committee for Veterinary Medicinal Products, shall set up the administrative structures and procedures allowing the development of advice for undertakings, as referred to in point (n) of Article 57(1), including advice on the use of novel methodologies and tools in research and development, particularly regarding the development of new therapies.

Those committees shall each establish a standing working party with the sole remit of providing scientific advice to undertakings.

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4. The Committee for Medicinal Products for Human Use and **►M8** the Committee for Veterinary Medicinal Products **◀** may, if they consider it appropriate, seek guidance on important questions of a general scientific or ethical nature.

▼B*Article 57***▼M8**

1. The Agency shall provide the Member States and the institutions of the Union with the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human use or veterinary medicinal products which is referred to it in accordance with the Union legislation relating to medicinal products for human use or veterinary medicinal products.

To that end, the Agency, acting particularly through its committees, shall carry out the following tasks:

- (a) coordinating the scientific evaluation of the quality, safety and efficacy of medicinal products for human use and of veterinary medicinal products which are subject to Union marketing authorisation procedures;
- (b) transmitting on request and making publicly available assessment reports, summaries of product characteristics, labels and package leaflets for the medicinal products for human use;
- (c) coordinating the monitoring of medicinal products for human use and of veterinary medicinal products which have been authorised in the Union and providing advice on the measures necessary to ensure the safe and effective use of those products, 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 and to veterinary medicinal products authorised in the Union by means of databases that are permanently accessible to all Member States;
- (e) assisting Member States with the rapid communication of information on pharmacovigilance concerns relating to medicinal products for human use to healthcare professionals and coordinating the safety announcements of the national competent authorities;
- (f) distributing appropriate information on pharmacovigilance concerns relating to medicinal products for human use to the general public, in particular by setting up and maintaining a European medicines web-portal;

- (i) coordinating, as regards medicinal products for human use and veterinary medicinal products, the verification of compliance with the principles of good manufacturing practice, good laboratory practice, good clinical practice and, as regards medicinal products for human use, the verification of compliance with pharmacovigilance obligations;
- (j) upon request, providing technical and scientific support in order to improve cooperation between the Union, its Member States, international organisations and third countries on scientific and technical issues relating to the evaluation of medicinal products for human use and of veterinary medicinal products, in particular in the context of discussions organised in the framework of international conferences on harmonisation;

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- (k) recording the status of marketing authorisations for medicinal products for human use and for veterinary medicinal products granted in accordance with Union marketing authorisation procedures;
- (l) creating a database on medicinal products for human use, to be accessible to the general public, and ensuring that it is updated, and managed independently of pharmaceutical companies; the database is to facilitate the search for information already authorised for package leaflets; it is to include a section on medicinal products for human use authorised for the treatment of children; the information provided to the general public is to be worded in an appropriate and comprehensible manner;
- (m) assisting the Union and its Member States in the provision of information to health-care professionals and the general public about medicinal products for human use and about veterinary medicinal products evaluated by the Agency;
- (n) advising undertakings on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products for human use and of veterinary medicinal products;
- (o) checking that the conditions laid down in Union legislation on medicinal products for human use and on veterinary medicinal products and in the marketing authorisations are met in the case of parallel distribution of medicinal products for human use and on veterinary medicinal products authorised in accordance with this Regulation or, as applicable, Regulation (EU) 2019/6;
- (p) drawing up, at the Commission's request, any other scientific opinion concerning the evaluation of medicinal products for human use and of veterinary medicinal products or the starting materials used in the manufacture of medicinal products for human use and of veterinary medicinal products;
- (q) with a view to the protection of public health, compiling scientific information concerning pathogenic agents which might be used in biological warfare, including the existence of vaccines and other medicinal products for human use and other veterinary medicinal products available to prevent or treat the effects of such agents;
- (r) coordinating the supervision of the quality of medicinal products for human use and of veterinary medicinal products placed on the market by requesting testing of compliance with their authorised specifications by an Official Medicines Control Laboratory or by a laboratory that a Member State has designated for that purpose;
- (s) forwarding annually to the budgetary authority any information relevant to the outcome of the evaluation procedures for medicinal products for human use and veterinary medicinal products;

▼M8

- (t) taking decisions as referred to in Article 7(1) of Regulation (EC) No 1901/2006 of the European Parliament and of the Council (¹);
- (u) contributing to the joint reporting with the European Food Safety Authority and European Centre for Disease Prevention and Control on the sales and use of antimicrobials in human and veterinary medicine as well as on the situation as regards antimicrobial resistance in the Union based on contributions received by Member States, taking into account the reporting requirements and periodicity in Article 57 of Regulation (EU) 2019/6. Such joint reporting shall be carried out at least every three years.

2. The database provided for in point (l) of paragraph 1 of this Article shall include the summaries of product characteristics, the package leaflet and the information shown on the labelling. That database shall be developed in stages, priority being given to medicinal products authorised under this Regulation and those authorised under Chapter 4 of Title III of Directive 2001/83/EC. The database shall subsequently be extended to include any medicinal product for human use authorised in the Union.

▼M5

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;

▼M6

- (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 in the Union, using the format referred to in point (a);

▼M5

- (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).

▼B

Where appropriate, the database shall also include references to data on clinical trials currently being carried out or already completed, contained in the clinical trials database provided for in Article 11 of Directive 2001/20/EC. The Commission shall, in consultation with the Member States, issue guidelines on data fields which could be included and which may be accessible to the public.

(¹) Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ L 378, 27.12.2006, p. 1).

▼B*Article 58*

1. The Agency may give a scientific opinion, in the context of co-operation with the World Health Organisation, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the ►M8 Union ◀. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with Articles 6 to 9. The provisions of Article 10 shall not apply.

2. The said Committee shall establish specific procedural rules for the implementation of paragraph 1, as well as for the provision of scientific advice.

Article 59

1. The Agency shall take care to ensure early identification of potential sources of conflict between its scientific opinions and those of other bodies established under ►M8 Union ◀ law carrying out a similar task in relation to issues of common concern.

2. Where the Agency identifies a potential source of conflict, it shall contact the body concerned in order to ensure that any relevant scientific information is shared and to identify the scientific points which potentially conflict.

3. Where there is a fundamental conflict over scientific points and the body concerned is a ►M8 Union ◀ agency or a scientific committee, the Agency and the body concerned shall work together either to resolve the conflict or to submit a joint document to the Commission clarifying the scientific points of conflict. This document shall be published immediately after its adoption.

▼M8

4. Unless otherwise provided for in this Regulation, Regulation (EU) 2019/6 or Directive 2001/83/EC, where there is a fundamental conflict over scientific points and the body concerned is a body in a Member State, the Agency and the national body concerned shall work together either to resolve the conflict or to prepare a joint document clarifying the scientific points of conflict. Such joint document shall be published immediately after its adoption.

▼B*Article 60*

At the request of the Commission, the Agency shall, in respect of authorised medicinal products, collect any available information on methods that Member States' competent authorities use to determine the added therapeutic value that any new medicinal product provides.

▼B*Article 61***▼M8**

1. Each Member State shall, after consultation of the Management Board, appoint, for a three-year term which may be renewed, one member and one alternate to the Committee for Medicinal Products for Human Use.

The alternates shall represent and vote for the members in their absence and may also be appointed to act as rapporteurs in accordance with Article 62.

Members and alternates shall be chosen for their role and experience in the evaluation of medicinal products for human use as appropriate and shall represent the national competent authorities.

2. The Committee for Medicinal Products for Human Use may co-opt a maximum of five additional members chosen on the basis of their specific scientific competence. Those members shall be appointed for a term of three years, which may be renewed, and shall not have alternates.

With a view to the co-opting of such members, the Committee for Medicinal Products for Human Use shall identify the specific complementary scientific competence of the additional member or members. Co-opted members shall be chosen among experts nominated by Member States or the Agency.

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3. The members of ►M8 the Committee for Medicinal Products for Human Use ◀ may be accompanied by experts in specific scientific or technical fields.

▼M8

4. The Executive Director of the Agency or his or her representative and representatives of the Commission shall be entitled to attend all meetings of the committees referred to in Article 56(1), working parties and scientific advisory groups and all other meetings convened by the Agency or its committees.

▼B

5. In addition to their task of providing objective scientific opinions to the ►M8 Union ◀ and Member States on the questions which are referred to them, the members of ►M8 the Committee for Medicinal Products for Human Use ◀ shall ensure that there is appropriate coordination between the tasks of the Agency and the work of competent national authorities, including the consultative bodies concerned with the marketing authorisation.

▼M8

6. Members of the Committee for Medicinal Products for Human Use and experts responsible for evaluating medicinal products shall rely on the scientific evaluation and resources available to national marketing authorisation bodies. Each competent national authority shall monitor the scientific level and independence of the evaluation carried out and facilitate the activities of nominated members of that Committee and experts. Member States shall refrain from giving those members and experts any instruction which is incompatible with their own individual tasks or with the tasks and responsibilities of the Agency.

▼M8

7. When preparing the opinion, the committees referred to in Article 56(1) shall use their best endeavours to reach a scientific consensus. If such a consensus cannot be reached, the opinion shall consist of the position of the majority of members and divergent positions, with the grounds on which they are based.

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8. ►M8 The Committee for Medicinal Products for Human Use ◀ shall establish its own rules of procedure.

These rules shall, in particular, lay down:

- (a) procedures for appointing and replacing the Chairman;
- (b) procedures relating to working parties and scientific advisory groups; and
- (c) a procedure for the urgent adoption of opinions, particularly in relation to the provisions of this Regulation on market surveillance and pharmacovigilance.

They shall enter into force after receiving a favourable opinion from the Commission and the Management Board.

▼MS*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.

▼M5

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.

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.

▼B*Article 62*

1. ►M5 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. ◀

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When consulting the scientific advisory groups referred to in Article 56(2), the Committee shall forward to them the draft assessment report or reports drawn up by the rapporteur or the co-rapporteur. The opinion issued by the scientific advisory group shall be forwarded to the chairman of the relevant committee in such a way as to ensure that the deadlines laid down in Article 6(3) are met.

The substance of the opinion shall be included in the assessment report published pursuant to Article 13(3).

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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

▼M5

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.

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2. Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products for human use and veterinary medicinal products 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.

The Agency shall establish and maintain a list of accredited experts. That list shall include the national experts referred to in the first subparagraph and any other experts appointed by the Agency or the Commission, and shall be updated.

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3. The provision of services by rapporteurs or experts shall be governed by a written contract between the Agency and the person concerned, or where appropriate between the Agency and his employer.

The person concerned, or his employer, shall be remunerated in accordance with a scale of fees to be included in the financial arrangements established by the Management Board.

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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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4. The performance of scientific services for which there are several potential providers may result in a call for an expression of interest, if the scientific and technical context allows, and if it is compatible with the tasks of the Agency, in particular to ensure a high level of public health protection.

The Management Board shall adopt the appropriate procedures on a proposal from the Executive Director.

5. The Agency or any of the committees referred to in Article 56(1) may use the services of experts for the discharge of other specific tasks for which they are responsible.

Article 63

1. The membership of the committees referred to in Article 56(1) shall be made public. When each appointment is published, the professional qualifications of each member shall be specified.

2. Members of the Management Board, members of the committees, rapporteurs and experts shall not have financial or other interests in the pharmaceutical industry which could affect their impartiality. They shall undertake to act in the public interest and in an independent manner, and shall make an annual declaration of their financial interests. All indirect

▼B

interests which could relate to this industry shall be entered in a register held by the Agency which is accessible to the public, on request, at the Agency's offices.

The Agency's code of conduct shall provide for the implementation of this Article with particular reference to the acceptance of gifts.

Members of the Management Board, members of the committees, rapporteurs and experts who participate in meetings or working groups of the Agency shall declare, at each meeting, any specific interests which could be considered to be prejudicial to their independence with respect to the items on the agenda. These declarations shall be made available to the public.

Article 64

▼M8

1. The Executive Director shall be appointed by the Management Board, on a proposal from the Commission, for a period of five years on the basis of a list of candidates proposed by the Commission following a call for expressions of interest published in the *Official Journal of the European Union* and, as appropriate, by other means. Before appointment, the candidate nominated by the Management Board shall be immediately invited to make a statement to the European Parliament and to answer any questions put by its Members. The mandate of the Executive Director may be renewed once by the Management Board, upon a proposal from the Commission. The Management Board may, upon a proposal from the Commission, remove the Executive Director from his or her post.

▼B

2. The Executive Director shall be the legal representative of the Agency. He shall be responsible:

(a) for the day-to-day administration of the Agency;

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(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

(c) for ensuring that the time-limits laid down in ►M8 Union ◀ legislation for the adoption of opinions by the Agency are complied with;

▼M5

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

▼B

(e) for the preparation of the draft statement of estimates of the Agency's revenue and expenditure, and execution of its budget;

(f) for all staff matters;

(g) for providing the secretariat for the Management Board.

3. Each year the Executive Director shall submit a draft report covering the activities of the Agency in the previous year and a draft work programme for the coming year to the Management Board for approval, making a distinction between the Agency's activities concerning medicinal products for human use, those concerning herbal medicinal products and those concerning veterinary medicinal products.

▼M8

The draft report covering the activities of the Agency in the previous year shall include information about the number of applications evaluated by the Agency, the time taken for completion of the evaluation, and the medicinal products for human use and veterinary medicinal products authorised, rejected or withdrawn.

▼B*Article 65*

1. The Management Board shall consist of one representative of each Member State, two representatives of the Commission and two representatives of the European Parliament.

In addition, two representatives of patients' organisations, one representative of doctors' organisations and one representative of veterinarians' organisations shall be appointed by the Council in consultation with the European Parliament on the basis of a list drawn up by the Commission which includes appreciably more names than there are posts to be filled. The list drawn up by the Commission shall be forwarded to the European Parliament, together with the relevant background documents. As quickly as possible, and within three months of notification, the European Parliament may submit its views for consideration to the Council, which shall then appoint the Management Board.

The members of the Management Board shall be appointed in such a way as to guarantee the highest levels of specialist qualifications, a broad spectrum of relevant expertise and the broadest possible geographic spread within the European Union.

2. The members of the Management Board shall be appointed on the basis of their relevant expertise in management and, if appropriate, experience in the field of medicinal products for human or veterinary use.

3. Each Member State and the Commission shall appoint their members of the Management Board as well as an alternate who will replace the member in his absence and vote on his behalf.

4. The term of office of the representatives shall be three years. The term of office may be renewed.

5. The Management Board shall elect its Chairman from among its members.

The term of office of the Chairman shall be three years and shall expire when he ceases to be a member of the Management Board. The term of office may be renewed once.

6. Decisions of the Management Board shall be adopted by a majority of two-thirds of its members.

7. The Management Board shall adopt its rules of procedure.

8. The Management Board may invite the chairmen of the scientific committees to attend its meetings, but they shall not have the right to vote.

9. The Management Board shall approve the annual work programme of the Agency programme and forward it to the European Parliament, the Council, the Commission and the Member States.

10. The Management Board shall adopt the annual report on the Agency's activities and forward it by 15 June at the latest to the European Parliament, the Council, the Commission, the European Economic and Social Committee, the Court of Auditors and the Member States.

▼B*Article 66*

The Management Board shall:

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- (a) adopt an opinion on the rules of procedures of the Committee for Medicinal Products for Human Use (Article 61 of this Regulation) and the Committee for Veterinary Medicinal Products (Article 139 of Regulation (EU) 2019/6);
- (b) adopt procedures for the performance of scientific services (Article 62);
- (c) appoint the Executive Director (Article 64);
- (d) adopt the annual work programme and forward it to the European Parliament, the Council, the Commission and the Member States (Article 65);
- (e) approve the annual report on the Agency's activities and forward it by 15 June at the latest to the European Parliament, the Council, the Commission, the European Economic and Social Committee, the Court of Auditors and the Member States (Article 65);
- (f) adopt the budget of the Agency (Article 67);
- (g) adopt the internal financial provisions (►M5 Article 68 ◀);
- (h) adopt provisions implementing the Staff Regulations (Article 75);
- (i) develop contacts with stakeholders and stipulate the conditions applicable (Article 78);

▼M8

- (k) adopt rules to ensure the availability to the public of information concerning the authorisation or supervision of medicinal products for human use and of veterinary medicinal products (Article 80).

▼B**Chapter 2****Financial Provisions***Article 67*

1. Estimates of all the revenue and expenditure of the Agency shall be prepared for each financial year, corresponding to the calendar year, and shall be shown in the budget of the Agency.
2. The revenue and expenditure shown in the budget shall be in balance.

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3. The Agency's revenue shall consist of:
 - (a) a contribution from the Union;
 - (b) a contribution from third countries participating in the work of the Agency with which the Union has concluded international agreements for this purpose;

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- (c) fees paid by undertakings:
 - (i) for obtaining and maintaining Union marketing authorisations for medicinal products for human use and for veterinary medicinal products and for other services provided by the Agency, as provided for in this Regulation and in Regulation (EU) 2019/6; and
 - (ii) for services provided 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;
- (d) charges for other services provided by the Agency;
- (e) Union funding in the form of grants for participation in research and assistance projects, in accordance with the Agency's financial rules referred to in Article 68(11) and with the provisions of the relevant instruments supporting the policies of the Union.

The European Parliament and the Council ('the budgetary authority') shall re-examine, when necessary, the level of the Union contribution, referred to in point (a) of the first subparagraph, on the basis of an evaluation of needs and by taking account of the level of fees referred to in point (c) of the first subparagraph.

▼MS

- 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.

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- 5. The expenditure of the Agency shall include staff remuneration, administrative and infrastructure costs, and operating expenses as well as expenses resulting from contracts entered into with third parties.
- 6. Each year the Management Board, on the basis of a draft drawn up by the Executive Director, shall produce an estimate of revenue and expenditure for the Agency for the following financial year. This estimate, which shall include a draft establishment plan, shall be forwarded by the Management Board to the Commission by 31 March at the latest.
- 7. The estimate shall be forwarded by the Commission to the budgetary authority together with the preliminary draft general budget of the European Union.

- 8. On the basis of the estimate, the Commission shall enter in the preliminary draft general budget of the European Union the estimates it deems necessary for the establishment plan and the amount of the subsidy to be charged to the general budget, which it shall place before the budgetary authority in accordance with Article 272 of the Treaty.

- 9. The budgetary authority shall authorise the appropriations for the subsidy to the Agency.

The budgetary authority shall adopt the establishment plan for the Agency.

- 10. The budget shall be adopted by the Management Board. It shall become final following final adoption of the general budget of the European Union. Where appropriate, it shall be adjusted accordingly.

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11. Any modification of the establishment plan and of the budget shall be the subject of an amending budget, which is forwarded for the purposes of information to the budgetary authority.

12. The Management Board shall, as soon as possible, notify the budgetary authority of its intention to implement any project which may have significant financial implications for the funding of its budget, in particular any projects relating to property such as the rental or purchase of buildings. It shall inform the Commission thereof.

Where a branch of the budgetary authority has notified its intention to deliver an opinion, it shall forward its opinion to the Management Board within a period of six weeks from the date of notification of the project.

▼M8*Article 68*

1. The Executive Director shall implement the budget of the Agency in accordance with Regulation (EU) 2018/1046 of the European Parliament and of the Council (¹) ('the Financial Regulation').

2. By 1 March of financial year n+1, the Agency's accounting officer shall send the provisional accounts for year n to the Commission's accounting officer and to the Court of Auditors.

3. By 31 March of financial year n+1, the Executive Director shall send the report on the budgetary and financial management for year n to the European Parliament, to the Council, to the Commission and to the Court of Auditors.

4. By 31 March of financial year n+1, the Commission's accounting officer shall send the Agency's provisional accounts for year n, consolidated with the Commission's provisional accounts, to the Court of Auditors.

On receipt of the Court of Auditors' observations on the Agency's provisional accounts pursuant to Article 246 of the Financial Regulation, the Agency's accounting officer shall draw up the Agency's final accounts and the Executive Director shall submit them to the Management Board for an opinion.

5. The Management Board shall deliver an opinion on the Agency's final accounts for year n.

(¹) Regulation (EU, Euratom) 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, amending Regulations (EU) No 1296/2013, (EU) No 1301/2013, (EU) No 1303/2013, (EU) No 1304/2013, (EU) No 1309/2013, (EU) No 1316/2013, (EU) No 223/2014, (EU) No 283/2014, and Decision No 541/2014/EU and repealing Regulation (EU, Euratom) No 966/2012 (OJ L 193, 30.7.2018, p. 1).

▼M8

6. The Agency's accounting officer shall, by 1 July of financial year n+1, send the final accounts, together with the Management Board's opinion, to the European Parliament, to the Council, to the Court of Auditors and to the Commission's accounting officer.

7. The final accounts for year n shall be published in the *Official Journal of the European Union* by 15 November of financial year n+1.

8. The Executive Director shall send to the Court of Auditors a reply to its observations by 30 September of financial year n+1. The Executive Director shall also send that reply to the Management Board.

9. The Executive Director shall submit to the European Parliament, at the latter's request, any information required for the smooth application of the discharge procedure for the financial year concerned, as laid down in Article 261(3) of the Financial Regulation.

10. The European Parliament, upon a recommendation from the Council, shall, before 15 May of financial year n+2, give a discharge to the Executive Director in respect of the implementation of the budget for year n.

11. The financial rules applicable to the Agency shall be adopted by the Management Board after the Commission has been consulted. They shall not depart from Commission Delegated Regulation (EU) No 1271/2013⁽¹⁾ unless specifically required for the Agency's operation and with the Commission's prior consent.

▼B*Article 69*

1. In order to combat fraud, corruption and other unlawful activities the provisions of Regulation (EC) No 1073/1999 of the European Parliament and of the Council of 25 May 1999 concerning investigations conducted by the European Anti-Fraud Office (OLAF)⁽²⁾ shall apply without restriction.

2. The Agency shall accede to the Interinstitutional Agreement of 25 May 1999 concerning internal investigations by the European Anti-Fraud Office (OLAF) and shall issue, without delay, the appropriate provisions applicable to all the employees of the Agency.

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⁽¹⁾ Commission Delegated Regulation (EU) No 1271/2013 of 30 September 2013 on the framework financial regulation for the bodies referred to in Article 208 of Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council (OJ L 328, 7.12.2013, p. 42).

⁽²⁾ OJ L 136, 31.5.1999, p. 1.

▼B**Chapter 3****General Provisions governing the Agency***Article 71*

The Agency shall have legal personality. In all Member States it shall enjoy the most extensive legal capacity accorded to legal persons under their laws. It may in particular acquire or dispose of movable and immovable property and may be a party to legal proceedings.

▼M7*Article 71a***The Agency shall have its seat in Amsterdam, the Netherlands.**

The competent authorities of the Netherlands shall take all necessary measures to ensure that the Agency is able to move to its temporary location no later than 1 January 2019 and that it is able to move to its permanent location no later than 16 November 2019.

The competent authorities of the Netherlands shall submit a written report to the European Parliament and the Council on the progress on the adaptations to the temporary premises and on the construction of the permanent building by 17 February 2019, and every three months thereafter, until the Agency has moved to its permanent location.

▼B*Article 72*

1. The contractual liability of the Agency shall be governed by the law applicable to the contract in question. The ►M8 Court of Justice of the European Union ◀ shall have jurisdiction pursuant to any arbitration clause contained in a contract concluded by the Agency.

2. In the case of non-contractual liability, the Agency shall, in accordance with the general principles common to the laws of the Member States, make good any damage caused by it or by its servants in the performance of their duties.

The Court of Justice shall have jurisdiction in any dispute relating to compensation for any such damage.

3. The personal liability of its servants towards the Agency shall be governed by the relevant rules applying to the staff of the Agency.

Article 73

Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents (¹) shall apply to documents held by the Agency.

The Agency shall set up a register pursuant to Article 2(4) of Regulation (EC) No 1049/2001 to make available all documents that are publicly accessible pursuant to this Regulation.

(¹) OJ L 145, 31.5.2001, p. 43.

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The Management Board shall adopt the arrangements for implementing Regulation (EC) No 1049/2001 within six months of entry into force of this Regulation.

Decisions taken by the Agency pursuant to Article 8 of Regulation (EC) No 1049/2001 may give rise to the lodging of a complaint with the Ombudsman or form the subject of an action before the Court of Justice, under the conditions laid down in Articles 195 and 230 of the Treaty respectively.

▼M1*Article 73a*

Decisions taken by the Agency under Regulation (EC) No 1901/2006 may form the subject of an action before the ►M8 Court of Justice of the European Union ▲ under the conditions laid down in Article 230 of the Treaty.

▼B*Article 74*

The ►M8 Protocol on the Privileges and Immunities of the European Union ▲ shall apply to the Agency.

*Article 75***▼M8**

The staff of the Agency shall be subject to the Staff Regulations of Officials of the European Union and the Conditions of Employment of Other Servants of the European Union. In respect of its staff, the Agency shall exercise the powers which have been devolved to the appointing authority.

▼B

The Management Board, in agreement with the Commission, shall adopt the necessary implementing provisions.

Article 76

Members of the Management Board, members of the committees referred to in Article 56(1), and experts and officials and other servants of the Agency, shall be required, even after their duties have ceased, not to disclose information of the kind covered by the obligation of professional secrecy.

▼M8*Article 77*

The Commission may, in agreement with the Management Board and the relevant committee, invite representatives of international organisations with an interest in the harmonisation of technical requirements applicable to medicinal products for human use and to veterinary medicinal products to participate as observers in the work of the Agency. The conditions for participation shall be determined in advance by the Commission.

▼B*Article 78*

1. The Management Board shall, in agreement with the Commission, develop appropriate contacts between the Agency and the representatives of the industry, consumers and patients and the health professions. These contacts may include the participation of observers in certain aspects of the Agency's work, under conditions determined beforehand by the Management Board, in agreement with the Commission.

▼M8

2. The committees referred to in Article 56(1) of this Regulation and any working parties and scientific advisory groups established in accordance with that Article or Article 139(3) of Regulation (EU) 2019/6 shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products for human use and of veterinary medicinal products, in particular patient organisations and healthcare professionals' associations. Rapporteurs appointed by those committees may, on an advisory basis, establish contacts with representatives of patient organisations and healthcare professionals' associations relevant to the indication of the medicinal product for human use or veterinary medicinal product concerned.

▼B*Article 80***▼M8**

To ensure an appropriate level of transparency, the Management Board shall, on the basis of a proposal by the Executive Director and in agreement with the Commission, adopt rules to ensure the availability to the public of regulatory, scientific or technical information concerning the authorisation or supervision of medicinal products for human use and of veterinary medicinal products which is not of a confidential nature.

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The internal rules and procedures of the Agency, its committees and its working groups shall be made available to the public at the Agency and on the Internet.

TITLE V

GENERAL AND FINAL PROVISIONS

Article 81

1. All decisions to grant, refuse, vary, suspend, withdraw or revoke a marketing authorisation which are taken in accordance with this Regulation shall state in detail the reasons on which they are based. Such decisions shall be notified to the party concerned.

2. An authorisation to place a medicinal product governed by this Regulation on the market shall not be granted, refused, varied, suspended, withdrawn or revoked except through the procedures and on the grounds set out in this Regulation.

Article 82

1. Only one authorisation may be granted to an applicant for a specific medicinal product.

However, the Commission shall authorise the same applicant to submit more than one application to the Agency for that medicinal product when there are objective verifiable reasons relating to public health regarding the availability of medicinal products to health-care professionals and/or patients, or for co-marketing reasons.

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2. As regards medicinal products for human use, Article 98(3) of Directive 2001/83/EC shall apply to medicinal products authorised under this Regulation.

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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), 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.

▼B*Article 83*

1. By way of exemption from Article 6 of Directive 2001/83/EC Member States may make a medicinal product for human use belonging to the categories referred to in Article 3(1) and (2) of this Regulation available for compassionate use.

2. For the purposes of this Article, 'compassionate use' shall mean making a medicinal product belonging to the categories referred to in Article 3(1) and (2) available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who can not be treated satisfactorily by an authorised medicinal product. The medicinal product concerned must either be the subject of an application for a marketing authorisation in accordance with Article 6 of this Regulation or must be undergoing clinical trials.

3. When a Member State makes use of the possibility provided for in paragraph 1 it shall notify the Agency.

4. When compassionate use is envisaged, the Committee for Medicinal Products for Human Use, after consulting the manufacturer or the applicant, may adopt opinions on the conditions for use, the conditions for distribution and the patients targeted. The opinions shall be updated on a regular basis.

5. Member States shall take account of any available opinions.

6. The Agency shall keep an up-to-date list of the opinions adopted in accordance with paragraph 4, which shall be published on its website.

►M5 Article 28(1) and (2) shall apply *mutatis mutandis*. ◀

7. The opinions referred to in paragraph 4 shall not affect the civil or criminal liability of the manufacturer or of the applicant for marketing authorisation.

8. Where a compassionate use programme has been set up, the applicant shall ensure that patients taking part also have access to the new medicinal product during the period between authorisation and placing on the market.

9. This Article shall be without prejudice to Directive 2001/20/EC and to Article 5 of Directive 2001/83/EC.

Article 84

1. Without prejudice to the ►M8 Protocol on the Privileges and Immunities of the European Union ◀, each Member State shall determine the penalties to be applied for infringement of the provisions of this Regulation or the regulations adopted pursuant to it and shall take all measures necessary for their implementation. The penalties shall be effective, proportionate and dissuasive.

▼B

Member States shall inform the Commission of these provisions no later than 31 December 2004. They shall notify any subsequent alterations as soon as possible.

2. Member States shall inform the Commission immediately of any litigation instituted for infringement of this Regulation.

▼M8*Article 84a*

1. The Commission may impose financial penalties in the form of fines or periodic penalty payments on the holders of marketing authorisations granted under this Regulation if they fail to comply with any of the obligations laid down in Annex II in connection with the marketing authorisations.

2. The Commission may, insofar as specifically provided for in the delegated acts referred to in point (b) of paragraph 10, impose the financial penalties referred to in paragraph 1 also on a legal entity or legal entities other than the marketing authorisation holder provided that such entities form part of the same economic entity as the marketing authorisation holder and that such other legal entities:

- (a) exerted a decisive influence over the marketing authorisation holder; or
- (b) were involved in, or could have addressed, such failure to comply with the obligation by the marketing authorisation holder.

3. Where the Agency or a competent authority of a Member State is of the opinion that a marketing authorisation holder has failed to comply with any of the obligations, as referred to in paragraph 1, it may request the Commission to investigate whether to impose financial penalties pursuant to that paragraph.

4. In determining whether to impose a financial penalty and in determining its appropriate amount, the Commission shall be guided by the principles of effectiveness, proportionality and dissuasiveness and take into consideration, where relevant, the seriousness and the effects of the failure to comply with the obligations.

5. For the purposes of paragraph 1, the Commission shall also take into account:

- (a) any infringement procedure initiated by a Member State against the same marketing authorisation holder on the basis of the same legal grounds and the same facts; and
- (b) any sanctions, including penalties, already imposed on the same marketing authorisation holder on the basis of the same legal grounds and the same facts.

6. Where the Commission finds that the marketing authorisation holder has failed, intentionally or negligently, to comply with its obligations, as referred to in paragraph 1, it may adopt a decision imposing a fine not exceeding 5 % of the marketing authorisation holder's Union turnover in the business year preceding the date of that decision.

▼M8

Where the marketing authorisation holder continues to fail to comply with its obligations referred to in paragraph 1, the Commission may adopt a decision imposing periodic penalty payments per day not exceeding 2,5 % of the marketing authorisation holder's average daily Union turnover in the business year preceding the date of that decision.

Periodic penalty payments may be imposed for a period running from the date of notification of the relevant Commission's decision until the failure to comply with the obligation by the marketing authorisation holder, as referred to in paragraph 1, has been brought to an end.

7. When conducting the investigation on a failure to comply with any of the obligations referred to in paragraph 1, the Commission may cooperate with national competent authorities and rely on resources provided by the Agency.

8. Where the Commission adopts a decision imposing a financial penalty, it shall publish a concise summary of the case, including the names of the marketing authorisation holders involved and the amounts of and reasons for the financial penalties imposed, having regard to the legitimate interest of the marketing authorisation holders for the protection of their business secrets.

9. The Court of Justice of the European Union shall have unlimited jurisdiction to review decisions whereby the Commission has imposed financial penalties. The Court of Justice of the European Union may cancel, reduce or increase the fine or periodic penalty payment imposed by the Commission.

10. The Commission is empowered to adopt delegated acts in accordance with Article 87b in order to supplement this Regulation by laying down:

- (a) procedures to be applied by the Commission when imposing fines or periodic penalty payments, including rules on the initiation of the procedure, measures of inquiry, rights of the defence, access to file, legal representation and confidentiality;
- (b) further detailed rules on the imposition by the Commission of financial penalties on legal entities other than the marketing authorisation holder;
- (c) rules on duration of procedure and limitation periods;
- (d) elements to be taken into account by the Commission when setting the level of and imposing fines and periodic penalty payments, as well as the conditions and methods for their collection.

▼B*Article 85*

This Regulation shall not affect the competences vested in the European Food Safety Authority created by Regulation (EC) No 178/2002 (¹).

(¹) Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (OJ L 31, 1.2.2002, p. 1).

▼M8*Article 86*

At least every 10 years, the Commission shall publish a general report on the experience acquired as a result of the operation of the procedures laid down in this Regulation and in Chapter 4 of Title III of Directive 2001/83/EC.

Article 86a

By 2019, the Commission shall review the regulatory framework for fees payable to the Agency in relation to medicinal products for human use and veterinary medicinal products. The Commission shall put forward, as appropriate, legislative proposals with a view to update that framework. When reviewing the regulatory framework for fees payable to the Agency, the Commission shall pay attention to potential risks related to the fluctuations in the fee revenue of the Agency.

Article 87

1. The Commission shall be assisted by the Standing Committee on Medicinal Products for Human Use established by Article 121 of Directive 2001/83/EC. That committee shall be a committee within the meaning of Regulation (EU) No 182/2011 of the European Parliament and of the Council (¹).

2. Where reference is made to this paragraph, Article 5 of Regulation (EU) No 182/2011 shall apply.

▼M5*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;

(¹) Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers (OJ L 55, 28.2.2011, p. 13).

▼M5

- (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).

▼M8*Article 87b*

1. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in this Article.
2. The power to adopt delegated acts referred to in Articles 10b(1), 14-a(9), 16a(3), the second paragraph of Article 16b, and Article 84a(10) shall be conferred on the Commission for a period of five years from 28 January 2019. The Commission shall draw up a report in respect of the delegation of power not later than nine months before the end of the five-year period. The delegation of power shall be tacitly extended for periods of an identical duration, unless the European Parliament or the Council opposes such extension not later than three months before the end of each period.
3. The delegation of power referred to in Articles 10b(1), 14-a(9), 16a(3), the second paragraph of Article 16b, and Article 84a(10) may be revoked at any time by the European Parliament or by the Council. A decision to revoke shall put an end to the delegation of the power specified in that decision. It shall take effect the day following the publication of the decision in the *Official Journal of the European Union* or at a later date specified therein. It shall not affect the validity of any delegated acts already in force.
4. Before adopting a delegated act, the Commission shall consult experts designated by each Member State in accordance with the principles laid down in the Interinstitutional Agreement of 13 April 2016 on Better Law-Making ⁽¹⁾.
5. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.
6. A delegated act adopted pursuant to Articles 10b(1), 14-a(9), 16a(3), the second paragraph of Article 16b, and Article 84a(10) shall enter into force only if no objection has been expressed either by the European Parliament or by the Council within a period of three months of notification of that act to the European Parliament and to the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by three months at the initiative of the European Parliament or of the Council.

⁽¹⁾ OJ L 123, 12.5.2016, p. 1.

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Article 88

Regulation (EEC) No 2309/93/EC is hereby repealed.

References to the repealed Regulation shall be construed as references to this Regulation.

Article 89

The periods of protection provided for in Articles 14(11) and 39(10) shall not apply to reference medicinal products for which an application for authorisation has been submitted before the date referred to in Article 90, second paragraph.

Article 90

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

By way of derogation from the first paragraph, Titles I, II, III and V shall apply from 20 November 2005 and point 3, fifth and sixth indent of the Annex shall apply from 20 May 2008.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

▼M8

ANNEX I

▼B

**MEDICINAL PRODUCTS TO BE AUTHORISED BY THE
►M8 UNION ◀**

1. Medicinal products developed by means of one of the following biotechnological processes:
 - recombinant DNA technology,
 - controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells,
 - hybridoma and monoclonal antibody methods.

▼M2

- 1a. Advanced therapy medicinal products as defined in Article 2 of Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products ⁽¹⁾

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3. Medicinal products for human use containing a new active substance which, on the date of entry into force of this Regulation, was not authorised in the ►M8 Union ◀, for which the therapeutic indication is the treatment of any of the following diseases:
 - acquired immune deficiency syndrome,
 - cancer,
 - neurodegenerative disorder,
 - diabetes,
 - auto-immune diseases and other immune dysfunctions,
 - viral diseases.

▼M2

After 20 May 2008, the Commission, having consulted the Agency, may present any appropriate proposal to amend this point and the European Parliament and the Council shall take a decision thereon in accordance with the Treaty.

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4. Medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

⁽¹⁾ OJ L 324, 10.12.2007, p. 121.

▼M8*ANNEX II***LIST OF THE OBLIGATIONS REFERRED TO IN ARTICLE 84A**

- (1) the obligation to submit complete and accurate particulars and documents in an application for marketing authorisation submitted to the Agency or in response to obligations laid down in this Regulation and in Regulation (EC) No 1901/2006 to the extent that the failure to comply with the obligation concerns a material particular;
- (2) the obligation to comply with conditions or restrictions included in the marketing authorisation and concerning the supply or use of the medicinal product for human use, as referred to in point (b) of Article 9(4) and in the second subparagraph of Article 10(1);
- (3) the obligation to comply with conditions or restrictions included in the marketing authorisation with regard to the safe and effective use of the medicinal product for human use as referred to in points (aa), (c), (ca), (cb) and (cc) of Article 9(4) and in Article 10(1);
- (4) the obligation to introduce any necessary variation to the terms of the marketing authorisation to take account of technical and scientific progress and enable the medicinal products for human use to be manufactured and checked by means of generally accepted scientific methods, as provided for in Article 16(1);
- (5) the obligation to supply any new information which may entail a variation to the terms of the marketing authorisation, to notify any prohibition or restriction imposed by the competent authorities of any country in which the medicinal product for human use is marketed, or to supply any information that may influence the evaluation of the risks and benefits of the product, as provided for in Article 16(2);
- (6) the obligation to keep product information up to date with current scientific knowledge, including the conclusions of the assessment and recommendations made public on the European medicines web-portal, as provided for in Article 16(3);
- (7) the obligation to provide, at the request of the Agency, any data demonstrating that the risk-benefit balance remains favourable, as provided for in Article 16(3a);
- (8) the obligation to place the medicinal product for human use on the market in accordance with the content of the summary of the product characteristics and the labelling and package leaflet as contained in the marketing authorisation;
- (9) the obligation to comply with the conditions referred to in Article 14(8) and Article 14-a;
- (10) the obligation to notify the Agency of the dates of actual marketing and of the date when the medicinal product for human use ceases to be on the market, and to provide to the Agency data relating to the volume of sales and the volume of prescriptions of the medicinal product for human use, as provided in Article 13(4);
- (11) the obligation to operate a comprehensive pharmacovigilance system for the fulfilment of pharmacovigilance tasks, including the operation of a quality system, maintenance of a pharmacovigilance system master file and performance of regular audits, in accordance with Article 21 of this Regulation in conjunction with Article 104 of Directive 2001/83/EC;

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- (12) the obligation to submit, at the request of the Agency, a copy of the pharmacovigilance system master file, as provided for in Article 16(3a);
- (13) the obligation to operate a risk management system as provided for in Article 14a and Article 21(2) of this Regulation in conjunction with Article 104(3) of Directive 2001/83/EC and Article 34(2) of Regulation (EC) No 1901/2006;
- (14) the obligation to record and report suspected adverse reactions for medicinal products for human use, in accordance with Article 28(1) of this Regulation in conjunction with Article 107 of Directive 2001/83/EC;
- (15) the obligation to submit periodic safety update reports, in accordance with Article 28(2) of this Regulation in conjunction with Article 107b of Directive 2001/83/EC;
- (16) the obligation to conduct post-marketing studies, including post-authorisation safety studies and post-authorisation efficacy studies, and to submit them for review, as provided for in Article 10a of this Regulation and Article 34(2) of Regulation (EC) No 1901/2006;
- (17) the obligation to ensure that public announcements relating to information on pharmacovigilance concerns are presented objectively and are not misleading and to notify them to the Agency, as provided for in Article 22 of this Regulation and Article 106a(1) of Directive 2001/83/EC;
- (18) the obligation to comply with the time limits for initiating or completing measures specified in the Agency's decision on deferral following the initial marketing authorisation of the medicinal product for human use concerned and in accordance with the definitive opinion referred to in Article 25(5) of Regulation (EC) No 1901/2006;
- (19) the obligation to place the medicinal product for human use on the market within two years of the date on which the paediatric indication is authorised, as provided for in Article 33 of Regulation (EC) No 1901/2006;
- (20) the obligation to transfer the marketing authorisation or to allow a third party to use documentation contained in the file of the medicinal product, as provided for in the first paragraph of Article 35 of Regulation (EC) No 1901/2006;
- (21) the obligation to submit paediatric studies to the Agency, including the obligation to enter information on third country clinical trials into the European database, as provided for in Articles 41(1) and (2), 45(1) and 46(1) of Regulation (EC) No 1901/2006;
- (22) the obligation to submit an annual report to the Agency as provided for in Article 34(4) of Regulation (EC) No 1901/2006 and to inform the Agency in accordance with the second paragraph of Article 35 of that Regulation.