Procedure file

Basic information

COD - Ordinary legislative procedure (ex-codecision procedure) Regulation	2001/0252(COD)
Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency Amended by 2004/0217(COD) Amended by 2005/0227(COD) Amended by 2007/0064(COD) Amended by 2008/0257(COD) Amended by 2012/0023(COD) Amended by 2014/0256(COD) Amended by 2017/0328(COD) Subject 3.10.08 Animal health requirements, veterinary legislation and pharmacy 4.20.04 Pharmaceutical products and industry 8.40.08 Agencies and bodies of the EU	Procedure completed

Key players

European Parliament

Committee responsible	Rapporteur	Appointed
ENVI Environment, Public Health, Consumer Policy	PSE MÜLLER Rosemarie	13/09/2001
Former committee responsible		
ENVI Environment, Public Health, Consumer Policy	PSE MÜLLER Rosemarie	13/09/2001
Former committee for opinion		
BUDG Budgets	PSE KUCKELKORN Wilfried	22/01/2002
CONT Budgetary Control	ELDR MULDER Jan	21/02/2002
JURI Legal Affairs and Internal Market	The committee decided not to give an opinion.	
ITRE Industry, External Trade, Research, Energy	PPE-DE SCAPAGNINI Umberto	23/01/2002
AGRI Agriculture and Rural Development	PPE-DE STURDY Robert	08/01/2002

Council of the European Union

Council configuration	Meeting	Date
Competitiveness (Internal Market, Industry, Research and Space)	2570	11/03/2004
Agriculture and Fisheries	2528	29/09/2003
Employment, Social Policy, Health and Consumer Affairs	2512	02/06/2003
Employment, Social Policy, Health and Consumer Affairs	2470	02/12/2002
Health	2440	26/06/2002

European Commission

Commission DG	Commissioner

	Internal Market, Industry, Entrepreneurship and SMEs

Key events

13/12/2001	Committee referral announced in Parliament, 1st reading		
26/06/2002	Debate in Council	2440	Summary
02/10/2002	Vote in committee, 1st reading		Summary
02/10/2002	Committee report tabled for plenary, 1st reading	A5-0330/2002	
22/10/2002	Debate in Parliament		
23/10/2002	Decision by Parliament, 1st reading	T5-0504/2002	Summary
02/12/2002	Debate in Council	2470	Summary
09/10/2003	Committee referral announced in Parliament, 2nd reading		
27/11/2003	Vote in committee, 2nd reading		Summary
16/12/2003	Debate in Parliament		
17/12/2003	Decision by Parliament, 2nd reading	T5-0576/2003	Summary
11/03/2004	Act approved by Council, 2nd reading		
31/03/2004	Final act signed		
31/03/2004	End of procedure in Parliament		
30/04/2004	Final act published in Official Journal		

Technical information

Procedure reference	2001/0252(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation
Legislative instrument	Regulation
	Amended by 2004/0217(COD) Amended by 2005/0227(COD) Amended by 2007/0064(COD) Amended by 2008/0257(COD) Amended by 2012/0023(COD) Amended by 2014/0256(COD) Amended by 2017/0328(COD)
Legal basis	EC Treaty (after Amsterdam) EC 095; EC Treaty (after Amsterdam) EC 152
Stage reached in procedure	Procedure completed
Committee dossier	ENVI/5/16943

Documentation gateway

Legislative proposal		COM(2001)0404	26/11/2001	EC	Summary
Committee draft report		PE286.276	16/05/2002	EP	
Committee opinion	AGRI	PE307.225/DEF	19/06/2002	EP	
Committee opinion	ITRE	PE316.247/DEF	20/06/2002	EP	
Committee opinion	CONT	PE305.679/DEF	21/06/2002	EP	
Committee opinion	BUDG	PE318.692/DEF	03/07/2002	EP	
Amendments tabled in committee		PE286.276/AM	29/08/2002	EP	
Economic and Social Committee: opinion, report		CES1007/2002	18/09/2002	ESC	
Amendments tabled in committee		PE286.276/AMC	30/09/2002	EP	
Committee report tabled for plenary, 1st reading/single reading		A5-0330/2002	02/10/2002	EP	
Text adopted by Parliament, 1st reading/single reading		T5-0504/2002 OJ C 300 11.12.2003, p. 0166-0308 E	23/10/2002	EP	Summary
Modified legislative proposal		COM(2002)0735	10/12/2002	EC	Summary
Council statement on its position		12155/1/2003	24/09/2003	CSL	
Council position		10949/2/2003 OJ C 297 09.12.2003, p. 0001-0040 E	29/09/2003	CSL	Summary
Commission communication on Council's position		SEC(2003)1082	07/10/2003	EC	Summary
Committee draft report		PE331.689	21/10/2003	EP	
Amendments tabled in committee		PE331.689/AM1	18/11/2003	EP	
Amendments tabled in committee		PE331.689/AM	19/11/2003	EP	
Committee recommendation tabled for plenary, 2nd reading		A5-0425/2003	27/11/2003	EP	
Text adopted by Parliament, 2nd reading		T5-0576/2003 OJ C 091 15.04.2004, p. 0133-0253 E	17/12/2003	EP	Summary
Commission opinion on Parliament's position at 2nd reading		COM(2004)0124	17/02/2004	EC	Summary
Implementing legislative act		32005R2049 OJ L 329 16.12.2005, p. 0004-0007	15/12/2005	EU	Summary
Implementing legislative act		32006R0507 OJ L 092 30.03.2006, p. 0006-0009	29/03/2006	EU	Summary
Follow-up document		C(2012)5562	08/08/2012	EC	
Follow-up document		C(2012)9279	14/12/2012	EC	
Follow-up document		COM(2015)0138	30/03/2015	EC	Summary
Follow-up document		COM(2016)0498	08/08/2016	EC	Summary
Follow-up document		SWD(2016)0284	08/08/2016	EC	

Follow-up document		COM(2019)0591	15/11/2019	EC	Summary
Follow-up document		COM(2021)0497	31/08/2021	EC	

Additional information

European Commission	EUR-Lex

Final act

Regulation 2004/726
OJ L 136 30.04.2004, p. 0001-0033 Summary

Final legislative act with provisions for delegated acts

Delegated acts

2014/2562(DEA)	Examination of delegated act

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

PURPOSE : regulation to establish the new procedures for the authorisation and supervision of medicinal products and to establish a European Agency for the Evaluation of Medicinal Products ("the Agency"). CONTENT : This regulation repeals Regulation 2309/93/EC. There are four main objectives: -to guarantee a high level of health protection, particularly by providing patients, as swiftly as possible, with innovative and reliable products and through increased market surveillance thanks to a strengthening of procedures. -to complete the internal market in pharmaceutical products taking account of globalisation and to establish a regulatory framework that favours the competitiveness of the European pharmaceutical sector. -to meet the challenges of enlargement. -to rationalise and simplify the system, improving transparency. The scope of the centralised procedure for medicinal products for human use still includes categories of products for which the procedure is obligatory and those for which it is optional. The procedure remains obligatory for products resulting from biotechnical processes, in particular those using recombinant DNA technology. The main amendment proposed seeks to make this procedure also compulsory for any new active substance appearing on the Community market. The procedure is optional for other products that constitute therapeutic innovation. Also, it is proposed to allow access to this procedure for medicinal products which, though innovative, may be of benefit if they are authorised from the outset at Community level. This may apply in particular to products that cannot be supplied without prescription. Member States have the option of authorising at national level the generic form of medicinal products authorised by the Community, on the condition that the harmonisation obtained at Community level is maintained. The manufacturers of these generic forms would henceforth have the choice between the two existing procedures (centralised and decentralised) for obtaining market authorisations. Other changes include: -two new ways of obtaining market authorisation. The applicant may apply for an accelerated assessment and decision, which has priority over other procedures. This refers particularly, but not exclusively, to products to treat cancer and HIV. The other procedure deals with the granting of a provisional authorisation of one year, subject to strict conditions and annual reassessment. -the five-yearly renewal of market authorisations is abolished. -Any authorisation not resulting in the actual marketing of the product concerned during two consecutive years ceases to be valid. -the Agency has additional tasks e.g, increasing the scientific advice it provides for companies at the research and development phases, before market authorisation procedures; participation in programmes for the compassionate use of human medicinal products; increased responsibilities regarding international scientific cooperation; and a procedure for solving potential conflicts with other bodies outside the field of product evaluation. The Agency's administrative and scientific structures are also modified. The changes are made with a view to enlargement and aim to adapt the composition of the Committees.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Council held a policy debate on the basis of a Presidency questionnaire on three proposals - a Regulation (the current text) and two Directives (COD/2001/0253) and (COD/2001/0254) - the main aims of which are to achieve completion of the single market in the medicinal products sector, to improve the competitiveness of the pharmaceutical industry (particularly small and medium-sized enterprises) and to simplify Community legislation. The Opinion of the European Parliament at first reading should be available in October 2002. Two topics were discussed at this stage following the proceedings of the Working Party: - the scope of the proposal for a Regulation: the text provides for extension of the compulsory centralised Community procedure to medicinal products for human or veterinary use containing new active substances; a majority of delegations wanted to be able to continue to choose between a centralised system and a system of national authorisations with the principle of mutual recognition. Some delegations, however, made distinctions depending on whether the medicinal product was for human or veterinary use. Some delegations said they could support an extension of the scope for medicinal products for human use only. Delegations which recommended an optional system put forward the following main arguments: several delegations wanted the Commission to provide a better definition of medicinal products containing new active substances; several delegations expressed concern regarding the situation of small and medium-sized enterprises and argued that some flexibility was the best solution for them; some delegations expressed fears that extension of a centralised procedure would not take sufficient account of the views of national authorities. As regards medicinal products for veterinary use, some delegations pointed out that, since in some cases their use and authorisation involved

only a few regional animal species (e.g. northern Finland), a national authorisation system would be preferable. Some delegations stressed in particular the need to improve the technical resources of the European Agency for the Evaluation of Medicinal Products (EMEA) - computerised files, national databases - and to extend its evaluation methods, along the lines of the methods available to the United States Food and Drug Administration. - the new composition of the Management Board of the European Agency for the Evaluation of Medicinal Products (EMEA): under the proposal this Board would consist of four representatives of the Member States, four representatives of the European Parliament, four representatives of the Commission and four representatives of patients and the industry; a very large majority of delegations wanted to maintain representation by Member States only. Two delegations stressed in particular the need for the Management Board to have a composition different from that of the European Food Safety Authority (EFSA) - a consultative body - taking account of the executive role of the EMEA in issuing authorisations for placing medicinal products on the market. The Council agreed to take account of these positions expressed by the Member States when continuing its discussions in the second half of 2002.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The committee adopted the report by Rosemarie MÜLLER (PES, D) amending the proposal under the codecision procedure (1st reading). The main amendments were as follows: - the name of the agency should be simplified, and the committee therefore proposed 'European Medicinal Products Agency' (EMPA); - the scope of the regulation should not be extended, as the Commission was proposing, so as to make it compulsory for all medical products for human use containing new active substances to be authorised centrally in future rather than on a national basis; the committee therefore deleted the new point which the Commission had added to the Annex; - there should be a scheme for establishing a European price for centrally authorised medicinal products; - generic drugs should be identified in all Member States with the same denomination of the internationally approved chemical name of the active substances and the name of the producer; - authorisation applications should include a confirmation that clinical trials for the medicinal product in question have not been carried out in developing countries unless that product is primarily geared to the domestic market in those countries; - where a new medicinal product submitted for authorisation is intended for paediatric use, the application should state that it has been tested for suitability for children; - the proposed database on medicinal products should also include information about which medicinal products are specifically authorised for administration to children; - assessment procedures should be speeded up, by reducing decision-making deadlines; - to ensure that the competent authorities are fully independent, there should be public funding of activities relating to pharmacovigilance, the operation of communications networks and market suveillance; - not only specialists but also patients should be able to notify any adverse reactions; - in the first five years after being placed on the market, the package leaflet must bear the phrase 'Newly authorised medicinal product. Please notify any adverse reactions'; - the committee introduced a number of measures aimed at ensuring greater transparency and public access to information, including ensuring that labels and package leaflets are written in simple clear language comprehensible to the public; - when evaluating a medicinal product, the Agency's scientific committees should establish contact with patients' representatives to take account of their experience in the relevant field; - with regard to the composition of the management board and the appointment of the Executive Director of the EMPA, the same rules should apply as for the European Food Safety Authority. ?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

In approving the Commission's proposal relating to the authorisation of pharmaceutical products, MEPs adopted a number of amendments, particularly designed to improve transparency and access by consumers to, in particular, information on new drugs. The report drafted by Mrs Rosemarie MULLER (PES, D) was adopted subject to amendments. These amendments are laid down in the decision of the committee responsible (please refer to the summary dated 02/10/02). In general, the Parliament is of the opinion that the existing 1989 directive designed to provide this is not working and that people using new drugs should be guaranteed access to new information on the product as quickly as possible. MEPS want the Commission to report as soon as possible on the workings of this directive. Parliament wants to see a databank providing neutral information on drugs enabling comparisons between different products to be made. This should also include specific effects relating to children and be publicly accessible free of charge to all EU citizens. All drugs given to children should be fully tested, MEPs believe. Furthermore, Parliament wants more women to take part in clinical trials. Parliament also voted for another amendment seeking to oblige pharmaceutical companies to provide a leaflet on every new drug within 5 years of its being placed on the market, carrying the description "Newly authorised medicinal products. Please notify any adverse reactions". MEPs also want to see more incentives for the industry to develop new drugs to combat diseases caused by poverty. The main amendments were as follows: - generic drugs should be identified in all Member States with the same denomination of the internationally approved chemical name of the active substances and the name of the producer; - authorisation applications should include a confirmation that clinical trials for the medicinal product in question have not been carried out in developing countries unless that product is primarily geared to the domestic market in those countries; - where a new medicinal product submitted for authorisation is intended for paediatric use, the application should state that it has been tested for suitability for children; - the proposed database on medicinal products should also include information about which medicinal products are specifically authorised for administration to children; - assessment procedures should be speeded up, by reducing decision-making deadlines; - to ensure that the competent authorities are fully independent, there should be public funding of activities relating to pharmacovigilance, the operation of communications networks and market suveillance; - create further incentives to carry out research into medicinal products against widespread tropical diseases; - the Commission should submit as soon as possible a report on the implementation of Directive 89/105/EC and proposals for its revision and enforcement. This Directive relates to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems provides for rapid patient access to new medicinal products, fixing the maximum duration of negotiations on prices and reimbursement at 180 days; - in the case of innovative medicinal products which can be used to treat incurable diseases, the Agency shall lay down a streamlined procedure with a view to making such medicinal products available as quickly as possible; - not only specialists but also patients should be able to notify any adverse reactions; - in the first five years after being placed on the market, the package leaflet must bear the phrase 'Newly authorised medicinal product. Please notify any adverse reactions; - introducing a number of measures aimed at ensuring greater transparency and public access to information, including ensuring that labels and package leaflets are written in simple clear language comprehensible to the public; - when evaluating a medicinal product, the Agency's scientific committees should establish contact with patients' representatives to take account of their experience in the relevant field; - with regard to the composition of the management board and the appointment of the Executive Director of the EMPA, the same rules should apply as for the European Food Safety Authority. The House also stated that provision should be made for a derogation for SMEs so that the cost of

marketing the medicinal products developed by these enterprises can be kept within reasonable bounds. The Commission should draw up, as a matter of urgency, a specific regulation aimed at resolving the problems concerning the availability of medicinal products for veterinary use and should in particular introduce a policy for 'orphan' medicinal products for veterinary use analogous to that established for human medicinal products. Such a Regulation should create the necessary mechanisms to ensure that all needs are covered by at least two therapeutic alternatives in the European Union, with the objective of guaranteeing both competition and the diversity of available protection options and thereby preventing the emergence of resistance. The Commission should submit a proposal within six months after the adoption of the present Regulation. With regard to the Agency's budget, it should be composed of fees paid by the private sector and contributions paid out of the Community budget to implement Community policies. On the basis of a duly reasoned request the Committee for Human Medicinal Products may require the duration of the scientific and clinical trials to be extended. The request must stipulate the additional length of time needed for the scientific and clinical trials to be carried out successfully. The request must be drawn up at least 15 days before the end of the period of scientific and clinical trial. The Agency shall publish an annual report on the recorded reactions and point out further research requirements.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Council held an exchange of views, on the basis of a progress report from the Presidency, on some of the key issues raised by the proposal for a Regulation of the European Parliament and of the Council aimed at amending the rules regarding the European Agency for the Evaluation of Medicinal Products. The Council requested the Permanent Representatives Committee to pursue work actively on the proposal, taking into account the positions expressed by delegations and the opinion of the European Parliament in first reading. In the light of this discussion, the President concluded that: - views continue to differ on the scope of the centralised authorisation procedure, with a slight majority opposed to its extension as regards medicinal products for Human use and a clear majority opposed as regards veterinary medicinal product; - a majority of delegations are favourable to each Member State being represented on the management board of the European Agency for the Evaluation of Medicinal Products; - a majority of delegations are in favour of maintaining a first renewal of market authorisations after five years, with unlimited validity thereafter.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission has accepted 45 amendments proposed by the European Parliament at first reading, including: - a negative risk/benefit analysis is included as a reason for withdrawing a medicinal product from the market; - two amendments aimed at strengthening the inspection of the manufacturing sites of the applicant for medicinal products for human and veterinary use; - four amendments aimed at shortening the time limit for the decision-making process; - the requirement to publish information concerning the refusals or negative opinions for applications for marketing authorisation; - the provisions aimed at altering the period of validity of the marketing authorisation in the case where this has not been followed by the placing on the market of the medicinal product. The same provision is introduced in the case of previously authorised medicinal products which have not been on the market for a certain period; - the introduction of a derogation from the rule that a marketing authorisation is valid for three years; - an amendment aimed at preventing the marketing authorisation holder from providing pharmacovigilance information without the consent of the Agency; - certain amendments aimed at modifying the method of nominating and of working of the Committees of the Agency - the functions of the Agency are modified, concerning inspections of compliance with good practices; - the contents of the database on medicinal products must be specified; - documents prepared must be published in the event of disagreements between the Agency and a scientific committee; - the contents of the code of conduct of the Agency must be specified, and the declarations of interest of the Members of the boards and the committees of the Agency must be published and made accessible on request; - the executive director shall cover the activities of the Committee on Herbal Medicinal Products in the context of his responsibilities; - two amendments aimed at modifying the composition of the Management Board; - provisions aimed at reviewing the finances of the Agency; - the possibility of helping small and medium-sized pharmaceutical firms at the time of submission of marketing authorisation applications or applications relating to diseases with a regional distribution is extended; - at the request of the Agency, the names of marketing authorisation holders subject to financial penalties from the Commission must be made public. The Commission accepted some 58 amendments in part or in principle. These include: - two amendments aimed at providing particular support to SMEs by reason of the extension of the scope of the centralised procedure to all medicinal products containing a new active substance. These measures are aimed at reducing the costs associated with the request for authorisation submitted to the Agency and to facilitate the requests for scientific advice. Rewording is necessary to indicate the possibility of a specificbut not dispensatory system for these companies and to indicate specifically, but not exclusively, the ability of SMEs to request scientific advice; - the introduction of an arrangement to provide for a reduction in fees payable by SMEs; - the reference to the principle of comparative efficacy. It is emphasised that the evaluation is not considered a necessary criterion for the application or authorisation of medicinal products; - the application of the ethical requirements of Directive 2001/20/EC on the implementation of good clinical practice in the conduct of clinical trials on medicinal products authorised by the Community as well as the application of the same requirements to clinical trials conducted outside the Community on medicinal products destined to be authorised by the Community; - the provision concerning Directive 89/105/EC and the conduct of a specific study on its implementation; - the principle concerning the naming of generic medicinal products of reference products authorised through the centralised procedure. The international non-proprietary name and its translation into the different languages of the Member States are considered as equivalent in all Member States; - the principle aimed at including an accelerated procedure for medicinal products used in certain treatments with a view to making them available to patients more quickly; - specific provisions for the publication of the opinions of the committee of the Agency concerning conditional authorisations, assessment reports, summaries of product characteristics, labels and package leaflets as well as information related to suspected adverse effects of medicinal products and urgent decisions aimed at suspending the use of a product, by reference to the implementation of Regulation 1049/2001; - the provision of public funding commensurate with the pharmacovigilance activities carried out by the Agency; - the role of patients in the communication of adverse effects; - the specification of the contents of the guidance developed for the verification and presentation of adverse reaction reports; - strengthened coordination between the national pharmacovigilance systems and the Agency. The Commission does not accept 50 amendments. These include: - an obligation for the Commission to prepare a specific regulation establishing a policy for orphan medicinal products for veterinary use - the provision that all new medicinal products authorised by the Agency must include the phrase "newly authorised medicinal product" as well as an invitation to patients to report any adverse effects and an obligation for the marketing authorisation holder to handle any information reported directly by the patient.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The common position, adopted by qualified majority, with the Belgian and Dutch delegations voting against and the German delegation abstaining is consistent with the aims of the Commission's proposal. It adopts 29 of Parliament's amendments adopted at first reading and accepts 68 in principle. Apart from changes introduced following amendments by the European Parliament and other changes on substance, the Council has agreed on a certain number of changes in order, in the first place, to clarify the provisions of the text, update terminology and to align the human and veterinary provisions to the largest extent possible. The more substantial changes are described below. - The Council has simplified the name of the European Agency for the Evaluation of Medicinal Products to "European Medicines Agency". - The Council has delineated the extension of the compulsory use of the centralised procedure to medicinal products for human use containing a new active substance for the treatment of 4 key disease areas (HIV/AIDS, cancer, neuro-degenerative disorders and diabetes). These disease areas are, in addition, broadly aligned with the areas in which specialist expertise is being developed at the Agency with the introduction of therapeutic advisory groups (which are now to be called scientific advisory groups). - In reaching agreement, the Council, in particular, had regard to the importance of maintaining national expertise for the evaluation of new active substances and the fact that existing legislation already allows the applicant to choose the centralised authorisation procedure for all medicinal products containing a new active substance. This option has been maintained for those products containing a new active substance that are not covered by paragraph 3 of the Annex. - In addition, the Council has inserted a review clause which will provide for the possibility to extend the range of products for which use of the centralised procedure is compulsory four years after the entry into force of the Regulation. The Council considers it appropriate to set out an ad hoc procedure for adoption of such decisions based on the Council's right to reserve implementing powers to itself in accordance with Article 202 of the Treaty. According to this procedure, the Commission may after consultation of the Agency, submit a proposal to the Council that shall act with a qualified majority. - For veterinary medicinal products, the Council has chosen to retain the applicants possibility to choose between the centralised procedure and the decentralised procedure to take account of the considerable regional differences in markets and disease patterns, e.g. animal species that only live in a limited part of the Community and some diseases only occurring in some geographical regions in the Community. In this context Article 79 should be borne in mind, which offers incentives to use the centralised procedure for veterinary products in order to improve availability. In addition, the "cascade" procedure set out in Directive 2001/82/EC is aimed at securing availability of veterinary products. - The provisions on the choice of Committee procedure in relation to decisions concerning marketing authorisations have been changed as the Council does not consider it consistent with Decision 1999/468/EC to have two different procedures fordecisions having the same object. The Council believes that the management procedure is the appropriate procedure to apply for these decisions. - The Council has provided for the possibility of adopting amendments to the arrangements concerning the periodic safety update reports through a Committee procedure in the light of experience gained. Article 59 on the setting up of an Advisory Board has been deleted. - In view of the changes agreed to the composition of the Management Board, there is no need for an Advisory Board. - The provisions of Title IV, in particular Chapter 2, have been amended and rearranged to take full account of the adoption of the Council Regulation of 18 June 2003 amending Regulation 2309/93/EEC as regards the financial rules governing the Agency. - As concerns Article 82 on the principle of one single authorisation for a medicinal product, the exemptions from that rule have been clarified and now explicitly include the admission of more than one application for co-marketing reasons. - A number of changes have been made to Article 83 on compassionate use. Article 5 of Directive 2001/83/EC allows Member States to make unauthorised medicinal products available to individual patients under the direct responsibility of a health care professional, e.g. for compassionate use reasons. The Council has considered that this provision should not be affected by this Regulation and has therefore chosen to provide for a complementary system based on making products available to groups of patients, and also made it clear that compassionate use can not be used by pharmaceutical companies as an alternative to applying for and obtaining a marketing authorisation. The paragraph on payment in relation to compassionate use products has been deleted as the Council believes that, in line with the principle set out in Article 1 (2), it should be up to each Member State to decide on the arrangements for the financing of the distribution of compassionate use products. Other changes include: - Adding a the possibility for Member States to ask for an opinion of the scientific committees, subject to the discretion of the relevant committee; - Adjusting some time limits in relation to the evaluation procedure; - Strengthening the supervision of the Agency by providing it with the explicit right to request the submission of data from the marketing authorisation holder at any time; - Extension of the duty of the marketing authorisation holder to report adverse reactions occurring in the territory of a third country; - Clarification of the wording of Article 37, including the alignment with the Annex (consistent use of the term "performance enhancers"). On the amendments of the European Parliament accepted partly or in principle, these refer to the following : - relative effectiveness; - the name of generic medicinal products; - benefit-risk analysis; - opinions of the Scientific Committees in the context of the mutual recognition procedure; - good clinical practice and clinical trials; - the exceptions from the principle of single name; - Directive 89/105/EEC on national procedures for the pricing and reimbursement of medicinal products; - conditions and restrictions in relation to the safe and effective use of medicinal products. However, as these conditions and restrictions should also be applied to third parties, the Council is of the opinion that a specific legal instrument is necessary to produce this effect. Therefore, Article 127a of Directive 2001/83/EC and 95a of Directive 2001/82/EC provides for adoption through comitology of decisions requiring Member States to implement such conditions and restrictions, including vis-?-vis third parties. Moreover, the Council considers it appropriate to use the term "recommendations" instead of "details" and to simplify the wording of the provision; - the accelerated procedure for the evaluation of certain medicines; - assessment reports; - the marketing authorisation holders' obligation to provide data on adverse reactions upon request to the European Medicines Agency; - the reference to Regulation 1049/2001/EC on access to documents. The Council has agreed on a new Article 73 which sets out that the aforementioned Regulation shall apply to documents held by the Agency; - authorisation of medicinal products under exceptional circumstances; - the accuracy of the documents and data submitted by the applicant; - setting out the same date protection period for medicinal products for human use authorised centrally as for products authorised nationally, except for those products where the use of the centralised procedure is compulsory. In coming to agreement on the issue of data protection, the Council has considered both the need to harmonise the widely differing data protection periods available in the Member States and the period of 10 years' data protection currently available to products using the centralised procedure. The Council therefore has decided that it is appropriate to retain the current 10 year's data protection for products for which use of the centralised procedure is compulsory. Furthermore, the Council has considered that offering an additional year's data protection for such products will be in line with encouraging innovation for these products. For products authorised nationally, the Council has considered that harmonising the period at 10 years would be difficult for some Member States but that a provision as the one agreed by Parliament, that allows generic companies to undertake all development work in the last two years of a ten year period (the "8+2" provision) would be acceptable. The Council felt that in view of the significant increase in data exclusivity that the "8+2" provision would be offering in a number of Member States, there was no justification for adding a further year's data exclusivity for nationally authorised products. ?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission supports the texts of the common position, adopted by qualified majority, for a regulation laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. The Commission takes note that the Council has accepted, partly, the European Parliament amendment, which aimed at establishing the data protection period automatically linked with the one applicable in the context of the medicinal products authorised through the national procedures. However, the Commission takes also note that the Council has limited the application of this amendment to the products to be authorised, on an optional basis, through the centralised procedure. For these products, the same data protection scheme as the one foreseen for the nationally authorised products is applicable. For the medicinal products to be authorised, on a mandatory basis, through the centralised procedure, the Council has agreed with the Commission proposal to keep the 10 years period as it is currently applied on the basis of the existing Regulation with the possibility to extend this period with one extra year when a new indication bringing a significant clinical benefit in comparison with existing therapies is approved.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The committee adopted the report by Rosemarie MÜLLER (PES, D) amending the Council's common position under the 2nd reading of the codecision procedure. It reinstated a number of Parliament's key amendments from 1st reading which had not been incorporated by the Council: - whereas the Council was stipulating that any extension of the centralised authorisation procedure should be the subject of a proposal, to be decided by the Council acting by a qualified majority, MEPs said that the current list of four indications in the annex should be extended automatically four years after the regulation's entry into force so that the centralised authorisation procedure would apply to all new active substances in medicinal products intended for human use; - whereas the Council's common position sought to provide data protection for a longer period for medicines approved under the centralised procedure, the committee said that medicinal products for human use authorised under this procedure should benefit from only an eight-year period of data protection and a ten-year period of marketing protection. Under certain circumstances, this latter period could be extended to a maximum of 11 years (known as the 8 + 2 + 1 compromise); - the Agency's management board should consist of one representative from each Member State, two representatives from the Commission, two representatives from Parliament and two representatives each from patients' and doctors' organisations, whereas the Council wanted only the Member States and the Commission to be represented; - for the purposes of authorising medicinal products for human use, clinical trials carried out in a developing country should not be recognised, unless the product concerned is primarily geared to the domestic market in that country; - the Agency's tasks should include ensuring that patient leaflets are easily readable. The committee also adopted a number of amendments aimed at ensuring the transparency of the Agency's decision-making, by making information publicly accessible. Finally, it called for particular incentives for research into paediatric medicinal products. MEPs said that medicinal products already long established for adult use should be tested for subsequent use by children and the database on medicinal products should also include information about which medicinal products were specifically authorised for children.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The European Parliament adopted a resolution drafted by Rosemarie MÜLLER (PES, Germany) making some amendments to the Council's common position. The main amendments are as follows: - a new recital states that pharmaceutical law should continue to ensure that only efficacious, safe and top-quality medicinal products are exported, and the Commission should consider creating further incentives to carry out research into medicinal products against widespread tropical diseases; - the Agency's budget should be composed of fees paid by the private sector and contributions paid out of the Community budget to implement Community policies; - the Committee must formulate an opinion whenever there is disagreement in the assessment of medicinal product through the mutual recognition procedure. The opinion of the Committee must be made publicly accessible; - two indents are added to point 3 of the Annex, adding auto-immune diseases and other immune dysfunctions, and viral diseases. Thereafter, the Commission, having consulted the Agency, may present any appropriate proposal modifying point 3 of the Annex and the Council shall take a decision on that proposal by qualified majority. - clinical trials carried out outside the EU meet the ethical requirements of Directive 2001/20/EC; - the duration of the analysis of the scientific data in the file concerning the application for marketing authorization must be at least 80 days, except in cases where the rapporteur and co-rapporteur declare that they have completed their assessment before that time. On the basis of a duly reasoned request, the Committee for Human Medicinal Products may call for the duration to be extended; - whereas the Council's common position sought to provide data protection for a longer period for medicines approved under the centralised procedure, the committee said that medicinal products for human use authorised under this procedure should benefit from only an eight-year period of data protection and a ten-year period of marketing protection. Under certain circumstances, this latter period could be extended to a maximum of 11 years (known as the 8 + 2 + 1 compromise); - the database must include a section on medicinal products authorized for the treatment of children; - the Management Board will consist of one representative of each Member State, two representatives of the Commission and two representatives of the European Parliament. In addition, two representatives of patients' organisations, one representative of doctors' organisations and one representative of veterinarians' organisations shall be appointed by the Council in consultation with the European Parliament on the basis of a list drawn up by the Commission which includes appreciably more names than there are posts to be filled. The members of the Management Board shall be appointed in such a way as to guarantee the highest levels of specialist qualifications, a broad spectrum of relevant expertise and the broadest possible geographic spread within the EU.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission can accept in full the 32 amendments to the Council's common position adopted by Parliament on the proposal for a regulation, the 30 amendments to the Council's common position adopted by Parliament on the proposal for a directive on medicinal products for human use and the 22 amendments to the Council's common position adopted by Parliament on the proposal for a directive on veterinary medicinal products. The Commission notes the convergence of views between the three institutions on the general approach and on the most important issues regarding the compulsory field of application of the centralised procedure, the administrative structure of the agency, the period of data protection, definitions, information for patients and the assessment of the environmental impact. The amendments adopted by Parliament mainly concern the issues of the compulsory field of application of the centralised procedure, the period of data protection and the administrative structure of the agency as far as the regulation is concerned, and the definitions, period of data protection, information for patients and assessment of the environmental impact as regards the two directives on medicinal products for human use and veterinary use.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

PURPOSE : to reform Community pharmaceutical legislation. LEGISLATIVE ACT : Regulation 726/2004/EC of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. CONTENT : the Council adopted a package of Community legislation on pharmaceuticals, updating the existing rules with the aim of responding to technical and scientific innovations whilst maintaining a high level of health protection and continuing to ensure the proper functioning of the EU's internal market in the pharmaceuticals sector. The four main objectives of this package are particularly relevant: - to guarantee a high level of public health protection, particularly by providing patients, as swiftly as possible, with innovative and reliable products and by increasing market surveillance by reinforcing monitoring and pharmacovigilance procedures; - to complete the internal market in pharmaceutical products while taking account of the implications of globalisation, and to establish a regulatory and legislative framework that favours the competitiveness of the European pharmaceuticals sector; - to meet the challenges of the future enlargement of the European Union; - to rationalise and simplify the system, thus improving its overall consistency and visibility, and the transparency of procedures. The new Regulation is aimed at improving the operation of centralised and decentralised authorisation procedures for the placing of medicinal products on the Community market and at amending administrative aspects of the European Medicines Agency. More specifically, the new rules will improve and speed up access to new and innovative pharmaceutical products, building on the proven success of the European Medicines Evaluation Agency (EMEA) set up in 1995. Changes include a new fast-track authorisation procedure, the possibility of conditional authorisation for products and a harmonised period during which test and other data is protected in order to reward innovation. The generic pharmaceutical industry also benefits through clearer rules and procedures and the possibility for them to start testing their products in advance of patent expiry. Finally, the new rules should streamline procedures and reduce red-tape, while at the same time strengthening the supervision of pharmaceutical products. The changes include: the opening of the centralised procedure to more types of new medicines. Currently, the centralised procedure must be used for the authorisation of biotechnology products. Under the new rules the centralised procedure will become mandatory for medicines to treat AIDS, cancer, diabetes, neurodegenerative disorders and orphan diseases and after 4 years this will be further extended to cover medicines for autoimmune diseases and viral diseases. A general review clause will enable further extension to other diseases. In addition, the role of scientific advice in the process is strengthened, as is the EMEA's in relation to scientific matters relating to medicinal products, international activities and its role in providingearly scientific advice to companies before they embark on the trials and tests necessary to obtain an authorisation for their products. With a view to increasing and accelerating availability of products, in terms of benefits for patients, the opportunity has been taken to respond to several challenges. The revised legislation aims to increase the availability and speed of access of new and innovative medicines to the European market, while at the same time ensuring that the basic criteria of safety, quality and efficacy are met: - a "fast-track" registration procedure for products of significant therapeutic interest has been introduced allowing these products to be assessed and authorised in an expedited way; - the possibility of a conditional marketing authorisation has been introduced, which allows for a one-year authorisation to be granted provided that there is an important expected health benefit for the patients concerned and that the company agrees to carry out additional monitoring and clinical studies, which will be reviewed at the end of this period; - subject to further additional provisions, a European wide system to make medicinal products available in advance of authorisation for a "compassionate use" will also be possible. This will help to ensure that patients are not discriminated against on the basis, in particular, of the location of the clinical trials performed by a particular company. In addition to the first two provisions, specific measures concerning the availability of veterinary medicinal products are also proposed as well as an incentive scheme to encourage companies to broaden the use of older products for example to cover other species. As regards better access to information for patients, the revised legislation provides for an overall increase in transparency and improves access to the results of the pharmaceutical decision making process, including assessment reports and the summaries of product characteristics. On the issue of promoting the competitiveness of the European pharmaceutical industry in a global context, the revised legislation introduces mechanisms to improve the competitiveness of innovative pharmaceutical, generic and OTC sectors. Concerning data submitted by companies for the approval of medicines, the legislation harmonises the rules governing data protection (data exclusivity). Following transposition of the legislation, whatever the authorisation procedure used, it will not be possible to market generics until ten years have elapsed. This can be extended by a further year if a further innovative indication for the medicine is authorised. This removes current ambiguities of application and allows the innovative pharmaceutical industry more time to recoup its investments before a generic product may be authorised. - for the generic pharmaceutical sector, the new rules introduce the possibility for companies to perform tests to support generic medicine authorisation in Europe and to obtain a marketing authorisation before the end of the data exclusivity period; - in addition, a new definition of generic medicines should provide greater legal security and better application of the regulatory procedures for generic medicines; - for "copies" of biological products, a proper definition of these products, so-called "bio-similar" medicinal product, isintroduced. For the Over The Counter (OTC) sector, one year of data exclusivity will be granted on the studies that allowed the switch of medicinal products from prescription only to OTC; - additionally, the revised legislation introduces the new possibility for an additional period of data protection in case of re-classification of a product as non-prescription ("switch") and in case of a new indication granted to a well-established product. In both cases, the protection will be of one year. The revised legislation includes important changes aiming to optimise, simplify and rationalise the current regulatory processes. The changes reduce the requirement to renew marketing authorisations while reinforcing pharmacovigilance and information sharing provisions. They also include measures to accelerate the Commission's decision making process so that the period between the scientific assessment and marketing a product is shortened. This Regulation sets out the responsibilities and the administrative structure of the European Medicines Agency. ENTRY INTO FORCE : 20/05/2004. Titles I (Definitions and scope), II (Authorisation and supervision of medicinal products for human use), III (Authorisation and supervision of veterinary products) and V (General and final provisions) shall apply from 20 November 2005.?

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

ACT : Commission Regulation 2049/2005/EC laying down, pursuant to Regulation 726/2004/EC of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises.

CONTENT : Regulation 726/2004/EC provides that the revenue of the European Medicines Agency must consist of a contribution from the Community and fees paid by companies, and states that the situation of micro, small and medium-sized enterprises (SMEs) has to be considered separately. This Regulation establishes the circumstances in which, by derogation from the relevant provisions of Regulation 297/95/EC, SMEs may pay reduced fees, defer payment of fees, or receive administrative assistance when submitting applications under Regulation 726/2004/EC to the Agency. The Regulation applies both to applications concerning medicinal products for human use and to applications concerning veterinary medicinal products.

Fee deferrals and reductions: The payment of certain fees is deferred until the notification of the final decision on the marketing authorisation is issued, or the application is withdrawn:

- the fee for an application for a marketing authorisation of a medicinal product;

- the fee for inspections undertaken for the purpose of assessing a marketing authorisation application for a medicinal product.

These fees are payable within 45 days of the date of the notification of the final decision on the marketing authorisation, or within 45 days of the date of the notification of withdrawal of the application.

The Regulation makes provision for a conditional fee exemption, where an application for marketing authorisation is submitted for a medicinal product on which scientific advice has already been given by the Agency. The fee payable to the Agency for the examination of that application will be due only if a marketing authorisation is granted.

Fee reductions:

- in the case of inspections a 90 % reduction to the inspection fee;

- in the case of scientific advice a 90 % reduction to the scientific advice fee;

- in the case of scientific services a 90 % reduction to the scientific service fee;

- scientific advice and scientific services for designated orphan medicinal products as referred to in Regulation 141/2000/EC shall be provided free of charge;

- a 90 % reduction to the full and additional maximum residue limits (MRL) fees, as referred to in Regulation 297/95/EC;

- there are provisions on multiple fee reductions.

SME Office: The Executive Director of the Agency shall set up dedicated administrative structures and specific procedures for the establishment of an SME Office, which will have the following tasks:

- to give advice to applicants on the administrative and procedural steps necessary to comply with the requirements laid down in Regulation 726/2004/EC;

- to ensure the appropriate monitoring of all requests and applications submitted by the same applicant and related to a particular medicinal product;

- to organise workshops and training sessions for applicants on the administrative and procedural steps necessary to comply with the requirements laid down in Regulation 726/2004/EC.

The Agency will publish a detailed User Guide on the administrative and procedural aspects of the provisions laid down in Regulation 726/2004/EC, which are of particular relevance for SMEs.

ENTRY INTO FORCE : 16/12/2005. The Regulation shall not apply to valid applications pending at the date of its entry into force.

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

LEGISLATIVE ACT : Commission Regulation 507/2006/EC on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation 726/2004/EC of the European Parliament and of the Council.

CONTENT : this Regulation lays down rules on the granting of a marketing authorisation subject to specific obligations in accordance with Article 14(7) of Regulation 726/2004/EC ("conditional marketing authorisation").

In the case of certain categories of medicinal products, in order to meet unmet medical needs of patients and in the interests of public health, it may be necessary to grant marketing authorisations on the basis of less complete data than is normally the case and subject to specific obligations.

This Regulation applies to medicinal products for human use that fall under Article 3(1) and (2) of Regulation 726/2004/EC and belong to one of the following categories:

- medicinal products which aim at the treatment, the prevention or the medical diagnosis of seriously debilitating diseases or life-threatening diseases;

- medicinal products to be used in emergency situations, in response to public health threats duly recognised either by the World Health

Organisation or by the Community in the framework of Decision 2119/98/EC;

- medicinal products designated as orphan medicinal products in accordance with Article 3 of Regulation 141/2000/EC.

ENTRY INTO FORCE: 02/04/2006.

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission presented a report on the exercise of the delegation of powers conferred on the Commission pursuant to:

- Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use;
- Regulation (EC) No 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

Delegation of power: pursuant to the aforementioned texts, the power to adopt delegated acts is conferred on the Commission for five years from January 2011. The Commission is required to report on its exercise of those powers at the latest six months before the end of this period.

Regulation (EC) No 726/2004, as amended by Regulation (EU) No 1235/2010, empowered the Commission to adopt delegated acts on post-authorisation efficacy studies (Article 10b).

Exercise delegated powers: to date, the Commission has exercised the delegated powers provided for by Regulation (EC) No 726/2004.

Under this Regulation, it may be necessary in specific situations to complement the data available at the time a medicinal product was granted marketing authorisation with additional information on its efficacy, to address concerns that could not be resolved before the authorisation was granted.

Under Article 10b of the Regulation, the Commission is empowered to specify the situations in which post-authorisation efficacy studies may be required.

Following the consultation with the Expert Group formed by the Pharmaceutical Committee, the Commission adopted the Delegated Regulation (EU) No 357/2014 and notified the European Parliament and the Council of it. Neither institution objected to the delegated act. The Commission Delegated Regulation was published in the Official Journal and entered into force on 30 April 2014.

In conclusion, the Commission considered that the delegated powers conferred by Article 10b of Regulation (EC) No 726/2004, as amended by Regulation (EU) No 1235/2010, should remain in force.

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission presented a report on pharmacovigilance related activities of Member States and the European Medicines Agency (EMA) concerning medicinal products for human use (2012 2014).

The EU legal framework of pharmacovigilance for medicinal products for human use is provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC. The legislation was amended in 2010 and 2012.

Pharmacovigilance, as defined by the World Health Organisation (WHO), is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

This report and the accompanying Staff Working Document describe the activities of the EUs networked and collaborative system for monitoring and controlling the safety of human medicines and is focused on activities since the start of operation of new legislation in 2012 until the end of 2014, but also includes information on some tasks and processes initiated up to July 2015.

The main conclusions of the report are as follows:

Strong collaboration between the European regulatory authorities: the medicines regulatory authorities in 31 European Economic Area (EEA) countries, the EMA and the European Commission closely collaborate and work in partnership as a network to discuss and deal swiftly with any emerging problem in the interest of patients' access to safe and efficacious medicines. The ability to take quick and robust regulatory action was enhanced through the legislation by:

- the creation of the Pharmacovigilance Risk Assessment Committee;
- strengthening of the Co-ordination group for Mutual recognition and Decentralised procedures human;
- the introduction of new procedures to fast-track decision-making when public health is at risk.

Continuing and future development of the network: over the period of the report and beyond, the pharmacovigilance network is focusing on training to develop understanding of pharmacovigilance and regulatory science to enable sharing of best practice, improving the efficiency and effectiveness of the processes, and building capacity.

The European pharmacovigilance network represents an example of successful co-operation at the European level, to the benefit of EU citizens. The networked system allows participants to share in the best available expertise and evidence and co-ordinate the regulatory actions, producing more efficient and consistent outcomes for everybody.

The regulatory tools made available under the revised legislation represent an increasingly proactive approach to medicines safety. These tools comprise the following:

- risk management planning: Pharmacovigilance Risk Assessment Committee (PRAC) reviewed 48 risk management plans (RMPs) in

JulyDecember 2012, 637 in 2013 and 597 in 2014. The Member States, collectively, received around 3 500 (2012), 7 500 (2013), and 9 000 (2014) RMPs for nationally authorised medicines;
- post-authorisation studies: between July 2012 and December 2014, PRAC reviewed protocols for 38 imposed non-interventional post authorisation safety studies (PASSs);
- signal detection and management at EU level: analysing reports of suspected side effects to identify signals. Some 193 unique signals were evaluated by PRAC between September 2012 and December 2014;
- periodic safety update reports: routine benefit-risk monitoring of medicines via periodic safety update reports (PSURs) and maintaining the list (EURD list) of schedules for submitting PSURs;
- inspections: carrying out inspections to ensure company pharmacovigilance systems comply with good pharmacovigilance practice.

The regulatory tools are complemented by improvements in regulatory action and communication when safety concerns are identified.

Increased transparency: mechanisms have been put in place to ensure that accurate safety information reaches the EU public in a timely manner. Engagement of key stakeholders such as patients and healthcare professionals is embedded in the system including through patient reporting of suspected side effects.

For the future, deepening involvement is foreseen, including the holding of public hearings for critical safety issues.

Improving service systems: work is proceeding on the infrastructure needed to support further development of the system, and to simplify and streamline existing processes where possible so that the regulatory burden is minimised for all stakeholders. Work concerns:

- delivery of the medical literature monitoring service of the new EudraVigilance system, of the PSUR repository;
- full use of EU product database (provided for by Article 57) of all authorised medicines (both centrally and nationally authorised) in the EU with information on over 580 000 medicines from nearly 4 300 marketing authorisation holders.

Work continues to complete the development and implementation of other systems such as centralised ADR reporting through the EudraVigilance database. Ongoing research in the field of regulatory science, such as the research supported through the EU Research Framework Programmes, will also support future improvements.

Authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

The Commission presents a report on the national and European Medicines Agency experience regarding the list of medicines for human use subject to additional monitoring.

Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and Directive 2001/83/EC on the Community code relating to medicinal products for human use provide the EU legal framework for pharmacovigilance for medicinal products for human use. The provisions on pharmacovigilance were amended in 2010 and 2012.

Additional monitoring

The 2010 revision introduced additional monitoring for certain medicines and a mandatory scope of new biological medicines or those containing a new active substance. The medicines which are subject to additional monitoring are identified by the inclusion of a black symbol (a black inverted triangle) in the product information. In 2012, the mandatory scope was extended to include medicines with certain post authorisation obligations.

This report is based on a joint report of the Heads of Medicines Agencies (HMA) and EMA and gives an overview of the experience in the three years after the introduction of the black triangle in 2013.

Main findings

The report noted, inter alia, that:

- both more time and more communication are needed to raise the awareness of AM [additional monitoring], as well as the need for adverse drug reaction (ADR) reporting in general. The EMA survey results suggest that knowledge of AM is higher in some groups than others and that these data could be used to target the messaging and intensity of communications;

- the EudraVigilance analysis investigating the effect of additional monitoring status on reporting of ADRs was not conclusive and the known disparate influences on ADR reporting raise doubts as to whether a longer period and larger product sample would enable the detection of an impact of AM on ADR reporting and signal detection, if such an effects exists;

- the inclusion of imposed post authorisation safety study (PASS) as a mandatory trigger for additional monitoring leads to large numbers of established products being included in the list and is of limited value;

- additional monitoring status being at product level combined with the inclusion of imposed PASS as a mandatory trigger for additional monitoring were highlighted as major issues with the additional monitoring concept. This is because of the resulting misunderstanding among patients and health care professionals, due to situations when several products containing the same active substance have different AM status. Most examples of this inconsistency could be resolved by removing imposed PASS as a mandatory trigger of additional monitoring status;

- the Pharmacovigilance Risk Assessment Committee (PRAC) would support reconsideration of the scope of additional monitoring, particularly the mandatory inclusion of products subject to imposed PASS.

Recommendations

On the basis of these findings, the report made the following recommendations.

Recommendation 1

Member States and EMA are encouraged to continue promoting ADR reporting and sharing their experience to further develop best practices.

Recommendation 2

The evidence does not allow a conclusion on the impact of additional monitoring on the reporting or detection of adverse events. It is recommended to continue to monitor the impact to strengthen the evidence base for future review of the scheme.

Recommendation 3

Competent authorities are invited to continue to collect data regarding the implementation of additional monitoring to allow at a later stage further assessment of the understanding of additional monitoring and its impact with respect to medicines with the same active substance, as well as experience concerning medicines with an imposed PASS.