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***I
REPORT

on the proposal for a regulation of the European Parliament and of the Council 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
(COM(2008)0664 – C6-0515/2008 – 2008/0257(COD))

Committee on the Environment, Public Health and Food Safety

Rapporteur: Linda McAvan

PR_COD_1am

Symbols for procedures

*	Consultation procedure *majority of the votes cast*
**I	Cooperation procedure (first reading) *majority of the votes cast*
**II	Cooperation procedure (second reading) *majority of the votes cast, to approve the common position* *majority of Parliament's component Members, to reject or amend the common position*
***	Assent procedure *majority of Parliament's component Members except in cases covered by Articles 105, 107, 161 and 300 of the EC Treaty and Article 7 of the EU Treaty*
***I	Codecision procedure (first reading) *majority of the votes cast*
***II	Codecision procedure (second reading) *majority of the votes cast, to approve the common position* *majority of Parliament's component Members, to reject or amend the common position*
***III	Codecision procedure (third reading) *majority of the votes cast, to approve the joint text*

(The type of procedure depends on the legal basis proposed by the Commission.)

Amendments to a legislative text

In amendments by Parliament, amended text is highlighted in ***bold italics*.** In the case of amending acts, passages in an existing provision that the Commission has left unchanged, but that Parliament wishes to amend, are highlighted in **bold**. Any deletions that Parliament wishes to make in passages of this kind are indicated thus: [...]. Highlighting in *normal italics* is an indication for the relevant departments showing parts of the legislative text for which a correction is proposed, to assist preparation of the final text (for instance, obvious errors or omissions in a given language version). Suggested corrections of this kind are subject to the agreement of the departments concerned.

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DRAFT EUROPEAN PARLIAMENT LEGISLATIVE RESOLUTION

on the proposal for a regulation of the European Parliament and of the Council 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
(COM(2008)0664 – C7-0515/2008 – 2008/0257(COD))

(Ordinary legislative procedure: first reading)

The European Parliament,

– having regard to the Commission proposal to the European Parliament and the Council (COM(2008)0664),

– having regard to Article 251(2) and Article 95 of the EC Treaty, pursuant to which the Commission submitted the proposal to Parliament (C6-0515/2008),

– having regard to the Communication from the Commission to the European Parliament and the Council entitled "Consequences of the entry into force of the Treaty of Lisbon for ongoing interinstitutional decision-making procedures" (COM(2009)0665),

– having regard to Article 294(3) and Article 114 and Article 168(4)(c) of the Treaty on the Functioning of the European Union,

– having regard to the opinion of the European Economic and Social Committee of 10 June 2009[1],

– having regard to the opinion of the Committee of the Regions of 7 October 2009[2],

– having regard to Rule 55 of its Rules of Procedure,

– having regard to the report of the Committee on the Environment, Public Health and Food Safety and the opinions of the Committee on Industry, Research and Energy and the Committee on the Internal Market and Consumer Protection (A7-0153/2010),

1. Adopts the the position at first reading hereinafter set out;

2. Calls on the Commission to refer the matter to Parliament again if it intends to amend the proposal substantially or replace it with another text;

3. Instructs its President to forward its position to the Council and the Commission.

[1] OJ C 306, 16.12.2009, p. 22.
[2] OJ C 79, 27.3.2010, p. 50.

Amendment 1

Proposal for a regulation – amending act
Citation 3 a (new)

Text proposed by the Commission	*Amendment*
	- having regard to the opinion of the European Data Protection Supervisor of 22 April 2009[1]

Amendment 2

Proposal for a regulation – amending act
Recital 2 a (new)

Text proposed by the Commission	*Amendment*
	(2a) The pollution of waters and soils with pharmaceutical residues is an emerging environmental problem and an emerging public health concern. Measures should be taken to monitor and evaluate adverse environmental effects of medicinal products, including those which impact on public health.
	The Commission should, based on data received from the Agency, the Environment Agency, and Member States, produce a report on the scale of the problem, along with an assessment on whether amendments to EU legislation on medicinal products or other relevant EU legislation are required.

Amendment 3

Proposal for a regulation – amending act
Recital 4

Text proposed by the Commission	*Amendment*
(4) The main tasks of the Agency in the area of pharmacovigilance laid down in	(4) The main tasks of the Agency in the area of pharmacovigilance laid down in

[1] OJ C 229, 23.9.2009, p. 19.

Regulation (EC) No 726/2004 should be maintained and further developed, in particular as regards the management of the Community pharmacovigilance database and data-processing network (hereinafter referred to as 'the Eudravigilance database') ***and*** the coordination of safety announcements by the Member States.	Regulation (EC) No 726/2004 should be maintained and further developed, in particular as regards the management of the Community pharmacovigilance database and data-processing network (hereinafter referred to as 'the Eudravigilance database')***,*** the coordination of safety announcements by the Member States ***and the provision of information regarding safety issues to the public***.

Justification

Consumers have the right to have more information regarding pharmacovigilance concerns and about the risk-benefit balance of their medicines. The Agency has an important role to play as a reliable independent source of information.

Amendment 4

Proposal for a regulation – amending act
Recital 5

Text proposed by the Commission	*Amendment*
(5) In order to allow all competent authorities to receive and access, at the same time, pharmacovigilance information for medicinal products for human use authorised in the Community, and share it, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose on marketing authorisation holders any additional reporting requirements.	(5) In order to allow all competent authorities to receive and access, at the same time, pharmacovigilance information for medicinal products for human use authorised in the Community, and share it, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose on marketing authorisation holders any additional reporting requirements. ***Instead, the Eudravigilance database should simultaneously notify the relevant Member States of reports submitted by market authorisation holders.*** ***In order to ensure high-quality information, Member States should support the development of national and regional pharmacovigilance centres' expertise. The national competent authorities should collect the reports from those centres and transfer the data to the***

	Eudravigilance database.
The database should be fully accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.	The database should be fully accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public :***in all the official languages of the Union***.

Justification

Member States should be alerted electronically when Market Authorisation Holders submit reports to Eudravigilance about serious suspected adverse reactions which happen on their territory, as an extra check to ensure that national competent authorities do not miss or overlook this information.

Amendment 5

Proposal for a regulation – amending act
Recital 6

Text proposed by the Commission	*Amendment*
(6) In order to increase transparency as regards pharmacovigilance issues, a European medicines safety web-portal should be created and maintained by the Agency.	(6) In order to increase transparency as regards pharmacovigilance issues, a European medicines safety web-portal should be created and maintained by the Agency ***in all the official languages of the Union*****.**

Amendment 6

Proposal for a regulation – amending act
Recital 9

Text proposed by the Commission	*Amendment*
(9) In order to ensure harmonised responses across the Community to safety concerns regarding medicinal products for human use, ***the Pharmacovigilance Risk Assessment Advisory Committee should support*** 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	(9) In order to ensure harmonised responses across the Community 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

November 2001 on the Community code relating to medicinal products for human use on any question relating to the pharmacovigilance of medicinal products for human use. However, for the sake of consistency and continuity of the assessments, the final responsibility for the risk-benefit assessment of medicinal products for human use authorised in accordance with this Regulation should remain with the Committee for Medicinal Products for Human Use of the Agency and with the authorities competent for the granting of marketing authorisations.	use ***should rely on the recommendation of the Pharmacovigilance Risk Assessment Committee*** on any question relating to the pharmacovigilance of medicinal products for human use. However, for the sake of consistency and continuity of the assessments, the final responsibility for the risk-benefit assessment of medicinal products for human use authorised in accordance with this Regulation should remain with the Committee for Medicinal Products for Human Use of the Agency and with the authorities competent for the granting of marketing authorisations.

Justification

If the Pharmacovigilance Risk Assessment Committee (PRAC) is to be a representative committee, its powers should be increased in relation to the CHMP and the coordination group. Neither the CHMP nor the coordination group is a specialist body on pharmacovigilance – their job is to balance overall the risks with benefits. The PRAC should be the only body in charge of pharmacovigilance and risk assessment, in order to avoid undue duplication of roles.

Amendment 7

Proposal for a regulation – amending act
Recital 15

Text proposed by the Commission	*Amendment*
(15) Where a medicinal product is authorized subject to the requirement to conduct a post-authorisation safety study or subject to conditions or restrictions with regard to the safe and effective use of the medicinal product, the medicinal product should be intensively monitored on the market. Patients and healthcare professionals should be encouraged to report all suspect adverse reactions to such medicinal products, and a publicly available list of such medicinal products should be kept up to date by the Agency.	(15) Where a medicinal product is authorized subject to the requirement to conduct a post-authorisation safety study or subject to conditions or restrictions with regard to the safe and effective use of the medicinal product, the medicinal product should be intensively monitored on the market. Patients and healthcare professionals should be encouraged to report all suspect adverse reactions to such medicinal products, ***identified by a symbol and a corresponding explanatory sentence on the summary of product characteristics and on the patient information leaflet***, and a publicly available list of such medicinal products should be kept up to date by the

Agency.

Amendment 8

Proposal for a regulation – amending act
Recital 20 a (new)

Text proposed by the Commission	*Amendment*
	(20a) This Regulation shall apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data[1] and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data[2]. In order to detect, assess, understand and prevent adverse reactions, and to identify and take action to reduce risks and increase benefits of medicinal products for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while complying with EU data protection legislation.
	[1]OJ L 281, 23.11.1995, p. 31.
	[2]OJ L 8, 12.1.2001, p. 1.

Justification

The proposal covers highly sensitive personal information which should be fully protected. See also the opinion of the European Data Protection Supervisor of April 2009.

Amendment 9

Proposal for a regulation – amending act
Recital 21 a (new)

Text proposed by the Commission	*Amendment*
	(21a) The purpose of safeguarding public health constitutes a substantial public interest which justifies the processing of identifiable health data as long as it is processed only when necessary and the parties involved assess the necessity of processing such data at every stage of the pharmacovigilance process.

Justification

The proposal covers highly sensitive personal information which should be fully protected. However, it should be possible to process personal data within the Eudravigilance system whilst also respecting EU data protection legislation.

Amendment 10

Proposal for a regulation – amending act
Article 1 - point 1
Regulation (EC) No 726/2004
Article 5 - paragraph 2

Text proposed by the Commission	*Amendment*
For the fulfilment of its pharmacovigilance tasks, it shall ***be assisted by*** the Pharmacovigilance Risk Assessment ***Advisory*** Committee referred to in Article 56(1)(aa).	For the fulfilment of its pharmacovigilance tasks, it shall ***rely on the recommendation of*** the Pharmacovigilance Risk Assessment Committee referred to in Article 56(1)(aa). *The word « Advisory » should be removed from the title of the Pharmacovigilance Risk Assessment Committee so that it better reflects the powers of the committee.* *If adopted the name will be changed throughout the text.*

Justification

If the Pharmacovigilance Risk Assessment Committee (PRAC) is to be a representative committee, its powers should be increased in relation to the CHMP. The CHMP is not a specialist body on pharmacovigilance – its job is to balance overall the risks with benefits. The PRAC should be the only body in charge of pharmacovigilance and risk assessment, in order to avoid undue duplication of roles.

Amendment 11

Proposal for a regulation – amending act
Article 1 - point 4
Regulation (EC)No 726/2004
Article 10a - paragraph 1

Text proposed by the Commission	*Amendment*
1. After the granting of a marketing authorisation, the Agency may require a marketing authorisation holder to conduct a post-authorisation safety study ***if there are concerns about the risks of an authorised medicinal product.*** The requirement shall be made in writing, provide a detailed justification and include the objectives and timeframe for submission and conduct of the study.	1. After the granting of a marketing authorisation, the Agency may require a marketing authorisation holder to conduct a post-authorisation safety study, ***or post-authorisation safety and efficacy studies where important questions relating to the efficacy of a product remain; or when scientific advances in the understanding of the disease or in the clinical methodology would significantly change previous efficacy evaluations. For this purpose the Commission shall provide guidelines.*** The requirement shall be made in writing, provide a detailed justification and include the objectives and timeframe for submission and conduct of the study. ***The Commission shall also, based on data received from the Agency and Member States, produce a report focusing on the concept of Clinical Effectiveness, studies and data required and methodologies for assessing it.***

Justification

At the moment, most drugs are subject to some kind of PASS as an extra safety precaution. However, although safety monitoring happens throughout the life of a drug, efficacy is only checked once, at the time of authorisation. There should be the possibility to monitor drug

efficacy post-authorisation as well - in real world populations and real-life conditions.

Amendment 12

Proposal for a regulation – amending act
Article 1 - point 4
Regulation (EC)No 726/2004
Article 10a - paragraph 3

Text proposed by the Commission	*Amendment*
3. On the basis of explanations submitted by the marketing authorisation holder, the Commission shall withdraw or confirm the requirement. Where the Commission confirms the requirement, the marketing authorisation shall be varied to include the requirement as a condition of the marketing authorisation and the risk management system shall be updated accordingly.	3. On the basis of explanations submitted by the marketing authorisation holder, the Commission shall withdraw or confirm the requirement. Where the Commission confirms the requirement, the marketing authorisation shall be varied to include the requirement as a condition of the marketing authorisation and the risk management system shall be updated accordingly. ***Irrespective of whether the requirement is confirmed or withdrawn, the Commission must state the grounds for its decision in detail, and the decision shall be duly recorded.***

Justification

At the moment, most drugs are subject to some kind of PASS as an extra safety precaution. However, although safety monitoring happens throughout the life of a drug, efficacy is only checked once, at the time of authorisation. There should be the possibility to monitor drug efficacy post-authorisation as well - in real world populations and real-life conditions.

Amendment 13

Proposal for a regulation – amending act
Article 1 – point 5 b
Regulation EC/726/2004
Article 14 – paragraph 3

Text proposed by the Commission	*Amendment*
3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the ***national*** competent authority decides, on justified	3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the competent authority decides, on justified grounds

grounds relating to pharmacovigilance ***or to insufficient exposure to the product***, to proceed with one additional five-year renewal in accordance with paragraph 2.”	relating to pharmacovigilance, to proceed with one additional five-year renewal in accordance with paragraph 2.”

Justification

The benefits of a harmonised and simplified approach pursued in the current proposal should be preserved. The new proposal should not regress on improvements introduced by the previous revision of the medicines legislation which aimed at reducing the number of renewal procedures. The original wording regarding the deciding authority should be maintained.

Amendment 14

Proposal for a regulation – amending act
Article 1 – point 11
Regulation EC/726/2004
Article 21 – paragraph 2 – subparagraph 2

Text proposed by the Commission	*Amendment*
The requirement shall be made in writing, provide a detailed justification**,** and include the timeframe for submission of the detailed description of the risk-management system.	The requirement shall be made in writing, provide a detailed justification ***on the basis of scientific arguments*** and include the timeframe for submission of the detailed description of the risk-management system.

Justification

Where a detailed description of the risk-management system is requested, it should be based on scientific reasons. The Commission proposal is not sufficiently precise on this point.

Amendment 15

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 24 – paragraph 1 – subparagraph 1

Text proposed by the Commission	*Amendment*
1. The Agency, in collaboration with the Member States and the Commission, shall set up and maintain a database and data processing network (hereinafter ‘the Eudravigilance database’) to collate	1. The Agency, in collaboration with the Member States and the Commission, shall set up and maintain a database and data processing network (hereinafter ‘the Eudravigilance database’) to collate

pharmacovigilance information regarding medicinal products authorised in the Community and to allow competent authorities to access the information at the same time and to share it.	pharmacovigilance information regarding medicinal products authorised in the Community and to allow competent authorities to access the information at the same time and to share it. ***Member States shall support the development of the expertise of national and regional pharmacovigilance centres. National competent authorities should collect the reports from those centres and should then transfer data to the Eudravigilance database.***

Amendment 16

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 24 - paragraph 2 - subparagraph 2

Text proposed by the Commission	*Amendment*
The Agency shall ensure that health-care professionals and the public have appropriate levels of access to the Eudravigilance database, with personal data protection being guaranteed.	The Agency shall ensure that health-care professionals and the public have appropriate levels of access to the Eudravigilance database, with personal data protection being guaranteed. ***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" to the Eudravigilance database.***

Justification

The rapporteur agrees that EMEA should not be left to define itself the "appropriate level" of public access to Eudravigilance - but should involve stakeholders. However, she does not support full data being publically available online instead of aggregate data, as the database will contain many ADR reports which are unconfirmed. She also notes that article 24 of the Regulation specifies that individual ADR reports are publically available on request.

Amendment 17

Proposal for a regulation – amending act
Article 1 – point 11
Regulation EC/726/2004
Article 25

Text proposed by the Commission	*Amendment*
The Agency, in collaboration with the Member States, shall develop standard ***web-based*** structured forms for the reporting of suspected adverse reactions by health-care professionals and patients.	The Agency, in collaboration with the Member States and ***all relevant stakeholders***, shall develop standard structured forms ***and procedures, including web-based forms,*** for the reporting of suspected adverse reactions by health-care professionals and patients. ***To ensure the identification of biological medicinal products prescribed, dispensed or sold in the territory of the Union, the standard forms and procedures shall include the name of the MAH (marketing authorisation holder), the INN (international non-proprietary name), the name of the medicinal product as defined in Article 1(2) and the batch number.*** ***The Agency shall also make available to the public other means for patients to report undesirable effects, such as a dedicated telephone number or special email address*** :***All citizens of the Union shall have the option of submitting online declarations in their mother tongue.***

Justification

Accurate identification of the product associated with a suspected adverse event is fundamental to a sound pharmacovigilance system. Due to the specificities of biological medicinal products compared to small molecule medicinal products it is thus necessary to provide a number of identifiers to clearly distinguish the products available on the market.

Therefore the proposed amendment requires the EMEA to develop standard forms and procedures to be used by health-care professionals and patients in reporting suspected adverse events which shall include means to accurately identify biological medicinal products and both strengthen and harmonize reporting requirements for such products.

Amendment 18

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 1

Text proposed by the Commission	*Amendment*
(1) the 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 referred to in Article 27 of Directive 2001/83/EC (hereinafter 'the coordination group'), together with their professional qualifications and with the declarations pursuant to Article 63(2) of this Regulation;	(1) the 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 referred to in Article 27 of Directive 2001/83/EC (hereinafter 'the coordination group'), together with their professional qualifications and with ***their*** declarations ***of interest,*** pursuant to Article 63(2) of this Regulation;

Justification

Many colleagues support a greater degree of transparency than is provided for in the Commission's proposal. The rapporteur supports nearly all of these amendments, and, by extension, does not support any attempt to dilute what the Commission proposes should be made public.
The rapporteur supports full details of every PRAC, CHMP and Coordination Group meeting to be made public, including details of votes and minority opinions. This is already required by Article126b of this same Directive, but is not implemented: "Member States shall ensure that the competent authority makes publicly accessible its rules of procedure and those of its committees, agendas for its meetings and records of its meetings, accompanied by decisions taken, details of votes and explanations of votes, including minority opinions". The USA Food and Drugs Association does make this information public - both in theory and in practice.
The web portal should also include a link to EMEA's European Public Assessment Report (EPAR) database, set up by article 13(3) of the Regulation: http://www.ema.europa.eu/htms/human/epar/eparintro.htm. The EPAR summaries are one-page information sheets about every centrally-authorised medicinal product. They set out what the medicine is, what it's for, what are the risks and benefits, why it was approved, the scientific discussions surrounding it, and the procedural steps involved before and after its authorisation. Both the EPAR and the EudraPharm websites should be promoted, in order to raise awareness amongst patients of these useful sources of independent information about medicinal products.
This compromise amendment should be read in conjunction with compromise amendment 6 on the Directive - as article 106 of the Directive sets out what Member States are responsible for publishing on their national web portal, and article 26 of the Regulation sets out what the Agency is responsible for publishing on the (linked) European web portal.
N.B. Amendment 217 of the Directive has also been included in this compromise, although will have to be voted separately in the voting list for the Directive.

Amendment 19

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 2

Text proposed by the Commission	*Amendment*
(2) ***a summary of*** each meeting of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities;	(2) ***details*** of each meeting of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities, ***including agendas for, and records of, each meeting, accompanied by decisions taken;***

Justification

see justification to Article 26 - point 1

Amendment 20

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 3

Text proposed by the Commission	*Amendment*
(3) risk management systems for medicinal products authorised in accordance with this Regulation;	(3) risk management systems, ***and a user-friendly summary of these systems,*** for medicinal products authorised in accordance with this Regulation;

Justification

see justification to Article 26 - point 1

Amendment 21

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 3 a (new)

Text proposed by the Commission	*Amendment*
	(3a) the link to the Agency's EudraPharm database which must include the most up-to-date electronic version of the package

	leaflet and summary of product characteristics for all existing and new medicinal products authorised in accordance with this Regulation and with Directive 2001/83/EC, as well as a link to the Agency's European Public Assessment Report summary database which publishes information sheets on centrally authorised products. These two resources shall be publicised to the general public by the Agency or the competent authorities.

Justification

see justification to Article 26 - point 1

Amendment 22

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 4

Text proposed by the Commission	*Amendment*
(4) the list of medicinal products ***under intensive monitoring*** referred to in Article 23 of this Regulation;	(4) the list of medicinal products referred to in Article 23 of this Regulation;

Justification

see justification to Article 26 - point 1

Amendment 23

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 - point 6

Text proposed by the Commission	*Amendment*
(6) information about how to report suspected adverse reactions to medicinal products and standard forms for ***their web-based*** reporting by patients and health-care professionals;	(6) information about how to report suspected adverse reactions to medicinal products and standard forms for reporting by patients and health-care professionals;

Justification

see justification to Article 26 - point 1

Amendment 24

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 26 - paragraph 1 a (new)

Text proposed by the Commission	*Amendment*
	Before the launch of the portal, and during subsequent reviews, the Agency shall consult relevant stakeholders (including patient and consumer groups, healthcare professionals and industry representatives).

Justification

see justification to Article 26 - point 1

Amendment 25

Proposal for a regulation – amending act
Article 1 - point 11
Regulation EC/726/2004
Article 27 – paragraph 1

Text proposed by the Commission	*Amendment*
1. The Agency shall monitor selected medical literature for reports of suspected adverse reactions to medicinal products for human use containing certain active substances. It shall publish the list of active substances being monitored and the publications subject to this monitoring.	1. The Agency shall monitor selected medical literature for reports of suspected adverse reactions to medicinal products for human use containing certain active substances. It shall publish the list of active substances being monitored and the publications subject to this monitoring. ***The Agency shall monitor all medical literature for reports of suspected adverse reactions to medicinal products for human use containing well established active substances.***

Justification

The proposal requires the marketing authorisation holder to monitor the EudraVigilance to see what the EMA has covered and to monitor other non-selected medical literature and non-covered medicines. For well established active substances, the European Medicines Agency can carry out this task since the databases searched are the same searched by all marketing authorisation holders who have well established ingredients in common. Consequently,

requiring the European Medicines Agency to do this task for all well established substances makes sense and is efficient (once only).

Amendment 26

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC) No 726/2004
Article 28 - paragraph 3 - subparagraph 4 a (new)

Text proposed by the Commission	*Amendment*
	It shall formulate a recommendation for the Committee for Medicinal Products for Human Use on the basis of the assessment report.

Justification

The opinion of the PRAC should carry more weight with the CHMP, who should only be able to overturn the recommendation of the PRAC if they justify their decision on the grounds of science and public health.

Amendment 27

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC) No 726/2004
Article 28 - paragraph 4

Text proposed by the Commission	*Amendment*
4. Within 30 days of receipt of the ***report*** by the Pharmacovigilance Risk Assessment ***Advisory*** Committee, the Committee for Medicinal Products for Human Use shall ***consider the report and*** adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned.	4. Within 30 days of receipt of the ***recommendation*** by the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned. ***The CHMP shall adopt an opinion which differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, only where there exist strong scientific and public health grounds for doing so. The CHMP shall explain such***

	grounds in a justification to be annexed to its opinion.
Where the opinion states that regulatory action 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 decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.	Where the opinion states that regulatory action 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 decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.

Justification

The opinion of the PRAC should carry more weight with the CHMP, who should only be able to overturn the recommendation of the PRAC if they justify their decision on the grounds of science and public health.

Amendment 28

Proposal for a regulation – amending act
Article 1 – point 11
Regulation EC/726/2004
Article 28 – paragraph 6

Text proposed by the Commission	*Amendment*
6. The opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.	6. The ***final*** opinions and ***final*** decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.

Justification

Information for publication on this web-portal should be complete but not complex.

Amendment 29

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC) No 726/2004
Article 28a - paragraph 2 a (new)

Text proposed by the Commission	*Amendment*
	2(a) For the purposes of that assessment, the Pharmacovigilance Risk Assessment Committee may hold a public hearing.
	Public hearings shall be announced by means of the European medicines safety web-portal. The announcement shall include information on how marketing authorisation holders and the public can participate.
	The Agency shall provide the opportunity, to all those who request it, to participate in the hearing either in person or through the use of web-based technology.
	Where a marketing authorisation holder or another person intending to submit information has commercially confidential data relevant to the issue of the procedure, he may request that he be allowed to present those data to the Pharmacovigilance Risk Assessment Committee in a non-public hearing.

Justification

This is an identical amendment to the Directive. It allows the Pharmacovigilance Risk Assessment Committee to draw on public hearings if it sees fit, in its assessment of medicines authorised both through the centralised and decentralised procedures.

Amendment 30

Proposal for a regulation – amending act
Article 1 – point 11
Regulation EC/726/2004
Article 28d

Text proposed by the Commission	*Amendment*
Upon request of the Commission, the Agency shall participate in collaboration with the Member States in international harmonization and standardization of technical measures in pharmacovigilance.	Upon request of the Commission, the Agency shall participate***,*** in collaboration with the Member States ***and all interested parties,*** in international harmonisation and standardisation of technical measures in pharmacovigilance. ***Such work shall be based on patient needs and be carried out***

from a scientific perspective.

Justification

Amendment to ensure consistency with the proposals for changes to Article 108 of Directive 2001/83/EC.

Amendment 31

Proposal for a regulation – amending act
Article 1 - point 11
Regulation EC/726/2004
Article 28f

Text proposed by the Commission	*Amendment*
The Agency shall perform regular audit of its pharmacovigilance tasks and report the results to its Management Board on a two-yearly basis.	The Agency shall perform regular ***independent*** audit of its pharmacovigilance tasks and report the results to its Management Board on a two-yearly basis.

Justification

The text of the draft directive proposes independent audit for the Member States (Amendment 13). Article 28f of the draft regulation, concerning the Agency, contains a similar provision which should be adapted accordingly to ensure consistency.

Amendment 32

Proposal for a regulation – amending act
Article 1 - point 11
Regulation (EC)No 726/2004
Article 29

Text proposed by the Commission	*Amendment*
The Commission shall adopt any amendments which may be necessary to update the provisions of this Chapter to take account of scientific and technical progress.	***deleted***
Those measures, designed to amend non-essential elements of this Regulation, shall be adopted in accordance with the regulatory procedure with scrutiny	

referred to in Article 87(2a).

Amendment 33

Proposal for a regulation – amending act
Article 1 - point 12 - point a
Regulation (EC) No 726/2004
Article 56 - paragraph 1 - point aa

Text proposed by the Commission	*Amendment*
(aa) the Pharmacovigilance Risk Assessment ***Advisory*** Committee, which shall be responsible for ***providing advice*** to the Committee for Medicinal Products for Human Use and the coordination group on any question relating to the pharmacovigilance of medicinal products for human use;	(aa) the Pharmacovigilance Risk Assessment Committee, which shall be responsible for ***making a recommendation*** to the Committee for Medicinal Products for Human Use and the coordination group on any question relating to the pharmacovigilance of medicinal products for human use;

Justification

This change is in line with amendments 3 and 4.

Amendment 34

Proposal for a regulation – amending act
Article 1 – point 12 – point b a (new)
Regulation EC/726/2004
Article 56 – paragraph 1 – point g

Text proposed by the Commission	*Amendment*
	(ba) point (g) is replaced by the following:
	"(g) an Executive Director General, who shall exercise the responsibilities set out in Article 64;"

Justification

The clarification reflects the structure, size and responsibilities of the Agency. During the last years the variety of new tasks increased considerably. Today, the Agency is the second largest agency in the EU with 600 members of staff. Therefore, the term Executive Director shall be replaced by Executive Director General and shall be changed throughout the Regulation.

Amendment 35

Proposal for a regulation – amending act
Article 1 – point 14
Regulation EC/726/2004
Article 61a – paragraph 1

Text proposed by the Commission	*Amendment*
1. The Pharmacovigilance Risk Assessment ***Advisory*** Committee shall be composed of the following:	1. The Pharmacovigilance Risk Assessment Committee shall be composed of the following:
(a) ten members and ten alternates appointed by the Management Board, on the basis of proposals by the national competent authorities;	(a) ten members and ten alternates appointed by the Management Board, ***following consultation with*** the national competent authorities ***and on the basis of their relevant expertise in pharmacovigilance and the risk assessment of medicinal products for human use, as laid down in paragraph 2***;
(b) five members and five alternates appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament.	(b) ***seven additional*** members and five alternates appointed by the Commission, ***including at least one healthcare professional representative, and at least one patient representative,*** on the basis of a public call for expressions of interest, after consulting the European Parliament.
	A Member State may request another Member State to represent it in the committee.
The alternates shall represent and vote for the members in their absence.	The alternates shall represent and vote for the members in their absence.
The Commission may adapt the number of members and alternates in the light of technical and scientific needs. Those measures, designed to amend non-essential elements of this Regulation, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 87(2a).	

Justification

The appointment of members to the PRAC by the Management Board shall foremost be based on their scientific expertise. Apart from the ten appointed members, Member States should have the opportunity to send additional representatives from the national competent authorities to attend and participate in the PRAC meetings. Furthermore, the additional

members appointed by the Commission should include at least two members from patient and health care representatives. This follows the precedent set by the following EMEA committees: the Committee on Orphan Medicinal Products, the Paediatric Committee and the Committee for Advanced Therapies.

Amendment 36

Proposal for a regulation – amending act
Article 1 – point 14
Regulation (EC) No. 726/2004
Article 61a – paragraph 1 – point (ba) (new)

Text proposed by the Commission	*Amendment*
	(ba) one representative and one alternate belonging to the EMEA working party of patients and consumers and one representative and one alternate belonging to the EMEA working party of healthcare professionals.

Justification

It is important to make use of all the experts who exist at EMEA in order to facilitate the practical implementation of the proposal. The presence of representatives of all parties involved thus reflects the requirements with regard to safeguards and transparency which protecting the health and welfare of citizens requires.

Amendment 37

Proposal for a regulation – amending act
Article 1 – point 14
Regulation EC/726/2004
Article 61a – paragraph 6

Text proposed by the Commission	*Amendment*
6. Representatives of the national competent authorities shall be entitled to attend all meetings of the Pharmacovigilance Risk Assessment ***Advisory*** Committee to facilitate appropriate coordination between the tasks of the Agency and the work of national competent authorities. ***They may provide clarification or information if invited to***	6. Representatives of the national competent authorities shall be entitled to attend all meetings of the Pharmacovigilance Risk Assessment Committee ***and to participate in discussions in order*** to facilitate appropriate coordination between the tasks of the Agency and the work of national competent authorities.

do so but shall not seek to influence discussions."

Justification

See justification to amendment to Article 61a - paragraph 1.

Amendment 38

Proposal for a regulation – amending act
Article 1 – point 15 – point b
Regulation EC/726/2004
Article 62 – paragraph 2 – subparagraph 1

Text proposed by the Commission	*Amendment*
"Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products who 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."	"Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products who 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***, and also of their degree of independence from pharmaceutical firms***."

Justification

Several instances of decisions which have been changed following the establishment of new groups of experts prompt a cautious approach with regard to the existence of interests linking such experts and pharmaceutical firms. Declarations of such links are not enough to free experts from pressure.

Amendment 39

Proposal for a regulation – amending act
Article 1 - point 18 - point b
Regulation (EC)No 726/2004
Article 67 - paragraph 4

Text proposed by the Commission	*Amendment*
4. Activities relating to pharmacovigilance, to the operation of communications	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 collection of fees to be paid by marketing authorisation holders for the carrying out of these activities by the Agency.	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 collection of fees to be paid by marketing authorisation holders for the carrying out of these activities by the Agency***, on condition that its independence is strictly guaranteed.***

Justification

The rapporteur can support part of amendment 81 - that pharmacovigilance can only be financed by fees if the independence of national competent authorities is guaranteed.

Amendment 40

Proposal for a regulation – amending act
Article 2 – paragraph 1

Text proposed by the Commission	*Amendment*
1. The requirement for the inclusion of a summary of the essential information necessary to use the medicine safely and effectively in the summary of the product characteristics and the package leaflet provided for in point 3a of Article 11 and in point (aa) of Article 59(1) of Directive 2001/83/EC as amended by Directive …/…/EC, which applies to medicinal products authorised pursuant to Regulation (EC) No 726/2004 by virtue of its Article 9(4)(a) and (d), shall apply to a marketing authorisation granted before the date set out in the second paragraph of Article 3 of this Regulation from renewal of that authorisation or from the expiry of a period of three years starting from that date, whichever is the earliest.	***deleted***

Justification

This amendment is consistent with the rapporteur's amendment to the point 3a of Article 11 and to the point (aa) of Article 59(1) of Directive 2001/83/EC.

EXPLANATORY STATEMENT

Pharmacovigilance is the system used to monitor the safety of medicines after they have been authorised for public use. Pharmacovigilance plays an important role in public health. An estimated 197,000 deaths per year are caused by Adverse Drug Reactions (ADRs) in the EU). Clinical trials can miss side effects from drugs if they are rare, only appear after long-term use or involve interaction with other drugs. Most of us will be aware of the tragedy of the drugs Thalidomide in the 1960s and Viox more recently. There can therefore be no doubt that systems for tracking drug use, reporting on ADRs and looking for patterns ("signal detection") are a priority for European public health policy.

Under current EU legislation, medicines can be authorised in two ways: a) through a central procedure where one application is made by a pharmaceutical company to the EMEA (European Medicines Agency) or b) through a system of mutual recognition where one country leads on the assessment of the new drug and coordinates with other Member States through mutual recognition.There is an obligation for certain kinds of new products to go through the centralised system e.g. Biotech, cancer, HIV, neurodegenerative drugs. Rules governing the centralised procedure are set out in EU Regulation 726/2004 and for the decentralised system in Directive 2001/83/EC. The Commission proposal to update the rules on pharmacovigilance therefore requires amendment of both pieces of legislation.Your rapporteur has similarly drafted amendments to both the Regulation and the Directive, but given the overlapping nature of the two pieces of legislation, the narrative below refers to both.

The essence of a good pharmacovigilance system is proper reporting of ADRs by healthcare professionals, companies and patients themselves and proper recording of these ADRs by the public authorities so that "signals" pointing to potential problems can be detected .These signals must then be followed up with action which can include changes to the way a medicine is prescribed, better information on how it is used or, where the nature of the ADR is severe, the withdrawal of the medicine altogether. The advantage of strengthening cooperation on pharmacovigilanvce at EU level is that the "pool" of reported ADRs is larger, meaning rarer patterns can be picked up more quickly, duplicate work on following up the same ADRs in different Member States can be avoided and unsafe medicines can be withdrawn quickly when required. "Signals" are picked up from spontaneous reports of ADRs to national competent authorities, from the periodic safety update reports (PSURs) that companies are required to present once a product is on the market and from expert review of medical research papers.The current system of pharmacovigilance in the EU has evolved in recent years to better coordinate work between Member States. A single Eudravigilance database which collects data is up and running and a working party meets to discuss issues. However, gaps in the current legislation mean that the approach is somewhat ad hoc and inconsistent.
The Commission therefore proposes changes to strengthen EU pharmacovigilance and rationalise procedures. Your rapporteur generally welcomes the Commission's approach but has strengthened its proposals in some areas. The following are, your rapporteur believes, the main points.

1. **Strengthened EU Committee on Pharmacovigilance:**

The rapporteur believes the Commission is right to replace the existing Phamacovigilance working party with the Pharmacovigilance Risk Assessment Advisory Committee (PRAAC). Most experts agree that the existing working party system works in a rather ad hoc manner, focusing only on drugs authorised through the central procedure and lacking the status to ensure its findings are acted on by the Committee for Medicinal Products for Human Use (CHMP) which oversees the whole system. However, the rapporteur believes that the PRAAC ‘s role can be strengthened still by giving it the power to recommend action to the CHMP rather than simply providing advice to it and be extending its membership to one representative per Member State.To reinforce the transparency of the work of the PRAAC , your rapporteur also proposes that two additional representatives be appointed to represent patients and healthcare professionals, as is the case with other EMEA Committees.

2. **The role of Member States in the system:**

Your rapporteur believes that Member States must remain key players in the EU pharmacovigilance system. As proposed by the Commission, the competent authority(CA) in each Member State should continue to act as the clearing house for all spontaneous reporting of ADRs and healthcare professionals and patients should continue to report ADRs to their CA and not directly to Eudravigilance (the EU database of ADRs). The rapporteur understands the concerns of Member States at the Commission proposal to allow a company to make a single report to Eudravigilance on an ADR rather than to every Member State (see point 2). She believes that Member States must be immediately informed if a company reports an ADR which happened on its territory to the Eudravigilance database and suggests that a system to alert relevant Member States simultaneously be established.

3. The role of companies in the system:

Several useful changes are proposed which affect companies. The rapporteur particularly welcomes proposals which ensure better follow up and coordination of the assessments of ADRs by preventing duplicate work in different Member States. She therefore supports direct reporting to Eudravigilance by companies (with the safeguards in point 3) and the work-sharing mechanisms for follow-up to Periodic Safety Reports coordinated through the PRAAC.

4. The role of Healthcare professionals:

Your rapporteur supports measures to encourage healthcare professionals to voluntarily report ADRs to their competent authority and wants to strengthen their role in informing and encouraging patients to report.

5. The role of patients:

Patients are key to “signal detection” of ADRs. Your rapporteur supports proposals to encourage the “informed patient” and strongly supports the new provisions to allow direct patient reporting of ADRs, though she believes this should be to competent authorities and not companies. At present, only a few Member States accept direct reporting but where it exists, the system has not overburdened the competent authority.The informed patient also needs to

know when they are taking new drugs. The rapporteur therefore also supports the proposal for Intensively Monitored Products and believes the system should not only inform patients who are prescribed a new product but encourage them to report ADRs. She has tabled a number of amendments to improve information on the Patient Information Leaflet (PIL) to that effect.

6. The Patient Information Leaflet (PIL):

A number of stakeholders are unhappy with the proposal by the European Commission to include the "black box" with essential information on the PIL.Your rapporteur understands those concerns, in particular that what is essential to one patient may not be essential to all patients. However, she also feels that the current PIL is not satisfactory from a patient point of view and that there needs to be a clearer indication of the main features of the drug for patients. It is possible that the best solution would be to remit this problem to a general review of the PIL. For this reason, she has not tabled any amendments herself to the Commission proposals .

7. The reporting of ADRs:

The new system proposes that all ADRs (and not just serious ones) are reported to the Eudravigilance database by Competent Authorities and Companies. This means that information on all ADRs will, for the first time, be centralised in one place in the EU. This can be a valuable research tool for all. The Commission needs to ensure, however, that Eudravigilance is able to cope with the surge of information and by putting systems in place so that the most serious ADRs are clearly flagged up. If all ADRs are recorded on Eudravigilance, the rapporteur sees the logic of cutting back on the requirement by companies to provide line by line reporting of ADRs in PSURs. Instead of just presenting raw data, companies will be required instead to analyse the ADRs and present summaries of their findings. This makes sense, particularly since the rapporteur has learned that competent authorities have often been overwhelmed by the sheer volume of PSURS they have received in the past, with the result that many have gone unread. The speed with which ADRs are reported to Eudravigilance is of paramount importance for patient safety. The rapporteur is therefore concerned to hear that both companies and Member States have failed to meet the current requirement to report ADRs within 15 days. However, Member States are by far the worst "offenders": 5% of company reports were late compared with 50% of Member State reports. The rapporteur has therefore sought to include provisions to ensure better compliance mechanisms.

8. Urgent action or "Community procedure":

Your rapporteur welcomes the inclusion of clearer provisions for when an urgent procedure is triggered. Member States need to work quickly together to act when a serious ADR occurs.

9. Transparency:

Your rapporteur welcomes the proposals to bring more transparency to the EU pharmacovigilance system. She welcomes the expansion of the web portal and the use of public hearings to gather evidence about ADRs. She believes public hearings should not only

be used in the case of urgent action, but could also be useful tools for normal pharmacovigilance and has therefore proposed an amendment along these lines.

16.4.2010

OPINION OF THE COMMITTEE ON INDUSTRY, RESEARCH AND ENERGY

for the Committee on the Environment, Public Health and Food Safety

on the proposal for a regulation of the European Parliament and of the Council 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
(COM(2008)0664 – C6-0515/2008 – 2008/0257(COD))

Rapporteur: Michèle Rivasi

SHORT JUSTIFICATION

These two proposals (a regulation and a directive) on pharmacovigilance place us right at the heart of current issues. The arguments surrounding the vaccine against AH1N1 influenza, which was put on the market following a very quick procedure, illustrate the public's loss of confidence in the ability of the authorities to guarantee their protection. A recent study shows that 61% of French doctors do not intend to have themselves vaccinated. This context further highlights (if it were necessary to do so) the need for the European Union to have an effective pharmacovigilance policy, to reassure and protect its citizens.

We are unfortunately able to point to several cases of medicinal products in recent years which, despite having been placed on the market upon completion of a traditional procedure, have produced substantial side-effects:

- rofecoxib (Vioxx®, Ceox®, Ceeoxx®): an anti-inflammatory which is no more effective than ibuprofene and which triggered thousands of fatal heart attacks; authorised in 1999 and withdrawn from the market in 2004;
- paroxetine: an anti-depressant (Deroxat®, Seroxat®) which increased the risk of suicide;
- rimonabant (Acomplia®): an anti-obesity medicine which was put on the market without adequate assessment and withdrawn from the European market a year and a half later.

Several court cases have shown that pharmaceutical companies have a tendency to conceal information about adverse reactions to their medicinal products, which might damage sales, for as long as possible.

In each of these cases we were able to see that the length of the decision-making process and the withholding of information about adverse reactions were harmful to patients.

The human cost of such side-effects is unacceptable; as for the financial costs, these are massive, and it is society as a whole which bears them, because they account for 5% of hospital admissions and 5% of the causes of hospital deaths.

From assessment, via supervision and information relating to medicinal products, to placing them on the market

Before medicinal products are granted marketing authorisation they have to be assessed. This is done over a limited period using a sample of selected patients. Pharmacovigilance's role is subsequently to extend our knowledge of adverse reactions, so as to limit the harm caused to the public.

Your rapporteur fears that the regulation will weaken the pharmacovigilance system, instead of strengthening it, for the reasons given below.

1. The risk management plans and other post-authorisation studies may be used as a backstop in order to reduce assessment before marketing authorisations are granted. This must remain an exception.

2. The ending of the requirement for funding to be public threatens to reduce the pharmacovigilance system to the status of service provider to pharmaceutical firms. The rapporteur proposes, instead, to strengthen the independent national and regional pharmacovigilance systems.

3. Companies' increased control over the collection, analysis and interpretation of the data places them in an untenable situation regarding conflicts of interest. Firms should be able to take part in the study of adverse reactions, but under the control of the authorities, and in no circumstances in a monopoly position.

4. The organisation of dilution of the data, which are stored directly in Eudravigilance, a mega-database, without any procedure to ensure that the quality of the content of Eudravigilance is safeguarded. Your rapporteur proposes that input to Eudravigilance be restricted to the Member States' relevant pharmacovigilance authorities (no direct input by patients, or by pharmaceutical firms, which might create too much background noise and thus making the relevant data unusable).

5. The very limited access to the Eudravigilance database for the public and independent experts. Transparency with regard to pharmacovigilance data is essential in order to restore public confidence in the health authorities.

Several proposals are still too cautious and should be strengthened.

1. The formal establishment of a European risk management advisory committee (PRAAC), without any more genuine authority or autonomy than the current Pharmacovigilance Working Party, does not contribute any significant added value.

2. Lack of transparency where pharmacovigilance data is concerned remains the rule: for instance, there is no access to PSURs, on the pretext of commercial confidentiality. PSURs

and all assessment reports should be published immediately.

To conclude:

- Strengthen the criteria **to enable marketing authorisation to be granted on surer grounds**, entailing the requirement for new medicinal products to bring genuine therapeutic advances; no widespread use of the fast-track procedure
- Ensure the quality of pharmacovigilance data
- Provide the resources to ensure **effective public pharmacovigilance**
- **Increase transparency**

AMENDMENTS

The Committee on Industry, Research and Energy calls on the Committee on the Environment, Public Health and Food Safety, as the committee responsible, to incorporate the following amendments in its report:

Amendment 1

Proposal for a regulation - amending act
Recital 4

Text proposed by the Commission	*Amendment*
(4) 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 Community pharmacovigilance database and data-processing network (hereinafter referred to as 'the Eudravigilance database') ***and*** the coordination of safety announcements by the Member States.	(4) 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 Community pharmacovigilance database and data-processing network (hereinafter referred to as 'the Eudravigilance database')***,*** the coordination of safety announcements by the Member States ***and the provision of information regarding safety issues to the public***.

Justification

Consumers have the right to have more information regarding pharmacovigilance concerns and about the risk-benefit balance of their medicines. The Agency has an important role to play as a reliable independent source of information.

Amendment 2

Proposal for a regulation – amending act
Recital 5

Text proposed by the Commission	*Amendment*
(5) In order to allow all competent authorities to receive and access, at the same time, pharmacovigilance information for medicinal products for human use authorised in the Community, and share it, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose on marketing authorisation holders any additional reporting requirements. The database should be fully accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.	(5) In order to allow all competent authorities to receive and access, at the same time, pharmacovigilance information for medicinal products for human use authorised in the Community, and share it, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose on marketing authorisation holders any additional reporting requirements. ***Instead, the Eudravigilance database should simultaneously notify the relevant Member States of reports submitted by market authorisation holders. In order to ensure the high quality of information, Member States should support the development of the expertise of national and regional pharmacovigilance centres. National competent authorities should collect the reports from those centres and should then transfer data to the Eudravigilance database.*** The database should be fully accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.

Amendment 3

Proposal for a regulation – amending act
Recital 7

Text proposed by the Commission	*Amendment*
(7) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Community level, it is appropriate to create	(7) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Community level, it is appropriate to create

a new scientific committee within the Agency, the Pharmacovigilance Risk Assessment Advisory Committee. That committee should be composed of independent scientific experts with competence in the safety of medicines including the detection, assessment, minimisation and communication of risk, and the design of post-authorisation safety studies and pharmacovigilance audit.	a new scientific committee within the Agency, the Pharmacovigilance Risk Assessment Advisory Committee. That committee should be composed of independent scientific experts with competence in the safety of medicines including the detection, assessment, minimisation and communication of risk, and the design of post-authorisation safety studies and pharmacovigilance audit. ***The scientific experts serving on the committee should be independent both in relation to authorisation holders and in relation to the Agency itself, especially when safety studies are being conducted on medicines.***

Justification

It is desirable to ensure that the experts will be completely independent, given that those who grant authorisation will hardly be inclined to withdraw medicines from the market once they have approved them.

Amendment 4

Proposal for a regulation - amending act
Recital 11

Text proposed by the Commission	*Amendment*
(11) In order to protect public health, there should be adequate funding of activities *related* to pharmacovigilance by the Agency. ***Provision should be made to allow adequate funding for pharmacovigilance activities through the collection of fees charged to marketing authorisation holders. The management of those collected funds should be under a permanent control of the Management Board in order to guarantee the independence of the Agency.***	(11) In order to protect public health, there should be adequate funding of activities *relating* to pharmacovigilance by the Agency.

Amendment 5

Proposal for a regulation – amending act
Recital 15

Text proposed by the Commission	*Amendment*
(15) Where a medicinal product is *authorized* subject to the requirement to conduct a post-authorisation safety study or subject to conditions or restrictions with regard to the safe and effective use of the medicinal product, the medicinal product should be intensively monitored on the market. Patients and healthcare professionals should be encouraged to report all suspect adverse reactions to such medicinal products, and a publicly available list of such medicinal products should be kept up to date by the Agency.	(15) ***For three years following the placing on the market of a newly authorised medicinal product or*** where a medicinal product is *authorised* subject to the requirement to conduct a post-authorisation safety study or subject to conditions or restrictions with regard to the safe and effective use of the medicinal product, the medicinal product should be intensively monitored on the market. Patients and healthcare professionals should be encouraged to report all suspect adverse reactions to such medicinal products, and a publicly available list of such medicinal products should be kept up to date by the Agency.

Justification

Special warnings for all new authorised products as well as intensively monitored medicines will help both the health professionals and the patients to identify new authorised medicines on the market for a period of less than three years and would increase their awareness of the need to report any adverse reaction that might appear.

Amendment 6

Proposal for a regulation - amending act
Recital 20 a (new)

Text proposed by the Commission	*Amendment*
	(20a) This Regulation should apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data[1] and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing

of personal data by the Community institutions and bodies and on the free movement of such data[2]. In order to detect, assess, understand and prevent adverse reactions, and to identify and take action to reduce risks and increase benefits from medicinal products for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while complying with EU data protection legislation.

[1] OJ L 281, 23.11.1995, p. 31.

[2] OJ L 8, 12.1.2001, p. 1.

Justification

The proposal covers highly sensitive personal information which should be fully protected. See also the opinion of the European Data Protection Supervisor of April 2009.

Amendment 7

Proposal for a regulation - amending act
Article 1 — point 1
Regulation (EC) No 726/2004
Article 5 – paragraph 2 – last sentence

Text proposed by the Commission	*Amendment*
For the fulfilment of its pharmacovigilance tasks, it shall be assisted by the Pharmacovigilance ***Risk Assessment Advisory*** Committee referred to in Article 56(1)(aa).	For the fulfilment of its pharmacovigilance tasks, it shall be assisted by the Pharmacovigilance Committee referred to in Article 56(1)(aa).

Justification

Horizontal change required throughout the proposal. The proposal establishes a European Pharmacovigilance Risk Assessment Advisory Committee and entrusts it with important pharmacovigilance tasks but with a mere advisory role and no authority. The committee's role should be strengthened and that is to be reflected in its title.

Amendment 8

Proposal for a regulation – amending act
Article 1 – point 4
Regulation (EC) No 726/2004
Article 10 a – paragraph 3

Text proposed by the Commission	*Amendment*
3. On the basis of explanations submitted by the marketing authorisation holder, the Commission shall withdraw or confirm the requirement. Where the Commission confirms the requirement, the marketing authorisation shall be varied to include the requirement as a condition of the marketing authorisation and the risk management system shall be updated accordingly.	3. On the basis of explanations submitted by the marketing authorisation holder, the Commission shall withdraw or confirm the requirement. Where the Commission confirms the requirement, the marketing authorisation shall be varied to include the requirement as a condition of the marketing authorisation and the risk management system shall be updated accordingly. ***Irrespective of whether the requirement is confirmed or withdrawn, the Commission shall justify its decision in detail, and the decision shall be duly recorded.***

Amendment 9

Proposal for a regulation - amending act
Article 1 – point 5 – point c
Regulation (EC) No 726/2004
Article 14 - paragraph 8

Text proposed by the Commission	*Amendment*
8. In exceptional circumstances and following consultation with the applicant, the authorisation may be granted subject to a requirement for the applicant to ***meet certain conditions***, in particular concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. This 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	8. In exceptional circumstances and following consultation with the applicant, the authorisation may be granted subject to a requirement for the applicant to ***introduce specific procedures***, in particular concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. This authorisation may be granted only 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 authorisation shall be linked to the annual reassessment of these

Directive 2001/83/EC. Continuation of the authorisation shall be linked to the annual reassessment of these conditions.	conditions.

Justification

The wording of the existing legislation ensures stricter criteria and better consumer protection against the risk of a premature marketing authorisation.

Amendment 10

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 23 – paragraph 3

Text proposed by the Commission	*Amendment*
The Agency shall keep the list up to date.	The Agency shall keep the list up to date. ***Medicinal products included on the list must be clearly identified as such on the package in order to provide patients and healthcare professionals with a source of information separate from the list.***

Amendment 11

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 24 – paragraph 1 – subparagraph 1

Text proposed by the Commission	*Amendment*
1. The Agency, in collaboration with the Member States and the Commission, shall set up and maintain a database and data processing network (hereinafter 'the Eudravigilance database') to collate pharmacovigilance information regarding medicinal products authorised in the Community and to allow competent authorities to access the information at the same time and to share it.	1. The Agency, in collaboration with the Member States and the Commission, shall set up and maintain a database and data processing network (hereinafter 'the Eudravigilance database') to collate pharmacovigilance information regarding medicinal products authorised in the Community and to allow competent authorities to access the information at the same time and to share it. ***Member States should support the development of the expertise of national and regional***

	pharmacovigilance centres. National competent authorities should collect the reports from those centres and should then transfer data to the Eudravigilance database.

Amendment 12

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 24 – paragraph 2 – subparagraph 2 a (new)

Text proposed by the Commission	*Amendment*
	The Agency shall work together with organisations representing healthcare professionals, patients and consumers to define 'the appropriate level of access'.

Amendment 13

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 25

Text proposed by the Commission	*Amendment*
The Agency, in collaboration with the Member States, shall develop standard ***web-based structured forms*** for the reporting of suspected adverse reactions by health-care professionals and patients.	The Agency, in collaboration with the Member States ***and relevant stakeholders***, shall develop standard ***content, formats and procedures*** for the reporting of suspected adverse reactions by health-care professionals and patients ***and the traceability of biological medicinal products prescribed, dispensed, or sold on EU territory***. ***Forms intended for patients must be designed according to technical criteria conforming to the principles of clear structure and simplified language accessible to the general public. They must be accessible on the internet and in pharmacies.***

The forms must include the information required to enable reports to be submitted to the authorities by pharmacies or directly by patients, by post, by fax, or electronically.

Justification

Accurate identification of the product associated with a suspected adverse event is fundamental to a sound pharmacovigilance system. The proposed amendment would require the Agency to develop user-friendly standard content, format and procedures for use by healthcare professionals and patients in reporting adverse events.

Amendment 14

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 25 – paragraph 1 a (new)

Text proposed by the Commission	*Amendment*
	To ensure the traceability of biological medicinal products prescribed, dispensed or sold on EU territory, the standard forms and procedures shall include the name of the marketing authorisation holder, the International Non-proprietary Name (INN), the name of the medicinal product as defined in point 20 of Article 1 of Directive 2001/83/EC and the batch number.

Justification

As biotech medicines vary from conventional medicines in so far as they are 'live products' it is appropriate to have separate rules for what kind of information health care professionals should report in case of adverse effects so as to ensure the traceability of the medicine and to be able to establish the cause of the adverse effect.

Amendment 15

Proposal for a regulation - amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 26 — point 2

Text proposed by the Commission	*Amendment*
(2) ***a summary*** of ***each meeting*** of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities;	(2) ***agendas for meetings and records*** of ***meetings, accompanied by decisions taken, details of votes and explanations of votes, including minority opinions,*** of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities;

Justification

According to Article 126b of Directive 2004/27/EC the 'Member States shall ensure that the competent authority makes publicly accessible its rules of procedure and those of its committees, agendas for its meetings and records of its meetings, accompanied by decisions taken, details of votes and explanations of votes, including minority opinions'. This is also already done by the US Food and Drug Administration, but is not implemented in Europe.

Amendment 16

Proposal for a regulation - amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 28 - paragraph 3

Text proposed by the Commission	*Amendment*
3. The Pharmacovigilance ***Risk Assessment Advisory*** Committee shall assess the periodic ***safety*** update reports.	3. The Pharmacovigilance Committee shall assess ***scientifically the risk-benefit balance of the medicinal product on the basis of all the information available, including*** the periodic update reports ***and the data entered in the Eudravigilance database.***
It shall prepare ***an assessment*** report within 90 days of receipt of the periodic safety update report and send it to the marketing authorisation holder.	It shall prepare ***a scientific*** report ***on the risk-benefit balance of the medicinal product*** within 90 days of receipt of the periodic safety update report and send it to the marketing authorisation holder.
Within 30 days of receipt of the assessment report, the marketing authorisation holder may submit comments to the ***Agency***.	Within 30 days of receipt of the assessment report, the marketing authorisation holder may submit comments to the ***Pharmacovigilance Committee***.
At its next meeting following the end of the period for comments by the marketing	At its next meeting following the end of the period for comments by the marketing

authorisation holder, the Pharmacovigilance ***Risk Assessment Advisory*** Committee shall adopt the assessment report with or without changes, taking into account any comments submitted ***by the marketing authorisation holder***.	authorisation holder, the Pharmacovigilance Committee shall adopt the assessment report with or without changes, taking into account any comments submitted. ***With effect from [indicate precise date, namely 18 months after the date referred to in Article 3] the assessment report shall be published immediately on the European medicines safety web-portal.***

Justification

The scientific assessment report drawn up by the rapporteur shall be based on the data supplied by firms (PSURs and data obtained from the clinical trials and studies carried out after marketing authorisation has been granted) and also on the data supplied by the pharmacovigilance systems in the various Member States (including notifications from health professionals and patients).

Amendment 17

Proposal for a regulation - amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 28 – paragraph 4 - subparagraph 1

Text proposed by the Commission	*Amendment*
4. Within 30 days of ***receipt*** of the report ***by the Pharmacovigilance Risk Assessment Advisory Committee***, the Committee ***for Medicinal Products for Human Use*** shall ***consider the report and*** adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned.	4. Within 30 days of ***adoption*** of the report, the ***Pharmacovigilance*** Committee shall adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned.

Amendment 18

Proposal for a regulation - amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 28 - paragraph 6

Text proposed by the Commission	*Amendment*
6. The opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.	6. The ***evaluation reports,*** opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.

Amendment 19

Proposal for a regulation - amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 28d

Text proposed by the Commission	*Amendment*
Upon request of the *Commission*, the Agency shall participate in collaboration with the Member States in international *harmonization* and *standardization* of technical measures in pharmacovigilance.	*At* the *Commission's request*, the Agency shall participate***,*** in collaboration with the Member States ***and all interested parties,*** in international *harmonisation* and *standardisation* of technical measures in pharmacovigilance. ***Such work shall be based on patient needs and be carried out from a scientific perspective.***

Justification

Amendment to ensure consistency with the proposals for changes to Article 108 of Directive 2001/83/EC.

Amendment 20

Proposal for a regulation - amending act
Article 1 – point 12 – point a
Regulation (EC) No 726/2004
Article 56 – paragraph 1 – point aa

Text proposed by the Commission	*Amendment*
(aa) the Pharmacovigilance ***Risk Assessment Advisory*** Committee, which shall be responsible for ***providing advice to*** the ***Committee for Medicinal Products for Human Use and the coordination group on any question relating to the pharmacovigilance of medicinal products for human use***;	(aa) the Pharmacovigilance Committee, which shall be responsible for the ***pharmacovigilance assessment, after marketing authorisation has been granted, of medicinal products placed on the market in accordance with the centralised procedure***;

Justification

This committee should have the same power to make recommendations as the European committee responsible for marketing authorisation (Committee for Medicinal Products for Human Use). Following analysis and discussion of the assessments carried out by the Member States under the committee's supervision (systems of rapporteurs and co-rapporteurs), it should be able to make a direct proposal to the Commission for a decision to revoke or modify a marketing authorisation, without having to work under the tutelage of the marketing authorisation committees (CMPHU or coordination group).

Amendment 21

Proposal for a regulation – amending act
Article 1 – point 14
Regulation (EC) No 726/2004
Article 61a – paragraph 1

Text proposed by the Commission	*Amendment*
1.The Pharmacovigilance Risk Assessment Advisory Committee shall be composed of the following: (a) ***ten members and ten alternates*** appointed by the ***Management Board, on the basis of proposals by the national competent authorities***; (b) ***five*** members and ***five*** alternates appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament.	1. The Pharmacovigilance Risk Assessment Advisory Committee shall be composed of the following: (a) ***one member and one alternate per Member State,*** appointed by the ***national competent authority in consultation with the Management Board***; (b) ***two additional*** members and ***two*** alternates***, one a representative of healthcare professionals and one a representative of patients,*** appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament. ***A Member State may request another Member State to take its place in the***

	committee.
The alternates shall represent and vote for the members in their absence. ***The Commission may adapt the number of members and alternates in the light of technical and scientific needs. Those measures, designed to amend non-essential elements of this Regulation, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 87(2a).***	The alternates shall represent and vote for the members in their absence.

Amendment 22

Proposal for a regulation - amending act
Article 1 – point 15 – point b
Regulation (EC) No 726/2004
Article 62 – paragraph 2 – subparagraph 1

Text proposed by the Commission	*Amendment*
Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products who 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.	Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products who 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***, and also of their degree of independence from pharmaceutical firms***.

Justification

Several instances of decisions which have been changed following the establishment of new groups of experts prompt a cautious approach with regard to the existence of interests linking such experts and pharmaceutical firms. Declarations of such links are not enough to free experts from pressure.

Amendment 23

Proposal for a regulation - amending act
Article 1 – point 18 – point b
Regulation (EC) No 726/2004
Article 67 - paragraph 4

Text proposed by the Commission	*Amendment*
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 collection of fees to be paid by marketing authorisation holders for the carrying out of these activities by the Agency***.	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. ***They shall receive adequate public funding commensurate with the tasks conferred***.

Justification

It is important that pharmacovigilance activities remain financed by public funds to avoid conflicts of interest. The text of the old paragraph 4 should be maintained.

PROCEDURE

Title	Pharmacovigilance of medicinal products (amendment of Regulation (EC) No 726/2004)
References	COM(2008)0664 – C6-0515/2008 – 2008/0257(COD)
Committee responsible	ENVI
Opinion by Date announced in plenary	ITRE 19.10.2009
Rapporteur Date appointed	Michèle Rivasi 16.9.2009
Discussed in committee	15.10.2009 27.1.2010
Date adopted	7.4.2010
Result of final vote	+: 47 –: 4 0: 0
Members present for the final vote	Jean-Pierre Audy, Zigmantas Balčytis, Bendt Bendtsen, Jan Březina, Maria Da Graça Carvalho, Giles Chichester, António Fernando Correia De Campos, Pilar del Castillo Vera, Lena Ek, Ioan Enciu, Adam Gierek, Norbert Glante, Robert Goebbels, Fiona Hall, Jacky Hénin, Edit Herczog, Sajjad Karim, Arturs Krišjānis Kariņš, Bogdan Kazimierz Marcinkiewicz, Marisa Matias, Judith A. Merkies, Ivari Padar, Jaroslav Paška, Aldo Patriciello, Miloslav Ransdorf, Michèle Rivasi, Jens Rohde, Paul Rübig, Amalia Sartori, Francisco Sosa Wagner, Konrad Szymański, Patrizia Toia, Evžen Tošenovský, Ioannis A. Tsoukalas, Claude Turmes, Niki Tzavela, Vladimir Urutchev, Adina-Ioana Vălean, Kathleen Van Brempt, Lambert van Nistelrooij, Alejo Vidal-Quadras
Substitute(s) present for the final vote	Lara Comi, Françoise Grossetête, Jolanta Emilia Hibner, Oriol Junqueras Vies, Bernd Lange, Vladko Todorov Panayotov, Markus Pieper, Mario Pirillo, Silvia-Adriana Ţicău
Substitute(s) under Rule 187(2) present for the final vote	Isabelle Durant

24.2.2010

OPINION OF THE COMMITTEE ON THE INTERNAL MARKET AND CONSUMER PROTECTION

for the Committee on the Environment, Public Health and Food Safety

on the proposal for a regulation of the European Parliament and of the Council 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
(COM(2008)0664 – C6-0515/2008 – 2008/0257(COD))

Rapporteur: Claude Turmes

SHORT JUSTIFICATION

Medicinal products contribute considerably to the health of EU citizens. They can however also have adverse effects, leading to about 5% of all hospital admissions according to the European Commission (underreporting does however not allow for accurate estimates). The rofecoxib (Vioxx) case, an anti-inflammatory that was withdrawn of the market in 2004 because of increased cardiovascular risks (more than 30.000 estimated strokes in the US, some of which were fatal) permitted to raise awareness about the need to strengthen pharmacovigilance.

Pharmacovigilance is the process and science of monitoring the safety of medicines, including the collection and management of data on the safety of medicines, the assessment of that data to detect whether there is a safety issue, action to address the possible safety issue including informing on this issue, and the evaluation of the procedure followed and results obtained.

As regards centrally authorised medicines the pharmacovigilance procedure is laid down by Regulation 726/2004. As regards nationally authorised medicinal products the procedure is laid down by Directive 2001/83. This opinion concerns the amendments to Regulation 726/2004.

The Commission wishes to improve the current system of pharmacovigilance by clarifying the roles of the various actors involved, simplifying procedures, enhanced transparency and communication, better data collection and evaluation procedures, more involvement of

stakeholders and the establishment of best practices.

Though the rapporteur for opinion welcomes the proposal, he is of the view that there is a room for further improvement, mainly with regard to consumer protection issues, transparency and data protection**.** He therefore proposes amendments along the following lines:

- The processing of personal data of users of medication taking place at several stages of the pharmacovigilance process, should take place in accordance with the data protection principles laid down by Directive 95/46/EC.
- The proposed summary of essential information about the safe and effective use of medicines should be rejected since the concept of 'essential information' is misleading and might be misunderstood.
- Patient reports can bring a new contribution to the understanding of adverse drug reactions (ADR) as it was the case for paroxetine (Deroxat/Seroxat), an antidepressant which was found, thanks to patient reports, to increase the risk of suicides and to cause a deprivation syndrome ("electric head") if the patients wanted to stop their treatment.
- Consumers should report directly to national authorities. Decentralised reporting systems whereby communication of all adverse drug reactions (reported whether by patients, health professionals and pharmaceutical companies) to the European database is coordinated at a national level, increase the safety for data protection and guarantees the quality of the data which are registered at the European level. Proximity also allows national health authorities to:
  - investigate the reports to add valuable information whereby they apply their particular expertise,
  - to have a clear view of the adverse effects occurring on their territory,
  - and to make this information accessible to their country's population in its own language (as the UK and the Netherlands already do).
- Consumers and Healthcare professionals should also have full access to the central European Eudravigilance database in order to prevent the repetition of preventable adverse drug reactions by making validated information easily available. It is an effective way to tackle inequalities of information on adverse drug reactions among Member States. This public access to Eudravigilance is needed to restore citizens' trust in health authorities' capacity to protect public health.
- The use of a web format for reporting should be supplemented by other means, such as mail, fax and phone as it is the case in the US and in the UK, in order to not exclude those who do not have access to or cannot use the internet and to improve patient reporting.
- All assessment reports concerning a medication in the framework of the national and European pharmacovigilance systems should be available to the public. When an overriding public interest is at stake, as it is the case concerning pharmacovigilance data, full disclosure has always to be guaranteed.
- The funding of the pharmacovigilance systems should remain public as recognition of the public authorities' responsibility to protect their populations, and in order to guarantee their independency.

AMENDMENTS

The Committee on the Internal Market and Consumer Protection calls on the Committee on the Environment, Public Health and Food Safety, as the committee responsible, to incorporate the following amendments in its report:

Amendment 1

Proposal for a regulation – amending act
Recital 7

Text proposed by the Commission	*Amendment*
(7) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Community level, it is appropriate to create a new scientific committee within the Agency, the Pharmacovigilance ***Risk*** Assessment Advisory Committee. That committee should be composed of independent scientific experts with competence in the safety of medicines including the detection, assessment, minimisation and communication of risk, and the design of post-authorisation safety studies and pharmacovigilance audit.	(7) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Community level, it is appropriate to create a new scientific committee within the Agency, the Pharmacovigilance ***Risk-Benefit*** Assessment Advisory Committee. That committee should be composed of independent scientific experts with competence in the safety of medicines including the detection, assessment, minimisation and communication of risk, and the design of post-authorisation safety studies and pharmacovigilance audit.

Justification

The name 'Pharmacovigilance Risk Assessment Advisory Committee' is too restrictive and overlooks the need for risk-benefit assessment of medicinal products, instead concentrating on risk analysis alone. After all, the committee's remit includes 'any question relating to (...) pharmacovigilance' (proposal for a regulation, Article 1(12)).

This amendment should be applied throughout the text of the proposal for a regulation.

Amendment 2

Proposal for a regulation – amending act
Article 1 — point 1
Regulation (EC) No 726/2004
Article 5 – paragraph 2

Text proposed by the Commission	*Amendment*
"For the fulfilment of its pharmacovigilance tasks, it shall be assisted by the Pharmacovigilance ***Risk***	'For the fulfilment of its pharmacovigilance tasks, it shall be assisted by the Pharmacovigilance ***Risk-***

Assessment Advisory Committee referred to in Article 56(1)(aa)."	***Benefit*** Assessment Advisory Committee referred to in Article 56(1)(aa).'

Justification

The name 'Pharmacovigilance Risk Assessment Advisory Committee' is too restrictive and overlooks the need for risk-benefit assessment of medicinal products, instead concentrating on risk analysis alone. After all, the committee's remit includes 'any question relating to (...) pharmacovigilance' (proposal for a regulation, Article 1(12)).

This amendment should be applied throughout the text of the proposal for a regulation.

Amendment 3

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 24 – paragraph 2

Text proposed by the Commission	*Amendment*
2. 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***.	2. 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***, healthcare professionals and the public, with personal data protection being guaranteed.***
The Agency shall ensure that health-care professionals and the public have appropriate levels of access to the Eudravigilance database, with personal data protection being guaranteed.	
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.	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.

Justification

The Pharmacovigilance system should be entirely transparent in order to guarantee full information of all stakeholders, notably in order to restore patients' and citizens' trust in Health authorities' accountability.

Amendment 4

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 24 – paragraph 3

Text proposed by the Commission	*Amendment*
3. Individual adverse reaction reports held on the Eudravigilance database may be requested by the public. Those reports shall be provided by the Agency or the national competent authority from which they are requested within 90 days, ***unless disclosure would compromise the anonymity of the subjects of the reports***.	3. Individual adverse reaction reports held on the Eudravigilance database may be requested by the public. Those reports shall be provided by the Agency or the national competent authority from which they are requested within 90 days, ***with personal data protection being guaranteed***.

Justification

The Pharmacovigilance system should be entirely transparent in order to guarantee full information of all stakeholders, notably in order to restore patients' and citizens' trust in Health authorities' accountability. Data protection regulations should be respected.

Amendment 5

Proposal for a regulation – amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 25

Text proposed by the Commission	*Amendment*
The Agency, in collaboration with the Member States, shall develop standard web-based structured forms for the reporting of suspected adverse reactions by health-care professionals and patients.	The Agency, in collaboration with the Member States, shall develop standard web-based structured forms for the reporting of suspected adverse reactions by health-care professionals and patients. ***All citizens of the Union shall have the option of submitting online declarations in their mother tongue.*** ***The Agency shall also make available to the public other means for patients to report undesirable effects, such as a dedicated telephone number or special email address.***

Amendment 6

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 26 – paragraph 1 – point 2

Text proposed by the Commission	*Amendment*
(2) ***a summary*** of each meeting of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities;	(2) ***detailed minutes*** of each meeting of the committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the coordination group as regards pharmacovigilance activities;

Justification

The Pharmacovigilance system should be entirely transparent in order to guarantee full information of all stakeholders, notably in order to restore patients' and citizens' trust in Health authorities' accountability.

Amendment 7

Proposal for a regulation – amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 26 — point 3

Text proposed by the Commission	*Amendment*
(3) risk management systems for medicinal products authorised in accordance with this Regulation;	(3) ***a summary of*** risk management systems for medicinal products authorised in accordance with this Regulation;

Justification

Information on national safety web portals should be presented in an easy and understandable way. Technical documents should be presented in a summary format and in lay version. The Package Leaflet (PL) and the Summary of Product Characteristics Additional should also be published in national safety web-portals as they contain basic information on the use of medicines which is key for their safe use.

Amendment 8

Proposal for a regulation – amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 26 – point 4 a (new)

Text proposed by the Commission	*Amendment*
	(4a) the most up-to-date electronic version of the package leaflet and summary of product characteristics for all existing and new medicinal products;

Justification

Information on national safety web portals should be presented in an easy and understandable way. Technical documents should be presented in a summary format and in lay version. The Package Leaflet (PL) and the Summary of Product Characteristics Additional should also be published in national safety web-portals as they contain basic information on the use of medicines which is key for their safe use.

Amendment 9

Proposal for a regulation – amending act
Article 1 — point 11
Regulation (EC) No 726/2004
Article 26 – point 4 b (new)

Text proposed by the Commission	*Amendment*
	(4b) a brief document history of changes made to the product information.
	All information on medicines safety web-portals, including all information set out in points 1 to 4b of this Article, shall be presented in a manner that is comprehensible to the general public.

Justification

Information on the EU safety web portal should be presented in an easy and understandable way. While this legislation provides for very detailed information to be published on the European web-portal, it does not include reference to key information to ensure safe use of medicines : This is why the package leaflet, the Summary of Product Characteristics or the European Public Assessment Reports should be made easily accessible to the public. Additionally, a brief document history of changes would allow patients and healthcare

professionals to see updates made to product information over time.

Amendment 10

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 26 – paragraph 1 a (new)

Text proposed by the Commission	*Amendment*
	Before the design and launch of this portal, the Agency consults relevant stakeholders (including patient groups, healthcare professionals and industry representatives) to get their opinion.

Justification

Before the launch of this website, it seems important to consult stakeholders who are involved in the information provided on the portal of the Agency.

Amendment 11

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 28 – paragraph 4 – subparagraph 1

Text proposed by the Commission	*Amendment*
4. Within 30 days of receipt of the report by the Pharmacovigilance Risk Assessment Advisory Committee, the Committee for Medicinal Products for Human Use shall ***consider the report and*** adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned.	4. Within 30 days of receipt of***the recommendation*** , by the Pharmacovigilance Risk Assessment Advisory Committee, the Committee for Medicinal Products for Human Use *(CHMP)* shall adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned. ***The CHMP shall adopt an opinion that differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, only where there exist strong scientific and public health grounds to do so. The CHMP shall explain such grounds in a justification to be annexed to***

	its opinion. That annex shall also be made available to the public.

Justification

Bringing it into line with the Agency's new structure, which strictly separates pharmacovigilance from marketing authorisations.

Amendment 12

Proposal for a regulation – amending act
Article 1 – point 11
Regulation (EC) No 726/2004
Article 28 – paragraph 6

Text proposed by the Commission	*Amendment*
6. The opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.	6. The ***assessment reports,*** opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines safety web-portal referred to in Article 26.

Justification

Bringing it into line with the Agency's new structure, which strictly separates pharmacovigilance from marketing authorisations.

Amendment 13

Proposal for a regulation – amending act
Article 1 – point 18 - point a
Regulation (EC) No 726/2004
Article 67 – paragraph 3

Text proposed by the Commission	*Amendment*
"The Agency's revenue shall consist of a contribution from the Community and fees paid by undertakings for obtaining and maintaining Community marketing authorisations and for other services provided by the Agency or the coordination group as regards the fulfilment of its tasks in accordance with in accordance with Articles 107c, 107e, 107g,	"The Agency's revenue shall consist of a contribution from the Community and fees paid by undertakings for obtaining and maintaining Community marketing authorisations and for other services provided by the Agency or the coordination group as regards the fulfilment of its tasks in accordance with in accordance with Articles 107c, 107e, 107g, 107l and 107r of Directive 2001/83/EC

107l and 107r of Directive 2001/83/EC.”	***and 28b of this Regulation. The budgetary authority, composed of the European Parliament and the Council, shall re-examine, as necessary, the level of the Community contribution on the basis of an evaluation of needs and taking account of the level of fees****."*

Justification

The agency has to have enough financial contributions in order to be able to fulfil its important tasks.

Amendment 14

Proposal for a regulation – amending act
Article 1 – point 18 - point b
Regulation (EC) No 726/2004
Article 67 – paragraph 4

Text proposed by the Commission	*Amendment*
“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 collection of fees to be paid by marketing authorisation holders for the carrying out of these activities by the Agency."	“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 ***and shall receive public funding,*** in order to guarantee the independence of the Agency. This shall not preclude the collection of fees to be paid by marketing authorisation holders for the carrying out of these activities by the Agency."

Justification

Public authorities are responsible for funding pharmacovigilance, because they are accountable to protect public health and because they have assumed responsibility for granting authorization.

Amendment 15

Proposal for a regulation – amending act
Article 2 – paragraph 1

Text proposed by the Commission	*Amendment*
1. The requirement for the inclusion of a summary of the essential information necessary to use the medicine safely and effectively in the summary of the product characteristics and the package leaflet provided for in point 3a of Article 11 and in point (aa) of Article 59(1) of Directive 2001/83/EC as amended by Directive …/…/EC, which applies to medicinal products authorised pursuant to Regulation (EC) No 726/2004 by virtue of its Article 9(4)(a) and (d), shall apply to a marketing authorisation granted before the date set out in the second paragraph of Article 3 of this Regulation from renewal of that authorisation or from the expiry of a period of three years starting from that date, whichever is the earliest.	***deleted***

Justification

This amendment is consistent with the rapporteur's amendment to the point 3a of Article 11 and to the point (aa) of Article 59(1) of Directive 2001/83/EC.

PROCEDURE

Title	Pharmacovigilance of medicinal products (amendment of Regulation (EC) No 726/2004)
References	COM(2008)0664 – C6-0515/2008 – 2008/0257(COD)
Committee responsible	ENVI
Opinion by Date announced in plenary	IMCO 19.10.2009
Rapporteur Date appointed	Claude Turmes 28.9.2009
Discussed in committee	2.12.2009 27.1.2010
Date adopted	23.2.2010
Result of final vote	+: 37 –: 0 0: 1
Members present for the final vote	Pablo Arias Echeverría, Adam Bielan, Cristian Silviu Buşoi, Lara Comi, Anna Maria Corazza Bildt, António Fernando Correia De Campos, Jürgen Creutzmann, Christian Engström, Evelyne Gebhardt, Louis Grech, Iliana Ivanova, Philippe Juvin, Sandra Kalniete, Alan Kelly, Eija-Riitta Korhola, Edvard Kožušník, Toine Manders, Tiziano Motti, Zuzana Roithová, Heide Rühle, Matteo Salvini, Christel Schaldemose, Andreas Schwab, Laurence J.A.J. Stassen, Catherine Stihler, Róża, Gräfin von Thun Und Hohenstein, Kyriacos Triantaphyllides, Emilie Turunen, Bernadette Vergnaud, Barbara Weiler
Substitute(s) present for the final vote	Cornelis de Jong, Frank Engel, Ashley Fox, Anna Hedh, Othmar Karas, Morten Løkkegaard, Konstantinos Poupakis, Oreste Rossi, Kerstin Westphal

PROCEDURE

Title	Pharmacovigilance of medicinal products (amendment of Regulation (EC) No 726/2004)
References	COM(2008)0664 – C6-0515/2008 – 2008/0257(COD)
Date submitted to Parliament	10.12.2008
Committee responsible Date announced in plenary	ENVI 19.10.2009
Committee(s) asked for opinion(s) Date announced in plenary	ITRE IMCO 19.10.2009 19.10.2009
Rapporteur(s) Date appointed	Linda McAvan 10.9.2009
Discussed in committee	5.11.2009 25.1.2010 26.4.2010
Date adopted	27.4.2010
Result of final vote	+: 52 –: 0 0: 0
Members present for the final vote	János Áder, Elena Oana Antonescu, Kriton Arsenis, Pilar Ayuso, Paolo Bartolozzi, Sandrine Bélier, Sergio Berlato, Martin Callanan, Nessa Childers, Chris Davies, Esther de Lange, Anne Delvaux, Bas Eickhout, Edite Estrela, Elisabetta Gardini, Julie Girling, Françoise Grossetête, Satu Hassi, Dan Jørgensen, Karin Kadenbach, Christa Klaß, Holger Krahmer, Jo Leinen, Corinne Lepage, Peter Liese, Linda McAvan, Radvilė Morkūnaitė-Mikulėnienė, Miroslav Ouzký, Gilles Pargneaux, Antonyia Parvanova, Andres Perello Rodriguez, Sirpa Pietikäinen, Mario Pirillo, Frédérique Ries, Anna Rosbach, Oreste Rossi, Dagmar Roth-Behrendt, Horst Schnellhardt, Richard Seeber, Theodoros Skylakakis, Bogusław Sonik, Catherine Soullie, Anja Weisgerber, Glenis Willmott, Sabine Wils, Marina Yannakoudakis
Substitute(s) present for the final vote	Christofer Fjellner, Matthias Groote, Alojz Peterle, Michèle Rivasi, Bernadette Vergnaud
Substitute(s) under Rule 187(2) present for the final vote	Mario Mauro