Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Text with EEA relevance)

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

of 15 December 2010

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(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

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

Having regard to the proposal from the European Commission,

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

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

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

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

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

Whereas:

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

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

(3) The pollution of waters and soils with pharmaceutical residues is an emerging environmental problem. Member States should consider measures to monitor and

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

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

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

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

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

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

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

(10) In order to ensure harmonised responses across the Union to safety concerns regarding medicinal products for human use, the Committee for Medicinal Products for Human Use and the coordination group established by Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use[6] should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee with regard to any question relating

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to the pharmacovigilance of medicinal products for human use. However, for the sake of consistency and continuity of the safety assessments, the final responsibility for issuing an opinion on the risk-benefit assessment of medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004 should remain with the Committee for Medicinal Products for Human Use and with the authorities competent for the granting of marketing authorisations.

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

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

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

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

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

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

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to enable the assessment of safety or efficacy of medicinal products for human use in everyday medical practice.

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

(18) Experience has shown that the responsibilities of marketing authorisation holders with regard to pharmacovigilance of authorised medicinal products for human use should be clarified. The marketing authorisation holder should be responsible for continuously monitoring the safety of its medicinal products for human use, for informing the authorities of any changes that might have an impact on the marketing authorisation, and for ensuring that the product information is kept up to date. As medicinal products for human use could be used outside the terms of the marketing authorisation, the marketing authorisation holder's responsibilities should include providing all available information, including the results of clinical trials or other studies, as well as reporting any use of the medicinal product which is outside the terms of the marketing authorisation. It is also appropriate to ensure that all relevant information collected on the safety of the medicinal product for human use is taken into account when the marketing authorisation is being renewed.

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

(20) As a result of the submission of all suspected adverse reaction data for medicinal products for human use authorised by the Member States directly to the Eudravigilance database, it is not necessary to provide for different reporting rules for medicinal

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products for human use authorised in accordance with Regulation (EC) No 726/2004. The rules on suspected adverse reaction recording and reporting laid down in Directive 2001/83/EC should therefore apply to medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004.

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

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

(23) This Regulation shall apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data[(7)] and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data[(8)]. In order to detect, assess, understand and prevent adverse reactions, and to identify and take actions to reduce the risks of, and increase the benefits from, medicinal products for human use for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while respecting the Union legislation relating to data protection. The purpose of safeguarding public health constitutes a substantial public interest and consequently the processing of personal data can be justified if identifiable health data are processed only when necessary and only when the parties involved assess this necessity at every stage of the pharmacovigilance process.

(24) This Regulation and Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use[(9)] widen the tasks of the Agency with regard to pharmacovigilance, including the monitoring of literature cases, the improved use of information technology tools and the provision of more information to the general public. The Agency should be enabled to fund these activities from fees charged to marketing authorisation holders. These fees should not cover tasks carried out by national competent authorities for which such authorities charge fees in accordance with Directive 2001/83/EC.

(25) The pharmacovigilance activities provided for in this Regulation require that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well as the minimum requirements for the