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NOTE

From:	General Secretariat of the Council
To:	Permanent Representatives Committee
No. prev. doc.:	6462/18 PHARM 10 VETER 16 SAN 65 MI 102 AGRILEG 31 CODEC 227
No. Cion doc.:	13240/14 PHARM 69 VETER 86 MI 666 AGRILEG 186 CODEC 1839
Subject:	Proposal for a Regulation amending Regulation (EC) No 726/2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency *- Confirmation of the final compromise text with a view to agreement*

I. INTRODUCTION

1. On 10 September 2014, the Commission transmitted to the European Parliament and to the Council the Proposal[1] for a Regulation amending Regulation (EC) No 726/2004[2]. This proposal was adopted together with a Proposal[3] for a Regulation on Veterinary Medicinal Products ("the VMP Regulation") and a Proposal[4] for a Regulation on Medicated Feed.

2. The legal basis for the proposed Regulation amending Regulation (EC) No 726/2004 is Article 114 and Article 168(4)(c) of the Treaty on the Functioning of the European Union ("TFEU"). The ordinary legislative procedure is applicable.

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1 13240/14 PHARM 69 VETER 86 MI 666 AGRILEG 186 CODEC 1839. Being part of the "Animal medicines package" it was not accompanied by a separate Impact Assessment.
2 OJ L 136, 30.4.2004, p. 1-33.
3 13289/14 AGRILEG 185 VETER 87 PHARM 70 MI 665 CODEC 1838
4 13196/14 AGRILEG 179 VETER 84 CODEC 1813

II. STATE OF PLAY

3. On 2 March 2018, the Committee endorsed the Tentative Agreement[5] on the text of the Regulation amending Regulation (EC) No 726/2004 that had been reached between the European Parliament and the Council in an informal trilogue held on 21 February 2018.

4. The Committee on that occasion also mandated the Presidency to make any technical adjustments to the Tentative Agreement that might become necessary once a compromise on the VMP Regulation had been negotiated between the Institutions.

5. The United Kingdom delegation at that stage maintained a Parliamentary scrutiny reservation, which has meanwhile been lifted.

6. In an informal trilogue, that took place on 5 June 2018, the European Parliament and the Council tentatively agreed on a compromise text for the VMP Regulation[6].

7. The Presidency has examined the texts of the Tentative Agreement on the Regulation amending Regulation (EC) No 726/2004 and of the compromise text for the VMP Regulation. Based on this examination, the Presidency concludes that the only technical adjustment needed is to clarify the wording providing that the Regulation amending Regulation (EC) No 726/2004 and the VMP Regulation should enter into force on the same date and that they should be applied from the same day. (See Article 2 on page 35.)

III. CONCLUSION

In the light of the above, the Permanent Representatives Committee is invited:

(a) to agree to the text set out in the Annex to this Note, thereby confirming its tentative agreement of 2 March 2018;

and

(b) to mandate the President to inform the European Parliament accordingly.

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[5] At that stage, the Commission indicated that it, for Institutional reasons, had reservations on a few specific provisions in the Tentative Agreement.The draft compromise text is set out in the "four-columns table" in document 6462/18 + ADD 1 + COR 1. A consolidated version of the draft compromise text is available in document 7259/18.

[6] 9763/18 + ADD 1.

ANNEX

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

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

Having regard to the proposal from the European Commission,

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

Having regard to the opinion of the European Economic and Social Committee[7],

Having regard to the opinion of the Committee of the Regions[8],

Acting in accordance with the ordinary legislative procedure,

Whereas:

[7] OJ C , , p. .

[8] OJ C , , p. .

(1) Directive 2001/82/EC of the European Parliament and of the Council[9] and Regulation (EC) No 726/2004 of the European Parliament and of the Council[10] constituted the Union regulatory framework for the manufacture, authorisation and distribution of veterinary medicinal products. In the light of the experience acquired and following the assessment by the Commission of the functioning of the internal market for veterinary medicinal products, the regulatory framework for veterinary medicinal products has been reviewed, and Regulation [*reference to the VMP Regulation*] of the European Parliament and of the Council[11] laying down procedures for the authorisation and supervision of veterinary medicinal products has been adopted, with a view to harmonisation of the laws of the Member States.

(2) It is appropriate to maintain certain provisions relating to veterinary medicinal products, in particular those relating to the European Medicines Agency, in Regulation (EU) No 726/2004, but as the procedures applicable to centralised marketing authorisations for veterinary medicinal products are laid down in Regulation [*reference to the VMP Regulation*], the parts of Regulation (EC) No 726/2004 that relate to procedures for those marketing authorisations and that are covered by Regulation [*reference to the VMP Regulation*] should be repealed.

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9 Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L 311, 28.11.2001, p. 1).

10 Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).

11 Regulation … of the European Parliament and of the Council of … … … on veterinary medicinal products (OJ L …, … … …, p. …).

(3) The costs of the procedures and services associated with the operation of this Regulation need to be recovered from those making medicinal products available on the market and from those seeking authorisation. As Council Regulation (EC) No 297/95[12] and Regulation (EU) No 658/2014 of the European Parliament and of the Council[13] establish the fees payable to the European Medicines Agency (hereinafter referred to as 'the Agency') for the services it provides it is not necessary to maintain any provisions on the structure and level of those fees in Regulation (EC) No 726/2004. In order to ensure that the entire current legal framework for fees payable to the Agency in relation to medicinal products for human use and veterinary medicinal products remains unchanged until an agreement of changes thereto has been reached, it is however appropriate to provide that Commission Regulation (EC) No 2049/2005[14] remain in force and continue to apply unless and until repealed. When reviewing the legal framework for fees payable to the Agency, the Commission should pay attention to potential risks related to the fluctuations in the fee revenue of the Agency.

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12 Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the Evaluation of Medicinal Products (OJ L 35, 15.2.1995, p. 1).

13 Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use.

14 Commission Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises. (OJ L 329, 16.12.2005, p. 4-7.)

(3a) Before a medicinal product for human use is authorised for placing on the market of one or more Member States, it generally has to undergo extensive studies to ensure that it is safe, of high quality and effective for use in the target population. In the case of certain categories of medicinal products, however, in order to meet unmet medical needs of patients and in the interests of public health, it may be necessary to grant marketing authorisations on the basis of less complete data than is normally the case. Those marketing authorisations should be granted subject to specific obligations. The categories concerned should be medicinal products, including orphan medicinal products, that aim at the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases, or that are intended to be used in emergency situations in response to public health threats. Detailed rules on marketing authorisations subject to specific obligations are specified in Commission Regulation (EC) No 507/2006[15]. Those rules should be maintained, but it is appropriate to consolidate them by moving the core provisions into the basic act, while maintaing a delegation of powers that allows the Commission to supplement Regulation (EC) No 726/2004 by adjusting the procedures and provisions for granting and renewal of such marketing authorisations and by specifying the categories of medicinal products that fulfill the requirements of Regulation (EC) No 726/2004 for being granted a marketing authorisation subject to specific obligations.

[15] OJ L 92, 30.3.2006, p. 6.

(3b) Marketing authorisations for medicinal products for human use are granted by a competent authority of a Member State pursuant to Direcive 2001/83/EC[16] or by the Commission pursuant to Regulation (EC) No 726/2004. Those basic acts also provide the legal bases for the examination of applications for variations to the terms of marketing authorisations. Directive 2009/53/EC of the European Parliament and of the Council[17] further harmonised the system for examination of applications for variations to cover also many medicinal products authorised under purely national procedures. That system as laid down in Commission Regulation (EC) No 1234/2008[18] should be maintained. It is however appropriate to consolidate it by moving its core elements into the basic acts, while maintaing a delegation of powers that allows the Commission to complement the core elements by laying down further necessary elements and to adapt the system currently in force to technical and scientific progress. As the provisions on variations in Directive 2001/83/EC should remain aligned to those in Regulation (EC) 726/2004 it is appropriate to make the same changes in both legal acts.

(3ba) Since 2015, the Agency, the European Food Safety Authority ('EFSA') and the European Centre for Disease Prevention and Control ('ECDC') have published Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Reports. It is appropriate to provide that the Agency should continue to contribute to periodic reporting on this issue that should be carried out at least every three[19] years. Considering the seriousness of the threat from Antimicrobial resistance (AMR), it is desirable to increase the reporting frequency within the limits set by feasibility and data reliability.

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16 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67–128).

17 Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009 amending Directive 2001/82/EC and Directive 2001/83/EC, as regards variations to the terms of marketing authorisations for medicinal products (OJ L 168, 30.06.2009, p. 33).

18 Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7).

19 This frequency of preparing JIACRA reports is not incompatible with what is provided in the VMP Regulation. (Compare Footnote 23.)

(3c) In order to ensure the enforcement of certain obligations connected with the marketing authorisation for medicinal products granted in accordance with this Regulation, the Commission may impose financial penalties. When assessing the responsibility for failures to observe those obligations and imposing such penalties, it is important to provide means to address the fact that marketing authorisation holders may be part of a wider economic entity. Otherwise, there is a clear and identified risk that the responsibility for infringements could be evaded, which might impact the ability to impose effective, proportional and dissuasive penalties.

(4) As a consequence of the entry into force of the Treaty of Lisbon, the powers conferred on the Commission under Regulation (EC) No 726/2004 should be aligned to Articles 290 and 291 of the Treaty on the Functioning of the European Union (TFEU). In order to supplement or amend certain non-essential elements of Regulation (EC) No 726/2004, the power to adopt acts in accordance with Article 290 TFEU should be delegated to the Commission in respect of determining the situations in which post-authorisation efficacy studies may be required, establishing procedures for the examination of applications for the transfer of marketing authorisations and laying down the procedure for investigating the infringements and the imposition of fines or periodic penalty payments to the holders of marketing authorisations granted under this Regulation as well as the conditions and methods for their collection.

(5) It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level, and that those consultations be conducted in accordance with the principles laid down in the Interinstitutional Agreement of 13 April 2016 on Better Law-Making[20]. In particular, to ensure equal participation in the preparation of delegated acts, the European Parliament and the Council receive all documents at the same time as Member States' experts, and their experts systematically have access to meetings of Commission expert groups dealing with the preparation of delegated acts.

[20] OJ L 123, 12.5.2016, p. 1.

(6) In order to ensure uniform conditions for the implementation of Regulation (EC) No 726/2004, implementing powers should be conferred on the Commission to adopt implementing acts in relation to marketing authorisations for medicinal products for human use. Those powers should be exercised in accordance with Regulation (EU) No 182/2011 of the European Parliament and of the Council[21].

(6a) The Agency should provide advice for the regulatory acceptance of innovative development methods in the context of research and development of medicinal products for human use and veterinary medicinal products.

(7) Regulation (EC) No 726/2004 should therefore be amended accordingly,

HAVE ADOPTED THIS REGULATION:

Article 1

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

(1) the title is replaced by the following:
'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';

(1a) the word 'Community' shall be replaced by 'Union' and any necessary grammatical changes shall be made, except in the second sub-paragraph of Article 13(1) and in Article 13(2);

[21] 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).

(2) in Article 1, the first paragraph is replaced by the following:

'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 (hereinafter referred to as 'the Agency') that shall undertake the tasks relating to medicinal products for human use and veterinary medicinal products that are laid down in this Regulation and other Union legislation.'

(3) in Article 2, the first paragraph is replaced by the following:

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

(1) "medicinal product" and "medicinal product for human use" means a medicinal product as defined in point (2) of Article 1 in Directive 2001/83/EC;

(2) "veterinary medicinal product" means a medicinal product as defined in point (1) of Article 4 in Regulation [*reference to the VMP Regulation*].

In addition, the other definitions of Article 1 of Directive 2001/83/EC shall apply for the purposes of this Regulation.';

(4) Article 3 is amended as follows:

(a) paragraph 2 is replaced by the following:

'2. Any medicinal product not appearing in Annex I may be granted a marketing authorisation by the Union in accordance with the provisions of 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 interests of patients health at Union level.',

(b) in paragraph 3, the introductory phrase and point (a) are replaced by the following:

'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;',

(c) paragraph 4 is deleted;

(5) Article 4(3) is deleted;

(5a) In Article 9(1), point (d) is replaced by the following:

'(d) the authorisation needs to be granted subject to the conditions provided for in Article 14(8) and in Article 14aa.';

(6) Article 10 is amended as follows:

(a) paragraph 2 is replaced by the following:

'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).',

(b) paragraph 5 is replaced by the following:

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

(7) Article 10b(1) is replaced by the following:

'The Commission is empowered to adopt delegated acts in accordance with Article 87b, 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).';

(7a) Article 14(1) is replaced by the following:

‘1. Without prejudice to paragraphs 4 and 5 of this Article and Article 14aa a marketing authorisation shall be valid for five years.’;

(7b) Article 14(7) is deleted.

(8) The following Article 14aa is added before Article 14a:

‘Article 14aa

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 positive and the applicant is likely to be able to provide comprehensive data.

4. Marketing authorisations granted pursuant to this Article shall be subject to certain specific obligations, to be reviewed annually by the Agency.

5. As part of the specific obligations, 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 positive.

6. Those obligations and, where appropriate, the time limit for compliance shall be specified in the conditions to the marketing authorisation. 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 those obligations.

7. By way of derogation from paragraph 1 of Article 14, such authorisation shall be valid for one year, on a renewable basis.

8. When the specific obligations 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 paragraphs 2 and 3 of Article 14.

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

(a) specifying the categories of medicinal products that fall under paragraph 1; and

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

(9) Article 16(4) is deleted;

(9a) The following Article 16a is added:

'Article 16a

1. For the purposes of this Regulation, 'variation' and 'variation to the terms of a marketing authorisation' mean an amendment to the contents of the particulars and documents referred to in:

(a) Article 8(3) and Articles 9 to 11 of Directive 2001/83/EC and Annex I thereto, in Article 6(2) of this Regulation, and in Article 7 of Regulation (EC) No 1394/2007; and

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

2. 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.

3. 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.

4. The Commission is empowered to adopt delegated acts in accordance with Article 87b 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.';

(9b) The following Article 16b is added:

‘Article 16b

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

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

(10) Article 20 is amended as follows:

(a) paragraph 3 is replaced by the following:

‘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).

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

(b) paragraph 6 is replaced by the following:

‘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.’;

(10a) The following Article 20a is inserted immediately after Article 20:

‘Article 20a

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

(10b) Article 55 is replaced by the following:

‘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.’;

(10c) Point (b) of Article 56(1) is replaced by the following:

‘(b) the Committee for Veterinary Medicinal Products established pursuant to Article 139(1) of Regulation [*reference to the VMP Regulation*];’;

(10d) The first subparagraph of Article 56(2) is replaced by the following:

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

(10e) Article 56(3) is replaced by the following:

‘3. The Executive Director, in close 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 Article 57(1)(n), including advice on the use of novel methodologies and tools in research and development, particularly regarding the development of new therapies.

Each committee shall establish a standing working party with the sole remit of providing scientific advice to undertakings.’;

(10f) In Article 56(4) ‘the Committee for Medicinal Products for Veterinary use’ is replaced by ‘the Committee for Veterinary Medicinal Products;’;

(10g) Article 57(1) is replaced by the following:

‘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 or veterinary medicinal products which is referred to it in accordance with the provisions of Union legislation relating to medicinal products.

To this end, the Agency, acting particularly through its committees, shall undertake the following tasks:

(a) coordination of 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 these medicinal products for human use;

(c) coordinating the monitoring of medicinal products for human use and of veterinary medicinal products which have been authorised within the Union and providing advice on the measures necessary to ensure the safe and effective use of those medicinal 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 data bases 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;

(k) recording the status of marketing authorisations for medicinal products for human use and for veterinary medicinal products granted in accordance with Union 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 shall facilitate the search for information already authorised for package leaflets; it shall include a section on medicinal products authorised for the treatment of children; the information provided to the public shall be worded in an appropriate and comprehensible manner;

(m) assisting the Union and 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 observed in the case of parallel distribution of medicinal products for human use and on veterinary medicinal products authorised in accordance with this Regulation or Regulation [*reference to the VMP Regulation*], as applicable;

(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, compilation of 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 to treat, the effects of such agents;

(r) coordination of 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;

(t) taking decisions as referred to in Article 7(1) of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use[22];

(u) contributing to the joint reporting with EFSA and ECDC 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 54 of Regulation [*reference to the VMP Regulation*]. Such reporting shall be carried out at least every three[23] years.';

(11) The first subparagraph of Article 57(2) is replaced by the following:

'2. The database provided for in paragraph 1(l) shall include the summaries of product characteristics, the package leaflet and the information shown on the labelling. The 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.';

(12) Article 59(4) is replaced by the following:

'4. Save as otherwise provided in this Regulation, in Regulation [*reference to the VMP Regulation*] or in 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. This document shall be published immediately after its adoption.';

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22 OJ L 378, 27.12.2006, p.1.

23 Article 54 of the VMP regulation lays down the reporting obligations on Member States regarding sales volumes and uses of antimicrobial medicinal products used in animals. It also obliges the Agency to prepare an annual report thereon. The provision on the Agency to report at least every three years concerns the JIACRA reports (compare Recital (3ba)). To prepare a JIACRA report every three years is not incompatible with Article 54.

(13) Article 61is amended as follows:

(a) paragraph 1 is replaced by the following:

‘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 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 competent national authorities.’;

(b) in paragraphs 2 and 6 ‘the committees’ is replaced by ‘the Committee for Medicinal Products for Human Use’;

(c) in paragraphs 3, 5 and 8 ‘each committee’ is replaced by ‘the Committee for Medicinal Products for Human Use’;

(d) in paragraph 4 ‘the committees’ is replaced by ‘the committees referred to in Article 56(1)’;

(e) in paragraph 7 ‘each committee’ is replaced by ‘the committees referred to in Article 56(1)’;

(13a) The third and fourth subparagraphs of Article 62(1) are replaced by the following:

‘When consulting the scientific advisory groups referred to in Article 56(2), the Committee shall forward to them the draft assessment report(s) 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).’;

(13b) Article 62(2) is replaced by the following:

‘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 keep an up-to-date list of accredited experts. The list shall include the experts referred to in the first subparagraph and any other experts appointed by the Agency or the Commission. The list shall be updated.’;

(14a) Article 64(1) is replaced by the following:

‘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 elsewhere. Before appointment, the candidate nominated by the Management Board shall be invited forthwith to make a statement to the European Parliament and to answer any questions put by its Members. His mandate 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 post.’;

(14b) The last sentence of Article 64(3) is replaced by the following:

‘The draft report covering the activities of the Agency in the previous year shall include information about the number of applications evaluated within 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.’;

(14c) Article 66 is amended as follows:

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

‘(a) adopt an opinion on the rules of procedures of the Committee for Medicinal Products for Human Use (Article 61) and the Committee for Veterinary Medicinal Products (Article 139(5) in Regulation [*reference to the VMP Regulation*]);’;

(b) point (j) is deleted;

(c) point (k) is replaced by following:

‘(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).’;

(15) Article 67(3) is replaced by the following:

‘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;

(c) fees paid by undertakings 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 [*reference to the VMP Regulation*], or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC;

(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.’;

(15a) Article 68 is replaced by the following:

‘Article 68

1. The Executive Director shall implement the budget of the Agency in accordance with the provisions of the Regulation on the financial rules applicable to the general budget of the Union.

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

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

4. By 31 March of the following financial year, the Commission's accounting officer shall send the Agency's provisional accounts, 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 148 of the Financial Regulation applicable to the general budget of the Union, the 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.

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

7. The final accounts shall be published in the Official Journal of the European Union by 15 November of the following year.

8. The Executive Director shall send to the Court of Auditors a reply to its observations by 30 September. He or she shall also send this 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 in question, in accordance with Article 165(3) of the Financial Regulation applicable to the general budget of the Union.

10. On a recommendation from the Council, the European Parliament shall, before 15 May of 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 unless specifically required for the Agency's operation and with the Commission's prior consent.';

(16) Article 70 is deleted.

(16a) Article 77 is replaced by following:

'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 regulations 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 beforehand by the Commission.';

(16b) Article 78(2) is replaced by following:

‘2. The committees referred to in Article 56(1) and any working parties and scientific advisory groups established in accordance with that Article or Article 139(3) of Regulation [*reference to the VMP Regulation*] 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 these 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.’;

(16c) The first subparagraph of Article 80 is replaced by following:

‘To ensure an appropriate level of transparency, the Management Board, on the basis of a proposal by the Executive Director and in agreement with the Commission, shall 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.’;

(16d) Article 82(3) is replaced by following:

‘3. Without prejudice to the unique, Union nature of the content of the documents referred to in points (a) to (d) of Article 9(4), 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.’;

(17) Article 84(3) is deleted.

(17a) The following Article 84a is inserted after Article 84:

‘Article 84a

1. The Commission may impose financial penalties on the holders of marketing authorisations granted under this Regulation if they fail to observe any of the obligations laid down in Annex II in connection with the marketing authorisations.

1a. The Commission may, insofar as specifically provided for in the delegated acts referred to in paragraph 9, point (b), impose the financial penalties referred to in paragraph 1 also on a different legal entity or entities provided that such entities form part of the same economic entity as the marketing authorisation holder and that such other legal entities:

(i) exerted a decisive influence over the marketing authorisation holder, or

(ii) were involved in, or could have addressed, the infringement by the marketing authorisation holder.

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

3. In determining whether to impose a financial penalty and in determining the appropriate financial penalty, 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 infringement.

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

– 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

– any sanctions, including penalties, already imposed on the same marketing authorisation holder on the basis of the same legal grounds and the same facts.

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

Where the marketing authorisation holder has not terminated the infringement, the Commission may, in the decision referred to in paragraph 1, impose periodic penalty payments per day not exceeding 2,5 % of the holder's average daily Union turnover in the business year preceding the date of the decision.

Periodic penalty payments may be imposed for a period running from the date of notification of that decision until the infringement has been brought to an end.

6. For the conduct of the investigation, the Commission may cooperate with national competent authorities and rely on resources provided by the Agency.

7. 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 in the protection of their business secrets.

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

9. The Commission is empowered to adopt delegated acts in accordance with Article 87b 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 fees and periodic penalty payments, as well as the conditions and methods for their collection.';

(18) Article 86 is replaced by the following:

'Article 86

At least every ten 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.';

(18a) The following Article is inserted:

'Article 86a

By 2019 the Commission shall review the legal 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 legal 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.';

(19) Article 87 is replaced by the following:

‘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. The Committee shall be a committee within the meaning of Regulation (EU) No 182/2011.

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

(20) Article 87b is replaced by the following:

‘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), 14aa(9), 16a(4), 16b and 84a(9) shall be conferred on the Commission for a period of 5 years from […[24]]. The Commission shall draw up a report in respect of the delegation of power not later than nine months before the end of the 5-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), 14aa(9), 16a(4), 16b and 84a(9) 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.

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24 Date to be decided based on current reporting obligations.

3a. 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 on Better Law-Making of 13 April 2016.

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

5. A delegated act adopted pursuant to Articles 10b(1), 14aa(9), 16a(4), 16b and 84a(9) shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of three months of notification of that act to the European Parliament and 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.';

(21) Articles 30 to 54, Articles 79, 87c and 87d and point 2 of the Annex are deleted*;*

(22) The Annex becomes Annex I;

(23) The Annex set out in the Annex to this Regulation is added as Annex II.

Article 1aa

Amendments to Directive 2001/83/EC

Directive 2001/83/EC is hereby amended as follows:

(1) in Article 23b, paragraphs 1, 2 and 3 are replaced by the following:

‘1. For the purposes of this Directive 'variation' and 'variation to the term of a marketing authorisation' means an amendment to the contents of the particulars and documents referred to in:

(a) Article 8(3) and Articles 9 to 11 of this Directive and its Annex I, Article 6(2) of Regulation (EC) No 726/2004 and in Article 7 of Regulation (EC) No 1394/2007; and

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

2. 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 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.

2a. 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 competent authority.

2b. The Commission is empowered to adopt delegated acts in accordance with Article 121a to supplement this Directive 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.

3. When adopting the delegated acts referred to in this Article, the Commission shall make efforts to make it possible to submit a single application for one or more identical changes made to the terms of a number of marketing authorisations.';

(2) in Article 23b(4) and in Article 23b(5), the words 'the implementing regulation' are replaced by 'Commission Regulation (EC) No 1234/2008'.

Article 1ab

Amendments to Regulation (EC) No 1901/2006

Regulation (EC) No 1901/2006 is hereby amended as follows:

In Article 49, paragraph 3 is replaced by the following:

'3. The Commission may, in relation to medicinal products authorised through the procedure laid down in Regulation (EC) No 726/2004, pursuant to Article 84a of that Regulation impose financial penalties in the form of fines or periodic penalty payments for the infringement of the obligations based on this Regulation that are listed in Annex II to Regulation (EC) No 726/2004.

Article 1a

1. Commission Regulation (EC) No 2049/2005[25] and Commission Regulation (EC) No 2141/96[26] shall remain in force and continue to apply unless and until repealed.

2. Commission Regulation (EC) No 507/2006[27] shall continue to apply unless and until repealed.

3. Commission Regulation (EC) No 658/2007[28] shall continue to apply unless and until repealed.

4. Commission Regulation (EC) No 1234/2008[29] shall continue to apply unless and until repealed as regards medicinal products for human use that are covered by Regulation (EC) No 726/2004 and Directive 2001/83/EC and that are not exempted from the provisions in that Commission Regulation by virtue of paragraphs 4 and 5 of Article 23b of Directive 2001/83/EC.

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25 Commission Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises. (OJ L 329, 16.12.2005, p. 4-7.)

26 Commission Regulation (EC) No 2141/96 of 7 November 1996 concerning the examination of an application for the transfer of a marketing authorization for a medicinal product falling within the scope of Council Regulation (EC) No 2309/93

27 Commission Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ L 92, 30.3.2006, p. 6)

28 Commission Regulation (EC) No 658/2007 of 14 June 2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ L 155, 15.6.2007, p.10)

29 Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7)

Article 2

This Regulation shall enter into force on [*the date of entry into force of the VMP Regulation*][30].

It shall apply from [*the date of application of the VMP Regulation*][31].

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

Done at Brussels,

For the European Parliament	*For the Council*
The President	*The President*

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[30] Previous text "… on the twentieth day following its publication in the *Official Journal of the European Union*." It is assumed that the OJ will take the necessary measures to ensure timely publishing allowing for entry into force on the same date as that of the VMP Regulation.

[31] The VMP Regulation shall be applied 36 months after entry into force. The previous text of Article 2 provided for application of the VMP-related provisions from the same date as that of the VMP regulation and for another (non-specified earlier) date for the other provisions. As this date was not discussed the Presidency proposes to stick to one and the same date for the entire Regulation, as originally proposed by the Commission.

‘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 infringement 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, as referred to in Article 9(4)(b) 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 as referred to in Article 9(4)(aa), (c), (ca), (cb) and (cc) and 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 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 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 Articles 16(3a);

(8) the obligation to place the medicinal product 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 14aa;

(10) the obligation to notify the Agency of the dates of actual marketing and of the date when the product 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 product, 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 read together with Article 104 of Directive 2001/83/EC;

(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) read together 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) read together Article 107 of Directive 2001/83/EC;

(15) the obligation to submit periodic safety update reports, in accordance with Article 28(2) read together 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 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 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 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 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 marketing authorisation dossier, as provided for in the first subparagraph 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 into the European database on third country clinical trials, as provided for in Article 41(1) and (2), Article 45(1) and Article 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 subparagraph of Article 35 of that Regulation.