Procedure file

Basic information

COD - Ordinary legislative procedure (ex-codecision procedure) Regulation	2008/0257(COD)
Medicinal products for human use: pharmacovigilance of products Amending Regulation (EC) No 726/2004, Community procedures 2001/0252(COD) Amending Regulation (EC) No 1394/2007 2005/0227(COD) See also 2008/0260(COD) Subject 4.20.04 Pharmaceutical products and industry 4.20.05 Health legislation and policy 4.60.08 Safety of products and services, product liability	Procedure completed

Key players

European Parliament	Committee responsible	Rapporteur	Appointed
	ENVI Environment, Public Health and Food Safety		10/09/2009
		S&D MCAVAN Linda	
	Former committee responsible		
	ENVI Environment, Public Health and Food Safety		
	Committee for opinion	Rapporteur for opinion	Appointed
	ITRE Industry, Research and Energy		16/09/2009
		Verts/ALE RIVASI Michèle	
	IMCO Internal Market and Consumer Protection		28/09/2009
		Verts/ALE TURMES Claude	
	Former committee for opinion		
	IMCO Internal Market and Consumer Protection		
	ITRE Industry, Research and Energy		
Council of the European Union	Council configuration	Meeting	Date
	Agriculture and Fisheries	3050	29/11/2010
	Employment, Social Policy, Health and Consumer Affairs	2980	30/11/2009
European Commission	Commission DG	Commissioner	
	Health and Food Safety	DALLI John	

Key events

09/12/2008	Legislative proposal published	COM(2008)0664	Summary
13/01/2009	Committee referral announced in Parliament, 1st reading		
19/10/2009	Committee referral announced in Parliament, 1st reading		
30/11/2009	Debate in Council	2980	Summary
27/04/2010	Vote in committee, 1st reading		Summary

10/05/2010	Committee report tabled for plenary, 1st reading	A7-0153/2010	
21/09/2010	Debate in Parliament		
22/09/2010	Results of vote in Parliament		
22/09/2010	Decision by Parliament, 1st reading	T7-0331/2010	Summary
29/11/2010	Act adopted by Council after Parliament's 1st reading		
15/12/2010	Final act signed		
15/12/2010	End of procedure in Parliament		
31/12/2010	Final act published in Official Journal		

Technical information

Procedure reference	2008/0257(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation
Legislative instrument	Regulation
	Amending Regulation (EC) No 726/2004, Community procedures 2001/0252(COD) Amending Regulation (EC) No 1394/2007 2005/0227(COD) See also 2008/0260(COD)
Legal basis	Treaty on the Functioning of the EU TFEU 168-p4; Treaty on the Functioning of the EU TFEU 114-p1
Other legal basis	Rules of Procedure EP 159
Stage reached in procedure	Procedure completed
Committee dossier	ENVI/7/00162

Documentation gateway

Legislative proposal		COM(2008)0664	10/12/2008	EC	Summary
Document attached to the procedure		SEC(2008)2670	10/12/2008	EC	
Document attached to the procedure		SEC(2008)2671	10/12/2008	EC	
Document attached to the procedure		JOC_2009/C/229/04 OJ C 229 23.09.2009, p. 0019	22/04/2009	EDPS	Summary
Economic and Social Committee: opinion, report		CES1023/2009	10/06/2009	ESC	
Committee draft report		PE430.928	17/12/2009	EP	
Committee opinion	IMCO	PE431.040	24/02/2010	EP	
Amendments tabled in committee		PE438.413	01/03/2010	EP	
Committee opinion	ITRE	PE430.771	16/04/2010	EP	
Committee report tabled for plenary, 1st reading/single reading		A7-0153/2010	10/05/2010	EP	

Text adopted by Parliament, 1st reading/single reading		T7-0331/2010	22/09/2010	EP	Summary
Commission response to text adopted in plenary		SP(2010)7193	13/10/2010	EC	
Draft final act		00046/2010/LEX	15/12/2010	CSL	

Additional information

National parliaments	IPEX
European Commission	EUR-Lex

Final act

Regulation 2010/1235
OJ L 348 31.12.2010, p. 0001 Summary

Corrigendum to final act 32010R1235R(01)
OJ L 201 27.07.2012, p. 0138 Summary

Final legislative act with provisions for delegated acts

Medicinal products for human use: pharmacovigilance of products

PURPOSE: to improve the functioning of Community rules on the pharmacovigilance of medicinal products for human use, with the overall objectives of better protecting public health, ensuring proper functioning of the internal market and simplifying the current rules and procedures.

PROPOSED ACT: Directive of the European Parliament and of the Council.

CONTENT: it is estimated that 5% of all hospital admissions are due to an adverse drug reaction, that 5% of all hospital patients suffer an adverse drug reaction and adverse drug reactions are the fifth most common cause of hospital death. Some adverse reactions will only be detected after a medicine has been authorised and the full safety profile of medicinal products can only be known once they have entered the market.

Community rules so far adopted have made a major contribution to the achievement of the objective that medicinal products authorised to be placed on the Community market are continuously monitored as regards their safety. However, in the light of the experience acquired and following an assessment by the Commission of the Community system of pharmacovigilance, it has become clear that new measures are necessary to improve the operation of the Community rules on the pharmacovigilance of medicinal products for human use.

Therefore, the proposals aim at the strengthening and rationalizing the Community pharmacovigilance system of medicinal products for human use through the amendment of the two legal acts governing this field, i.e. Directive 2001/83/EC (see COD/2008/0260) and Regulation (EC) No 726/2004. The specific objectives are:

- providing for clear roles and responsibilities for the key responsible parties and clear obligations against which they perform their roles;
- rationalising EU decision-making on drug safety issues;
- strengthening medicines safety transparency and communication;
- strengthening companies' pharmacovigilance systems;
- ensuring the proactive and proportionate collection of high quality data relevant to the safety of medicines through risk management and structured data collection;
- involving stakeholders in pharmacovigilance;
- simplification of the current Community pharmacovigilance procedures.

The key elements of the proposals can be summarised as follows:

Clear roles and responsibilities:

- the key tasks of the Agency in the area of pharmacovigilance are overall maintained, but the Agency's coordinating role at the centre of the Community pharmacovigilance system is reinforced;
- the Member States should remain core to the operation of pharmacovigilance in the Community, with increased cooperation and work-sharing mechanisms;
- the pharmacovigilance responsibilities of marketing authorisation holders are also clarified, in particular as regards the scope of the obligation of marketing authorisation holders to continuously monitor the safety of products to ensure that all information available is brought to the attention of the authorities;
- a new scientific committee responsible for pharmacovigilance is created within the Agency: the Pharmacovigilance Risk Assessment Advisory Committee. This Committee is intended to play a key role in the pharmacovigilance assessments in the Community;
- the mandate of the coordination group composed of Member States representatives is enhanced;
- the Community procedure for the assessment of serious safety issues for nationally authorised products is stream-lined through clear and binding initiation criteria for the Member States.

Transparency and communication in terms of drug safety issues:

- strengthening of the Eudravigilance database, which should become the single point of receipt of pharmacovigilance information for medicinal products for human use authorised in the Community;
- Community coordination of communication about safety issues and establishment of a European medicines safety web-portal;
- introduction of a new ?key information' section in the summary of the product characteristics and the package leaflet which accompany every medicinal product placed on the Community market.

Pharmacovigilance obligations of the marketing authorisation holder: the proposals simplify the requirement that a ?detailed description of the pharmacovigilance system? be submitted in marketing authorisation applications. In the marketing authorisation application, only key elements of the pharmacovigilance system should be submitted, but this is balanced with a requirement for companies to maintain a detailed pharmacovigilance system master file on site.

Risk management planning and non-interventional safety studies:

- the establishment of a risk management system for each medicinal product to be newly authorised in the Community (or for existing products on the basis of safety concerns), which should be proportionate to the identified risks, potential risks, and the need for additional information on the medicinal product;
- the establishment of harmonised guiding principles and a procedure for the supervision of non-interventional post-authorisation safety studies (i.e. safety studies of authorised products that are not clinical trials), in particular to ensure that they are non promotional, and the follow-up of any safety data generated in such studies.

Adverse drug reaction case reports: the proposals are intended to make reporting proportionate to risks, to empower patients to report their side effects, and to ensure that overdoses and medication errors are reported. The following has therefore been proposed:

- simplification of adverse reaction reporting by providing that all adverse reaction data are reported directly to the Eudravigilance database;
- requiring the Agency to assume the role of monitoring scientific literature by the Agency and to enter case reports of adverse effects into the Eudravigilance database;
- clarification of the definition of adverse drug reaction to make clear that companies report medication errors that result in an adverse reaction to the competent authorities for medicines and ensure that all the relevant Member State authorities share data;
- clarification of the legal basis for patients to report suspected adverse drug reactions.

Periodic safety update reports and other safety related assessments: the proposals simplify periodic safety update report submission by industry and make it proportional to the knowledge about the safety/risk of the product. They introduce work-sharing mechanisms for the assessments, with a prominent role in all cases by the Pharmacovigilance Risk Assessment Advisory Committee, and faster updating of product information through the establishment of clear procedures.

Medicinal products for human use: pharmacovigilance of products

OPINION OF THE EUROPEAN DATA PROTECTION SUPERVISOR 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, and on the proposal for a Directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

Recall: on 10 December 2008, the Commission adopted two proposals relating to the amendment of the actual pharmacovigilance system. The general intention of the two proposals is to remedy these weaknesses and to improve and strengthen the Community pharmacovigilance system with the overall objective of better protecting public health, ensuring proper functioning of the internal market and simplifying the current rules and procedures (see COD/2008/0260). The overall operation of the current pharmacovigilance system relies on the processing of personal data. These data are included in the adverse drug reactions reporting and can be considered as data relating to health of the persons concerned since they reveal information about drug use and associated health problems.

Processing of such data is subject to strict data protection rules as laid down in Regulation (EC) No 45/2001 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 and Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

Despite this, no reference to data protection is included in the current text of Regulation (EC) No 726/2004 and Directive 2001/83/EC, except for one specific reference in the Regulation. The EDPS regrets that data protection aspects are not considered within the proposed amendments and that he was not formally consulted on both proposals for amendments. The EDPS recommends that a reference to this opinion is included in the preamble of both proposals.

Content of the Opinion: this Opinion will first proceed with a simplified explanation of the system of pharmacovigilance in the EU as it follows from Regulation (EC) No 726/2004 and Directive 2001/83/EC in their present state. Subsequently, the necessity of processing of personal data in the context of pharmacovigilance will be analysed. After this, the proposals of the Commission for improving the current and envisaged legal framework will be discussed and recommendations will be made on how to ensure and improve the data protection standards.

Conclusions and recommendations: the EDPS takes the view that the lack of a proper assessment of the data protection implications of pharmacovigilance constitutes one of the weaknesses of the current legal framework set out by Regulation (EC) No 726/2004 and Directive 2001/83/EC. The current amendment of Regulation (EC) No 726/2004 and Directive 2001/83/EC should be seen as an opportunity to introduce data protection as a full-fledged and important element of pharmacovigilance.

A general issue to be addressed thereby is the actual necessity of processing personal health data at all stages of the pharmacovigilance process. As explained in this Opinion, the EDPS seriously doubts this need and urges the legislator to reassess it at the different levels of the process. It is clear that the purpose of pharmacovigilance can in many cases be achieved by sharing information on adverse effects which is anonymous in the meaning of the data protection legislation. Duplication of reporting can be avoided through the application of well structured data reporting procedures already at national level.

The proposed amendments envisage a simplified reporting system and a strengthening of the EudraVigilance database. The EDPS has explained that these amendments lead to increased risks for data protection, especially when it involves the direct reporting of patients to the EMEA or the EudraVigilance database.

In this respect, the EDPS:

1. strongly advocates a decentralised and indirect reporting system whereby communication to the European webportal is coordinated through using the national webportals;
2. emphasises that privacy and security should be part of the design and implementation of a reporting system through the use of web-portals (?privacy by design?);
3. underlines that once data concerning health about identified or identifiable natural persons is processed, the person responsible for such processing should comply with all the requirements of the Community data protection legislation.

More specifically, the EDPS recommends:

- to include a reference to this Opinion in the preamble of both proposals, to introduce in both Regulation (EC) No 726/2004 and Directive 2001/83/EC a recital stating the importance of data protection in the context of pharmacovigilance, with references to the relevant Community legislation;
- to introduce in Regulation (EC) No 726/2004 and Directive 2001/83/EC a new Article having a general nature which states that: (i) the provisions of Regulation (EC) No 726/2004 and Directive 2001/83/EC are without prejudice to the rights and obligations stemming from the provisions of Regulation (EC) No 45/2001 and Directive 95/46/EC respectively, with specific reference to Article 10 of Regulation (EC) No 45/2001 and Article 8 of Directive 95/46/EC respectively; (ii) identifiable health data shall only be processed when strictly necessary and parties involved should assess this necessity at every single stage of the pharmacovigilance process;
- to include in the proposed Article 24(2) of Regulation (EC) No 726/2004 a sentence stating that the accessibility of the EudraVigilance database shall be regulated in conformity with the rights and obligations stemming from the Community legislation on data protection;
- to add a paragraph to the proposed Article 24 stating that measures shall be put in place which ensure that the data subject can exercise his right of access to personal data concerning him as provided for by Article 13 of Regulation (EC) No 45/2001;
- to add to the proposed Article 101 of Directive 2001/83/EC a paragraph which states that in case of processing of personal data the individual shall be properly informed in accordance with Article 10 of Directive 95/46/EC;
- to include in the newly proposed Articles 25 and 26 of Regulation (EC) No 726/2004 and Article 106 of Directive 2001/83/EC, which deal with the development of a reporting system for adverse effects through the use of web- portals, an obligation to incorporate proper privacy and security measures at an even level across Member States, taking into account the basic principles of confidentiality, integrity, accountability and availability of data.

Medicinal products for human use: pharmacovigilance of products

On the basis of progress reports, the Presidency informed the Council of the state of play in the negotiations on two parts of the "pharmaceutical package": preventing falsified medicines from entering into the legal supply chain of medicinal products and the strengthening and rationalising of the current pharmacovigilance system.

Under the Swedish Presidency, the preparatory bodies of the Council pursued their work with high priority on these two parts of the package.

1) Concerning the draft directive on preventing the entry into the legal supply chain of falsified medicinal products, the working group reached tentative agreement on a number of technical aspects, including:

- the definition of "falsified medicinal products";
- the proposed definition of "trading of medicinal products" has been changed to "brokering of medicinal products" and amended, thereby clarifying which actors in the supply chain should be subject to the responsibilities of brokers. The proposed introduction of obligations for brokers aim to reinforce the traceability of medicinal products;
- a clarification of the relationship between the proposed new provisions in Directive 2001/83/EC and Community legislation on intellectual property rights.

Other elements of the proposal still need further discussion, notably with regard to the strengthening of controls of non active substances used in pharmaceuticals (excipients) and the proposed safety features aiming to render falsification more difficult.

The proposal includes provisions requiring the accreditation of third party auditors of Good Manufacturing Practices and Good Distribution Practices. A majority of delegations object to accreditation, since they maintain that such a system could result in a transfer of responsibility from manufacturers and importers as well as make enforcement by national competent authorities more difficult. The Presidency has therefore proposed to delete the provisions regarding accreditation from the text. Some delegations have expressed an interest in the possibility of establishing third party accreditation at a national level.

2) Concerning the proposals for a regulation and a directive on strengthening the EU system for the safety monitoring of medicinal products ("pharmacovigilance"), the working group reached tentative agreement on a number of questions including:

- a clarification of the relation between the proposed new provisions in Directive 2001/83/EC and Regulation (EC) 726/2004 on the one hand and the Community legislation on protection of personal data on the other hand;
- a strengthening of the role of the Pharmacovigilance Risk Assessment Committee (PRAC) in relation to the Committee for Medicinal Products for Human Use and to the Coordination Group set up by Article 27 of Directive 2001/83/EC (CMD), including an obligation for these last two bodies to explain any differences in opinion compared to the PRAC;
- a change in the composition of the PRAC and in the method for nominating the PRAC members so that all Member States will be represented;
- the inclusion of a requirement for the Agency, in collaboration with the Member States and the Commission, to draw up functional specifications for the Eudravigilance database which will take account of the role and experience of national competent authorities

for pharmacovigilance. The new reporting obligations to Eudravigilance will not apply until these specifications are met and to this end a transitional period is envisaged;

- the legal status of CMD opinions and how they are implemented in Member States. Here, text redrafting proposals are under legal scrutiny.

The Working Party has continued to discuss other central provisions of the proposals, mainly in relation to the Community Procedure and Referrals, the Recording and Reporting of adverse reactions, the Periodic Safety Update Reports and the Post Authorisation Safety Studies.

A number of issues still require further examination, such as the recording and reporting of adverse reactions and the proposed list of medicinal products for human use under intensive monitoring.

At this stage, all delegations have a general scrutiny reservation on the entire proposal while the Danish, Maltese and United Kingdom delegations have parliamentary scrutiny reservations.

3) With regard to the third part of the "pharmaceutical package", the proposals for a regulation and a directive concerning information for the general public on medicinal products, the Presidency recalled the strong concerns of many Member States. The Commission made it clear that it is prepared to show flexibility in order to find a common basis for the future negotiations.

Medicinal products for human use: pharmacovigilance of products

The Committee on the Environment, Public Health and Food Safety adopted the report by Linda MACAVAN (S&D, UK) 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. It recommended that the European Parliament?s position at first reading under the ordinary legislative procedure (formerly known as the codecision procedure) should be to amend the Commission proposal as follows:

A Pharmacological Risk Assessment Committee (PRAC) with greater powers: 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 on the Community code relating to medicinal products for human 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.

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.

Post-authorisation safety and efficacy studies: 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 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.

Renewal of marketing authorisation: the committee deleted the words « insufficient exposure to the product » as a criterion for restricting renewal to a five-year period. 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.

Pharmacovigilance: the report adds that 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.

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.

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 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.

The Agency must make public the declaration of committee members? interests and agendas for, and records of, each meeting, accompanied by decisions taken. It must also make public 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 the 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.

The Agency shall monitor all medical literature for reports of suspected adverse reactions to medicinal products for human use containing well established active substances.

Assessment report following periodic safety update reports: PRAAC shall formulate a recommendation for the Committee for Medicinal Products for Human Use on the basis of the assessment report. 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.

Public hearings: in assessing updates to the risk management systems, 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.

Lastly, the committee amended provisions relating to the composition of the Pharmacovigilance Risk Assessment Advisory Committee and stressed that its independence must be guaranteed.

Medicinal products for human use: pharmacovigilance of products

The European Parliament adopted by 559 votes to 7, with 12 abstentions, a 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.

The Parliament adopted its position at first reading under the ordinary legislative procedure (formerly known as the codecision procedure). The amendments adopted in plenary are the result of a compromise reached between the European Parliament and the Council. They amend the Commission?s position as follows:

Strengthened Risk Assessment Committee: in order to ensure harmonised responses across the Union to safety concerns regarding medicinal products for human use, the Committee for Medicinal Products for Human Use and the coordination group established by Directive 2001/83/EC on the Community code relating to medicinal products for human 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.

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

Market authorisation: post authorisation efficacy and safety studies: the amended text stipulates that it is necessary from a public health perspective to complement the data available at the time of authorisation with additional data about the safety and, in certain cases, also about the efficacy of medicinal products authorised. The Commission should therefore be empowered to require the marketing authorisation holder to conduct post-authorisation studies on safety and on efficacy. It should be possible to impose this requirement at the time of granting the marketing authorisation or later, and it should be part of the marketing authorisation. These additional studies may be aimed at collecting data to enable the assessment of safety or efficacy of medicinal products in everyday medical practice. The supervisory authorities for pharmacovigilance may, as considered necessary, conduct pre-authorisation pharmacovigilance inspections to verify the accuracy and successful implementation of the pharmacovigilance system as described by the applicant in support of the application.

Products authorised subject to additional monitoring: some medicinal products are authorised subject to additional monitoring. This includes all medicinal products with a new active substance and biological medicinal products including biosimilars for which pharmacovigilance activities are prioritised. This may also apply, at the request of the competent authorities, to specific products, 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 that will be specified in the risk management plan.

Risk management plans are normally required for new active substances, biosimilars, medicinal products for paediatric use and for products involving a significant change in the marketing authorisation, including a new manufacturing process of a biotechnologically-derived product. Products subject to additional monitoring should be identified as such by a black symbol, which will be selected by the Commission on a recommendation by the Pharmacovigilance Risk assessment Committee, and a relevant standard 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.

Data protection: this Regulation shall apply without prejudice to Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data and Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Union institutions and bodies and on the free movement of such data.

In order to detect, assess, understand and prevent adverse reactions, identify and take actions 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 respecting EU data protection legislation.

Tasks of the Agency: the amended text specifies that the Regulation and Directive amending Directive 2001/83/EC on the Community Code relating to medicinal products for human use widen the task of the Agency with regard to pharmacovigilance, including literature monitoring, improved information technology tools and provision of more information to the general public. The Agency should be enabled to fund these activities from fees paid by marketing authorisation holders. These fees should not cover tasks carried out by national competent authorities for which such authorities charge fees in accordance with the provisions of Directive 2001/83/EC.

Uniform conditions: a recital states that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well the minimum requirements of the quality system for the performance of pharmacovigilance activities by the national competent authorities and marketing authorisation holders, the use of internationally agreed terminology, formats and standards for the conduct of pharmacovigilance, and the minimum requirements for the monitoring of data in the Eudravigilance database to determine whether there are new or changed risks.

The format and content of electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders, the format and content of electronic periodic safety update reports and risk management plans and the format of protocols, abstracts and final study reports for the post-authorisation safety studies should also be established. In this respect, pending the adoption of a new Regulation based on Article 291 of the TFEU, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of

implementing powers conferred on the Commission continues to apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.

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

Medicinal products for human use: pharmacovigilance of products

PURPOSE: to improve the functioning of Community rules on the pharmacovigilance of medicinal products for human use, with the overall objectives of better protecting public health, ensuring proper functioning of the internal market and simplifying the current rules and procedures.

LEGISLATIVE ACT: Regulation (EU) No 1235/2010 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, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products.

CONTENT: following first reading agreement with the European Parliament, the Council adopted a Directive on the Community pharmacovigilance system (COD/2008/0260) and this Regulation on medicinal products for human use. The EU pharmacovigilance system seeks to prevent, detect and assess adverse reactions to medicinal products placed on the Union market. It also ensures that any product which presents an unacceptable level of risk can be withdrawn rapidly from the market.

Roles and responsibilities: Member States will remain central for the operation of a pharmacovigilance system, but their responsibilities are clarified. Under the new rules they will collect information on suspected adverse drug reactions not only if the product was used within the terms of the marketing authorisation, but also in case of overdose, misuse, abuse and medication errors.

A new scientific committee, the Pharmacovigilance Risk Assessment Committee, is created within the European Medicines Agency (EMEA), and will advise the EMEA's Committee for medicinal products for human use, which remains responsible for issuing an opinion, on the risk-benefit assessment of centrally-authorised medicinal products for human use.

The mandate of the EMEA?s coordination group, responsible for the approval of risk management systems and monitoring their effectiveness, is expanded. From now on, this group will also examine matters in the area of pharmacovigilance, on the basis of opinions drawn up by the Pharmacovigilance Risk Assessment Committee, for all medicinal products authorised by the Member States, as well as questions regarding changes in the conditions of the market authorisations issued by the Member States. Under the current rules, the coordination group?s mandate is limited to examining questions regarding the market authorisation of a medicinal product in two or more Member States.

It is planned to provide adequate funding for pharmacovigilance activities by charging fees to undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, as well as competent national authorities.

Transparency and communication: the existing EU pharmacovigilance database, the "Eudravigilance database", is strengthened and becomes the single point of receipt of pharmacovigilance information for medicinal products for human use authorised in the EU, thus facilitating early discovery of adverse reactions. This reporting system will be gradually introduced, following development of the necessary capacity of the data base. In order to ensure transparency in pharmacovigilance issues, the EMEA will create and maintain a European medicines webportal.

Concerning the readability of the summaries of product characteristics and the packaging leaflets, the Commission is invited to present an assessment report and, if appropriate, table proposals to improve the layout and the content of the summaries of product characteristics and of the packaging leaflet.

Pharmacovigilance obligations by industry: as under the current rules, the marketing authorisation holder must establish a pharmacovigilance system to ensure the monitoring and supervision of its authorised medicinal products. The requirements for applications are, however, simplified. Marketing authorisation holder will have to submit only key elements of their pharmacovigilance system, rather than a detailed description of the system. On the other hand, they will have to maintain a detailed file on site for possible inspections by the competent authorities.

The marketing authorisation holders will have continuously to monitor the safety of their products, inform the authorities of any changes that might have an impact on the marketing authorisation, and for ensuring that the product information is kept up to date. In addition, the Commission is empowered to require marketing authorisation holders to conduct post authorisation studies on safety and on efficacy, as part of the marketing authorisation.

Risk management planning and non-interventional safety studies: EMEA may require a marketing authorisation holder to operate a risk management system if there are concerns about the risks affecting the risk-benefit balance of an authorised medicinal product.

In order to ensure that non-interventional post-authorisation safety studies (i.e. safety studies of authorised products that are not clinical trials) requested by competent authorities are non promotional, harmonised guiding principles and regulatory supervision are strengthened.

Adverse drug reaction case reports: Member States will have to take appropriate measures to enable patients, besides of doctors, pharmacists and other health-care professionals to report suspected adverse reactions to the national competent authority. Member States will have to report all suspected adverse reactions that occur in their territory to the Eudravigilance database.

Marketing authorisation will be required to submit electronically information on all suspected adverse reactions that occur in the EU and in third countries to the Eudravigilance database.

Periodic safety update reports and other safety related assessments: as under the current rules, marketing authorisation holders will have to submit to EMEA periodic safety update reports. In the future, these periodic safety update reports will, however, constitute a scientific evaluation of the risk-benefit balance of the medicinal product, rather than a detailed presentation of individual case reports, since that information will already have been reported to the Eudravigilance data base.

In addition, there may be a single periodic safety update report for products that contain the same active substance or combination thereof but are subject to different marketing authorisations.

For medicinal products with a new active substance and biological medicinal products, the pharmacovigilance will be strengthened by making the authorisation subject to additional monitoring activities and a requirement that they should be identified by a black symbol and an explanatory sentence that encourages reporting of adverse reactions on the summary of product characteristics and on the patient information leaflet. This requirement may also apply, at the request of the competent authorities, to other products.

Member States are invited to consider measures to monitor and evaluate the risk of environmental effects of medicinal products. The Commission is called upon to produce a report on the scale of the problem and assess if the EU legislation in this field should be amended.

This Regulation and the Directive mentioned above (COD/2008/0260) form part of the pharmaceutical package which also includes a draft directive on falsified pharmaceutical products, as well as a draft directive and a draft regulation concerning information on prescription drugs.

ENTRY INTO FORCE: 01/01/2011

APPLICATION: 2/07/2012.

Medicinal products for human use: pharmacovigilance of products

Corrigendum to Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (Regulation first published in the OJ L 348 of 31.12.2010).

Article 1(7) should read:

In Article 16, paragraphs 1, 2 and 3 are replaced by the following:

3. The marketing authorisation holder shall ensure that the product information is kept up to date with the current scientific knowledge including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal established in accordance with Article 26.

3a. In order to be able to continuously assess the risk-benefit balance, the Agency may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance remains favourable. The marketing authorisation holder shall answer fully and promptly any such request.

The Agency may at any time ask the marketing authorisation holder to submit a copy of the pharmacovigilance system master file. The marketing authorisation holder shall submit the copy at the latest seven days after receipt of the request.