Procedure file

Basic information

COD - Ordinary legislative procedure (ex-codecision procedure) Directive	2008/0260(COD)
Medicinal products for human use: pharmacovigilance of products Amending Directive 2001/83/EC, Community code 1999/0134(COD) See also 2008/0257(COD) Subject 4.20.04 Pharmaceutical products and industry 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	S&D MCAVAN Linda	10/09/2009
Former committee responsible		
ENVI Environment, Public Health and Food Safety		

Committee for opinion	Rapporteur for opinion	Appointed
ITRE Industry, Research and Energy	Verts/ALE RIVASI Michèle	16/09/2009
IMCO Internal Market and Consumer Protection	Verts/ALE TURMES Claude	28/09/2009
Former committee for opinion		
ITRE Industry, Research and Energy		
IMCO Internal Market and Consumer Protection		

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

10/12/2008	Legislative proposal published	COM(2008)0665	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
02/06/2010	Committee report tabled for plenary, 1st reading	A7-0159/2010	
21/09/2010	Debate in Parliament		
22/09/2010	Results of vote in Parliament		
22/09/2010	Decision by Parliament, 1st reading	T7-0332/2010	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		
25/01/2011	Final act published in Official Journal		

Technical information

Procedure reference	2008/0260(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation
Legislative instrument	Directive
	Amending Directive 2001/83/EC, Community code 1999/0134(COD) See also 2008/0257(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/7/00153

Documentation gateway

Legislative proposal		COM(2008)0665	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		CES1024/2009	10/06/2009	ESC	
Committee draft report		PE430.927	17/12/2009	EP	
Committee opinion	IMCO	PE431.039	05/03/2010	EP	
Amendments tabled in committee		PE438.412	15/03/2010	EP	
Committee opinion	ITRE	PE430.773	15/04/2010	EP	

Committee report tabled for plenary, 1st reading/single reading		A7-0159/2010	02/06/2010	EP	
Text adopted by Parliament, 1st reading/single reading		T7-0332/2010	22/09/2010	EP	Summary
Commission response to text adopted in plenary		SP(2010)7193	13/10/2010	EC	
Draft final act		00047/2010/LEX	15/12/2010	CSL	

Additional information

National parliaments	IPEX
European Commission	EUR-Lex

Final act

Directive 2010/84
OJ L 348 31.12.2010, p. 0074 Summary

Corrigendum to final act 32010L0084R(01)
OJ L 021 25.01.2011, p. 0008 Summary

Corrigendum to final act 32010L0084R(02)
OJ L 276 21.10.2011, p. 0063

Final legislative act with provisions for delegated acts

Medicinal products for human use: pharmacovigilance of products

PURPOSE: to amend, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

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 (ADR), and that ADR is 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. Pharmacovigilance rules are therefore necessary for the protection of public health in order to prevent, detect and assess adverse effects of medicinal products.

The proposals aim at the strengthening and rationalising the Community pharmacovigilance system of medicinal products for human use The specific objectives are:

- providing clear roles and responsibilities for the key responsible parties and clear obligations;
- strengthening transparency and communication on medicine?s safety issues to increase the understanding and trust of patients and health professionals and improve the penetration of key warnings;
- strengthening companies' pharmacovigilance systems, allowing companies to improve their systems regularly whilst reducing administrative burden;
- introducing a risk management planning for each new medicinal product
- strengthening the reporting system for adverse reactions by rationalising current system and involving all stakeholders in pharmacovigilance
- ensuring the proactive and proportionate collection of high quality data relevant to the safety of medicines through risk management and structured data collection.

In addition to achieving better protection of public health the proposals will also simplify the current EU procedures with consequent efficiency gains for both the pharmaceutical industry and medicines? regulators.

Clear roles and responsibilities:

- Member States should remain central to the operation of pharmacovigilance, with increased cooperation and work-sharing mechanisms (Member States not the Commission).
- companies? responsibilities are clarified, in particular as regards the scope of their obligation to continuously monitor the safety of products thereby ensuring that all information available is brought to the attention of the authorities.
- a new scientific committee, the Pharmacovigilance Risk Assessment Advisory Committee, is created within the EMEA and it will play a key role in the pharmacovigilance assessments in the EU.
- the mandate of the coordination group composed of Member States representatives is enhanced for the sake of closer cooperation between the Member States and in order to increase work-sharing.
- the EU 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: clear, EU coordinated messages about specific safety risk issues:

- the Eudravigilance database should become the single point of receipt of pharmacovigilance information for medicinal products authorised in the EU.
- EU 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.

Pharmacovigilance obligations by industry: currently legislation requires a ?detailed description of the pharmacovigilance system? to be submitted in marketing authorisation applications. These proposals simplify the existing requirement by introducing the "Pharmacovigilance system master file". In the applications only key elements of the pharmacovigilance system should be submitted, but this is balanced with a requirement for companies to maintain a detailed file on site.

Risk management planning and non-interventional safety studies: in the existing provisions, companies may provide a risk management system for specific medicinal products if considered appropriate, and there is no explicit legal basis for competent authorities to request it. These proposals require:

- a risk management system for each new medicinal product (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.
- 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 date generated in such studies.

Adverse drug reaction case reports: current reports are submitted to several authorities if a product is authorised in more than one Member State , and lead to duplicative assessments as there is no provision to group assessments by products or substances. The proposals are intended:

- to make reporting proportionate to risks;
- to empower patients to report their side effects;
- to ensure that overdoses and medication errors are reported;
- to simplify adverse reaction reporting. It is proposed to report all adverse reaction data directly to the Eudravigilance database.
- for the Agency to take on a new task for the monitoring of selected scientific literature and for entering case reports of adverse effects onto the Eudravigilance database.
- for medication errors that result in an ADR to be reported to the competent authorities for medicines. Member State authorities should ensure that data is shared (including between the authorities for medicines and any authorities for patient safety) and make clear the legal basis for patients to report suspected adverse drug reactions.

Periodic safety update reports and other safety related assessments: as there is currently no provision for group submissions and assessments on products or substances, this leads to duplicative submissions and assessments. The update of product information as a result of these assessments is not governed in detail by the actual legislation. The proposals:

- simplify periodic safety update report submission by industry and make it proportional to the knowledge about the safety/risk of the product;
- would 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;
- amend the scope of periodic safety update reports to become an analysis of the risk-benefit balance of a medicinal product rather than a detailed presentation of individual case reports as a result of the submission of all ADR data directly to the Eudravigilance database,;
- make the requirements for periodic safety update reports proportional to the risks posed by medicinal products, and routine reporting is no longer necessary for products considered low risk or where reporting would be duplicative (with the possibility for ad-hoc requests for such products).
- make explicit provision for the regulatory follow-up of assessments of periodic safety update reports, to ensure a clear link between pharmacovigilance evaluations and the review and updating of marketing authorisations authorised in the EU.
- create the framework for the shared use of resources between competent authorities for the assessment and follow-up of periodic safety update reports, with a strong involvement of the Agency's Pharmacovigilance Risk Assessment Advisory Committee.
- introduce a single assessment of periodic safety update reports for medicinal products authorised in more than one Member State,(including all products containing the same active substance),. This will also be the case for products authorised by the Member States and/or by the Commission.

Lastly, the proposal also contains two provisions to improve the availability of medicine in Member States, in particular the smaller ones.

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 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. 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 more robust risk assessment committee: Members propose increasing the powers of the Pharmacovigilance Risk Assessment Committee (PRAC) in relation to the coordination group. The coordination group is not a specialist body on pharmacovigilance. The PRAC should be the only body in charge of pharmacovigilance and risk assessment, in order to avoid undue duplication of roles.

The Committee for Medicinal Products for Human Use shall adopt an opinion which differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, only if there exist strong scientific and public health grounds for doing so. The Committee for Medicinal Products for Human Use shall explain these grounds in a justification to be annexed to its opinion.

Summary of Essential Information: the Commission had proposed this summary to be included in the Package Information Leaflet. However, the committee deleted this and inserted a clause specifying that for medicinal products included on the list referred to in Article 23 of Regulation (EC) No 726/2004, the statement, preceded by a black symbol which shall be decided on by means of delegated acts: ?This medicinal product is subject to additional safety monitoring. All suspected adverse reactions should be reported to your doctor, pharmacist, healthcare professional, or to name and web-address, postal address and / or telephone number of the national competent authority.?

For medicinal products not included in the list referred to in Article 23 of Regulation (EC) No 726/2004, the following statement should be included: ?All suspected adverse reactions should be reported to your doctor, pharmacist, healthcare professional, or to name and web-address, postal address and/or telephone number of the national competent authority.

The report adds that it is important for healthcare professionals and patients to identify easily the most relevant information about the medicines they use. In order to facilitate such identification, the Commission should review the summary of the product characteristics and the package leaflet within 18 months.

Within 18 months of the entry into force of the Directive, the Commission shall present to the European Parliament and the Council an assessment report on how the summary of product characteristics and the package leaflet should meet the needs of patients and healthcare professionals. On the basis of this, the Commission shall issue proposals in order to improve the readability, layout and content of these documents.

The summary of essential information is deleted from the text.

Marketing authorisations and post-authorisation safety and efficacy studies: marketing authorisation may be subject to the requirement to conduct post-authorisation safety studies 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, on studies and data required and on methodologies for assessing it.

The competent authorities shall have the power and appropriate resources to immediately suspend or revoke the marketing authorisation in the event that the conditions included in the marketing authorisation are not fulfilled by the relevant deadline.

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. It states that the words introduce a degree of uncertainty especially for products, such as orphan drugs, for which exposure is unlikely to ever be sufficient (sufficient exposure is a very difficult threshold/ benchmark to achieve). 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.

Reporting of adverse drug reactions: Member States must take all appropriate measures to encourage patients, doctors, pharmacists and other health-care professionals to report suspected adverse reactions to the national competent authority; these measures shall include training for health professionals and a public information campaign for patients. Patients? and consumer organisations shall be involved in providing information to patients and in developing public information campaigns in cooperation with regulatory bodies.

Member States must also:

- facilitate direct patient reporting through the provision of alternative reporting formats in addition to web-based formats;
- ensure that the public is given important information in good time on pharmacovigilance concerns relating to the use of a medicinal product through publication on the web portal and through other means of public information as necessary;
- pensure that any biological medicinal product prescribed, dispensed, or sold in their territory which is the subject of a report on a suspected adverse reaction is identifiable by, where available, the name of the MAH, the INN, the name of the medicinal product and the batch number, using the standard forms and procedures developed in accordance with Regulation (EC) No 726/2004 and taking due account of the developments within the EudraVigilance system.

Reporting of suspected adverse reactions due to medication errors should be on a 'no blame' basis, and should be legally privileged.

Transparency and medicine safety: each Member State shall set up and maintain a national medicines web-portal, including a dedicated medicine safety web page which shall be linked to the European medicines web-portal. Member States must provide:

- the most up-to-date electronic version of the leaflets of the medicines available on the national market in the national language (and where applicable the link to the Agency's EudraPharm database);
- for each medicinal product which Member States have authorised, the most up-to-date electronic version of the summary of the product characteristics and any conditions established, together with any deadlines for their fulfilment;
- assessment reports for medicinal products authorised in accordance with this Directive (and where applicable the link to the EPAR summary).

Reporting pharmacovigilance data: the Eudravigilance database should simultaneously and electronically notify the relevant Member States of reports submitted by market authorisation holders. From this perspective, and in order to achieve the objectives referred to above, Member States should not impose any further requirements on marketing authorisation holders in respect of the prompt and regular reporting of suspected adverse reactions. The Eudravigilance database and the national database should be fully interoperable.

The proposed new requirement for pharmaceutical companies to report all non serious suspected adverse reactions (including non-medically confirmed consumer reports) will have a massive impact on the workload of both the industry and regulatory authorities since the majority of cases are non-serious unconfirmed consumer reports. The committee states that certain holders of authorisations will be exempt.

Concerning suspected adverse reactions reported by patients, Member States may decide whether those are reported directly or via healthcare professionals.

Reporting by healthcare professionals should be particularly encouraged in cases where their contribution is essential in order to understand the significance of the adverse reaction and of adverse reactions derived from medication errors. To facilitate this type of reporting and to protect the citizen, access to data contained in patients? medical files should be accessible to healthcare professionals.

Data protection: the Directive should apply without prejudice to Directive 95/46/EC and Regulation 45/2001/EC 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. The purpose of safeguarding public health constitutes a substantial public interest which justifies the processing of identifiable health data as long as this is processed only when necessary and the parties involved assess the necessity of processing such data at every stage of the pharmacovigilance process.

Guidelines on good pharmacovigilance practice : the Commission, in cooperation with the Agency, Member States and stakeholders, shall prepare detailed guidelines on good record-keeping practices for pharmacies and others that dispense or administer medicinal products, to ensure retention of records necessary for filing a pharmacovigilance report or to provide information needed by a marketing authorisation holder conducting an evaluation of an adverse event and to facilitate follow-up investigations by the marketing authorisation holder and national competent authorities.

Environmental supervision and protection: Member States shall appoint one or several national authorities to monitor adverse environmental effects of medicinal products on public health or the environment. If one of these authorities identifies an environmental risk that is higher than that indicated in the evaluation or if it finds new adverse environmental effects, it shall forthwith transmit all findings to the European Medicines Evaluation Agency and to the competent authority. The Agency shall, upon receiving such information, assess whether the risk-benefit balance remains favourable when taking into account the new findings. This must not lead to the withdrawal of the authorisation for drugs necessary for treating life-threatening or serious diseases.?

Medicinal products for human use: pharmacovigilance of products

The European Parliament adopted by 569 votes to 8, with 15 abstentions, a legislative resolution 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.

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:

Market autorisation: the national competent authorities shall make publicly available without delay the marketing authorisation together with the package leaflet, the summary of the product characteristics, together with any deadlines for the fulfilment of the conditions where necessary for each medicinal product which they have authorised. The public assessment report shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

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.

Products 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.

Products subject to additional monitoring should be identified as such by a black 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 maintained up to date by the European Medicines Agency.

For all medicinal products, a standard text shall be included expressly asking healthcare professionals to report any suspected adverse reaction in accordance with the national spontaneous reporting system. Different ways of reporting, including electronic reporting, shall be available.

Suspicion of an adverse drug reaction: the suspicion of an adverse drug reaction, meaning that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, should be sufficient reason for reporting. Without prejudice to the existing Union and national provisions and practices on medical confidentiality, Member States should ensure that reporting and processing of personal data related to suspected adverse reactions including those associated with medication errors is on a confidential basis.

The text stipulates that Member States should operate a pharmacovigilance system to collect information useful in the surveillance of medicinal products including information on suspected adverse drug reactions, arising from use of a product within the terms of the marketing authorisation as well as from any other use, including overdose, misuse, abuse and medication errors, and those occurring after occupational exposure and ensure its quality through the follow up of suspected adverse drug reaction cases.

The Eudravigilance database should be equipped to immediately forward reports on suspected adverse reactions received from marketing authorisation holders to the Member States on whose territory the reaction occurred.

Assessment report: in the two years following the publication of the Directive, the Commission shall, in collaboration with EMA and national competent authorities and following consultations with organisations representing patients, consumers, doctors and pharmacists, social health insurers, and other interested parties, present to the European Parliament and the Council an assessment report regarding the readability of the summaries of product characteristics and the packaging leaflets and their value to the healthcare professionals and the general public. The Commission shall, if appropriate, bring forward proposals to improve the layout and the content of the summaries of product characteristics and of the packaging leaflet to ensure they are a valuable source of information for healthcare professionals and the general public as appropriate.

Strengthened Risk Assessment Committee: in order to fulfil its new tasks, the coordination group should be further strengthened through the adoption of clear rules as regards the expertise required, the procedures for reaching agreements or postions, transparency, independence and professional secrecy of its members, and the need for cooperation between Union and national bodies. With a view to ensuring that the same level of scientific expertise in the area of pharmacovigilance decision-making at both Union and national levels, when fulfilling pharmacovigilance tasks the coordination group should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee.

Regardless of whether the urgency procedure or the normal procedure is applied, and whether the medicinal product was authorised through the centralised or non-centralised procedure, the Pharmacovigilance Risk Assessment Committee should always give its recommendation when the reason for taking action is based on pharmacovigilance data. It is appropriate that the coordination group and the Committee for Medicinal Products for Human Use should rely on this recommendation when performing their assessment of the issue.

Inspections: the competent authority of the Member State concerned shall, in cooperation with the Agency, ensure that the legal requirements governing medicinal products are complied with, by means of inspections, if necessary unannounced, and, where appropriate, by asking an Official Medicines Control Laboratory or a laboratory designated for that purpose to carry out tests on samples. This cooperation shall consist in sharing information on planned and conducted inspections with the Agency. Member States and the Agency shall cooperate in the coordination of inspections in third countries.

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.

Transitional provisions: with regard to the requirements for the marketing authorisation holder to submit information on suspected adverse reactions electronically to the Eudravigilance database, the Member States shall ensure that these requirements apply 6 months after the functionalities of the database are established and have been announced by the Agency.

Until the Agency can ensure the functionalities of the Eudravigilance database:

- marketing authorisation holders shall be required to report, within 15 days of the day on which the holder concerned gained knowledge of the event, all serious suspected adverse reactions that occur in the Union, to the competent authority of the Member State on whose territory the incident occurred and shall report all serious suspected adverse reactions that occur on the territory of a third country to the Agency and, if requested, to the competent authorities of the Member States in which the medicinal product is authorised;
- the competent authority of a Member State may require marketing authorisation holders to report to it all non-serious suspected adverse reactions that occur on the territory of that Member State, within 90 days of the day on which the marketing authorisation holder concerned gained knowledge of the event.

During this period, Member States shall ensure that reports that occurred in their territory are made available promptly to the Eudravigilance database, and in any case within 15 days of the notification of suspected serious adverse reactions.

With regard to the requirements for the marketing authorisation holder to submit periodic safety update reports to the Agency, the national competent authorities shall ensure that these requirements apply 12 months after the functionalities of the repository have been established and have been announced by the Agency.

Until the Agency can ensure the functionalities agreed for the repository of the periodic safety update reports, the marketing authorisation holders shall be required to submit the periodic safety reports to all Member States in which the product has been authorised.

Medicinal products for human use: pharmacovigilance of products

PURPOSE: Corrigendum to Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use (originally published in OJEU L 348 of 31 December 2010).

CONTENT: the corrigendum relates to Article 2 which relates to transitional provisions. The text should read as follows:

With regard to the obligation on the part of the marketing authorisation holder to maintain and make available on request a pharmacovigilance system master file in respect of one or more medicinal products provided for in Article 104(3)(b) of Directive 2001/83/EC as amended by this Directive, the Member States shall ensure that that obligation applies to marketing authorisations granted before 21 July 2012:

a) the date on which those marketing authorisations are renewed; or

b) the expiry of a period of 3 years starting from 21 July 2015,

whichever is earlier.

The Member States shall ensure that the procedure provided for in Articles 107m to 107q of Directive 2001/83/EC as amended by this Directive applies only to studies which have commenced after 21 July 2012.

Medicinal products for human use: pharmacovigilance of products

PURPOSE: to strengthen the Community pharmacovigilance system of medicinal products for human use.

LEGISLATIVE ACT: Directive 2010/84/EU 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.

CONTENT: following first reading agreement with the European Parliament, the Council adopted a Regulation on pharmacovigilance (COD/2008/0257) and this Directive aimed at strengthening the EU system for the safety monitoring of medicinal products for human use ("pharmacovigilance"), and thereby better protecting public health. 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 agreeing and monitoring risk management systems, is enlarged. In the future, based on the advice from the Pharmacovigilance Risk Assessment Committee, this group will also examine questions related to the pharmacovigilance of all medicinal products authorised by Member States and to variations to the terms of marketing authorisations granted by Member States. Under the current rules, the coordination group's mandate is limited to the examination of questions relating to a marketing authorisation of a medicinal product in two or more Member States.

Provision is made to allow adequate funding for pharmacovigilance activities through the collection of fees charged to marketing authorisation holders for obtaining and maintaining EU marketing authorisations and for other services provided by EMEA and national competent authorities. However, the management of those collected funds will be under the permanent control of the national competent authorities in order to guarantee their independence in the performance of those pharmacovigilance activities.

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 Directive and the Regulation on pharmacovigilance (COD/2008/0257) 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.

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