Procedure file

Basic information

COD - Ordinary legislative procedure (ex-codecision procedure) Regulation	1997/0197(COD)	Procedure completed
Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials Amended by 2004/0217(COD) Repealed by 2012/0192(COD) Amended by 2021/0431(COD) Subject 4.20.02.06 Clinical practice and experiments 4.20.04 Pharmaceutical products and industry		

Key players

European Parliament	Committee responsible	Rapporteur	Appointed
	ENVI Environment, Public Health, Consumer Policy	PPE-DE LIESE Peter	11/09/2000
	Former committee responsible		
	ENVI Environment, Public Health and Consumer Protection	NI AMADEO Amedeo	08/10/1997
	Former committee for opinion		
	BUDG Budgets	The committee decided not to give an opinion.	
	ENER Research, Technological Development and Energy	UPE SCAPAGNINI Umberto	08/10/1997
Council of the European Union	Council configuration	Meeting	Date
	Agriculture and Fisheries	2332	26/02/2001
	Health	2319	14/12/2000
	Budget	2285	20/07/2000
	Competitiveness (Internal Market, Industry, Research and Space)	2265	25/05/2000

Key events

03/09/1997	Legislative proposal published	COM(1997)0369	Summary
19/09/1997	Committee referral announced in Parliament, 1st reading		
29/10/1998	Vote in committee, 1st reading		Summary
29/10/1998	Committee report tabled for plenary, 1st	A4-0407/1998	

	reading		
16/11/1998	Debate in Parliament		
17/11/1998	Decision by Parliament, 1st reading	T4-0648/1998	Summary
26/04/1999	Modified legislative proposal published	COM(1999)0193	Summary
20/07/2000	Council position published	08878/1/2000	Summary
07/09/2000	Committee referral announced in Parliament, 2nd reading		
21/11/2000	Vote in committee, 2nd reading		Summary
21/11/2000	Committee recommendation tabled for plenary, 2nd reading	A5-0349/2000	
11/12/2000	Debate in Parliament		
12/12/2000	Decision by Parliament, 2nd reading	T5-0548/2000	Summary
26/02/2001	Act approved by Council, 2nd reading		
04/04/2001	Final act signed		
04/04/2001	End of procedure in Parliament		
01/05/2001	Final act published in Official Journal		

Technical information

Procedure reference	1997/0197(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation
Legislative instrument	Regulation
	Amended by 2004/0217(COD) Repealed by 2012/0192(COD) Amended by 2021/0431(COD)
Legal basis	EC Treaty (after Amsterdam) EC 095
Stage reached in procedure	Procedure completed
Committee dossier	ENVI/5/13000

Documentation gateway

Legislative proposal		COM(1997)0369 OJ C 306 08.10.1997, p. 0009	03/09/1997	EC	Summary
Economic and Social Committee: opinion, report		CES0099/1998 OJ C 095 30.03.1998, p. 0001	28/01/1998	ESC	Summary
Committee report tabled for plenary, 1st reading/single reading		A4-0407/1998 OJ C 379 07.12.1998, p. 0005	29/10/1998	EP	
Text adopted by Parliament, 1st reading/single reading		T4-0648/1998 OJ C 379 07.12.1998, p. 0017-0034	17/11/1998	EP	Summary
Modified legislative proposal		COM(1999)0193 OJ C 161 08.06.1999, p. 0005	26/04/1999	EC	Summary

Council position		08878/1/2000 OJ C 300 20.10.2000, p. 0032	20/07/2000	CSL	Summary
Commission communication on Council's position		SEC(2000)1293	26/07/2000	EC	Summary
Committee recommendation tabled for plenary, 2nd reading		A5-0349/2000 OJ C 232 17.08.2001, p. 0010	21/11/2000	EP	
Text adopted by Parliament, 2nd reading		T5-0548/2000 OJ C 232 17.08.2001, p. 0035-0052	12/12/2000	EP	Summary

Additional information

European Commission	EUR-Lex

Final act

Directive 2001/20
OJ L 121 01.05.2001, p. 0034 Summary

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

OBJECTIVE: approximation of legislative provisions relating to the conduct of clinical trials on medicinal products for human use. SUBSTANCE: the proposal for a directive seeks to provide the same level of protection for patients taking part in a clinical trial and to harmonize technical standards and also rationalize documentary and administrative procedures involved in multi-centre clinical trials, whilst taking account of experience acquired by the Member States. The proposal contains a number of internationally approved definitions codifying the terms used in the Member States, facilitating an international exchange of data relating to clinical trials within the European Union. In addition, the proposal harmonizes the procedures to be followed with regard to information to facilitate ongoing safety monitoring and introduces monitoring in the form of inspections. It is important to note that this proposal is in fact a rationalization of legislation, since overall the administrative and bureaucratic requirements will be reduced in line with a 'risk-based' approach, thus allowing new medicines to be made available in a timely manner. It is also intended to simplify the regulatory burden for small and medium companies (e.g. companies starting up in biotechnology) for which the current complexity of national requirements makes it almost impossible to conduct trials in more than one Member State. ?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

In assessing the proposal, the Committee feels it desirable to seek to strike a balance between the need to: simplify red tape; respect the deadlines for commencement of the clinical trial; and the need to provide the utmost guarantees for trial subjects; coordinate findings so that the efficacy and safety of a new medicinal product can be rigorously assessed. However, the Committee thinks that forms of cooperation should be encouraged for the purpose of gradually moving towards a single EU procedure. Use should be made here of the scientific skills and knowhow available at the European Agency for the Evaluation of Medicinal Products (EMEA), especially as regards "orphan" medicinal products and gene and cell therapy. In order to boost cooperation, it is essential that an EU database be provided as part of EudraNet (a telematic network linking the relevant national authorities, the EMEA and the Commission). This would be used to coordinate and circulate information between the Member States involved in a multi-centre international trial, with an access key to guarantee the utmost confidentiality and the safeguarding of industrial protection. The goal must be a clear and simple legal framework which allows trials to be launched simultaneously in different countries. This presupposes respect for the deadlines laid down for the favourable opinion from the ethics committees and for the acceptance of any requests from the relevant authorities for modifications (these authorities have 30 days to notify their opinion to the sponsor). It is also essential that persons undergoing trials are guaranteed the best possible risks-benefits ratio. To this end, the Commission must obtain greater guarantees regarding the participation of third countries in multi-centre trials. The sponsor should be asked to ascertain that third countries involved in trials on a particular medicinal product are familiar with the Community guidelines and are therefore able to apply them properly. ?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The Committee adopted a report by Mr Amedeo AMADEO (independent, It) on a Commission proposal designed to ensure that similar standards of good clinical practice are observed throughout the union when trials are carried out on human beings with a view to developing new medicines. There are two main concerns: (1) to ensure the safety of those who have volunteered to take part in the trials (thousands of people may be involved in more than one Member State) and (2) to eliminate red-tape so that patients suffering from serious diseases such as

Aids or cancer have access to new pharmacological discoveries as early as possible. The committee adopted a number of amendments with this in mind. In particular, it insisted on the right of participants to physical and mental integrity as well as to privacy and stipulated that they give written consent to their participation. Compensation should be available in the event of death or injury. Recruitment of volunteers must be suspended in the event of unexpected side-effects. Medicines used in trials ("investigational medicinal products") must accord with good manufacturing practices, regardless of whether they have been produced in a Member State or imported from a third country. Those responsible for approving such medicines must have received appropriate training. Trials should not begin before the relevant ethics committee has given a favourable opinion. They may be deferred or terminated if good clinical practice is not respected. Detailed rules must be adopted to protect the mentally handcapped and children. The person responsible for a clinical trial must be a doctor. The committee also deleted from the proposal a reference to a related Council of Europe convention. Under the Commission proposal a database is to be set up in connection with such trials. The committee insisted that the confidentiality of the data recorded be strictly observed. Moreover, no information must be included which would adversely affect the industrial property rights or competitiveness of a trial's sponsor. With a view to cutting red-tape, the committee criticised the existence of several diverse procedures for obtaining opinions from ethics committees: a single opinion for each Member State concerned would normally suffice. The committee also accepted the rapporteur's view that those sponsoring a clinical trial could simply notify the authorities of their intention: they did not need to submit a prior application for authorization. ?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

In adopting the report by Mr Amedeo AMADEO (NI, I), the European Parliament called for trials to begin only after the ethics committee had issued a favourable opinion. At the same time, trials on any person incapable of giving informed consent should be banned unless they were of direct benefit to the person concerned. Member States were asked to adopt detailed regulations, if they did not already exist, to protect such persons (e.g. the mentally handicapped or children) against any abuse. It should not be possible for individuals who were incapable of giving their informed consent to participate in clinical trials unless a legally responsible person had consented after clarification of the circumstances. Similarly, if a trial participant was incapable of entering into legal transactions, the informed consent of relatives, the guardian and/or a legal representative was required. Parliament considered that a clinical trial could be undertaken only if: - the right of the participant in the trial to physical and mental integrity was respected, as well as the right to privacy, - the participant in the trial had given his written consent after being informed of the nature, significance and implications of the clinical trial, - an appropriately qualified doctor was responsible for the medical care given to, and medical decisions made on behalf of, subjects. Compensation must be available in the event of injury to or death of a trial participant which was attributable to the clinical trial. If trials had unexpected side-effects, Parliament considered that the sponsor should suspend all recruitment for the study concerned. Substances used in trials must be used in accordance with the principle of good practice, whatever their place of origin. Those responsible for approving 'investigational substances' must possess appropriate training. Parliament called for the outer or immediate packaging of investigational medicinal products to state in, at least, the national languages that the medicinal product was being used for a clinical trial and that it was not for sale.?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The Commission's amended proposal introduces new measures to take into account the European Parliament's opinion. The main amendments focus on the following points : 1) informed consent : with a view to strengthening the guarantees concerning the protection of participants in clinical trials, the Commission introduced an operational definition, as well as procedures for the exercise or withdrawal of consent, particularly in the case of minors or of incapacitated adults. The amended text also lays down clearer conditions for clinical trial subjects who wish to have access to an independent contact able to supply them with further information. To this end, the responsibility of the sponsor to organise the corresponding arrangements is clearly established ; 2) ethics committee : the amended proposal gives the ethics committee a more important role, one that is no longer limited almost exclusively to the phase preceding commencement of the clinical trial. In this way, the content of the information to be submitted to the ethics committee has been widened substantially to cover the entire clinical trial, from before commencement to completion. It has also been made clear that the ethics committee must be consulted again if the sponsor makes substantial amendments to the protocol being followed which could impair subjects' safety, and, therefore, call into question the original favourable opinion ; 3) exchanges of information : the amended proposal reinforces the original text by adding provisions on the practical arrangements for centralisation at Community level of the results of the clinical trials and clearly defining the role played by the Commission in organising and coordinating such exchanges of information vis-à-vis the competent authorities and the sponsor of the clinical trial ; 4) compatibility with existing Community legislation : it is essential that the European Agency for the Evaluation of Medicinal Products receives a copy of the notification of commencement of a clinical trial so that it can assess the content thereof in preparation for subsequent evaluation of the product should it fall under Part A of the Annex to Regulation 2309/93/EEC. If the product falls under Part B of the same Annex, the sponsor has the option of deciding whether or not to notify the Agency ; 5) procedure for the commencement of a clinical trial : the new procedure opts for simplification, which should lead to greater speed and efficiency, by putting the accent on the notification procedure. For the sponsor, this entails informing the competent authorities of any plans to proceed with a clinical trial , by means of a "notification". The notification of the clinical trial must be accompanied by a written authorisation granted by the competent authorities of the Member States concerned within fixed time limits.?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The Council's common position is essentially based on the amended Commission proposal, and therefore includes the letter or spirit of most of the amendments suggested by Parliament and taken up by the Commission. An important exception concerns the procedure for starting a clinical trial, which has been substantially amended by the Council in order to simplify and speed up decision-making by the competent authorities of the Member States. Another exception concerns the provisions for the subjects in clinical trials, in particular certain aspects to minors and incapacitated adults which could only be partly accepted by the Council and the Commission, both institutions nevertheless

considering that the protection guarantees for subjects in clinical trials would not be reduced as a result. In addition, the Council has also introduced a number of editorial changes to the text of the common position. Some original provisions to which the European Parliament's proposals for amendments refer have consequently undergone subsequent re-drafting or re-editing. The amendments accepted by the Council without modification, with minor editorial modifications or in principle relate in particular to: - the definition of "informed consent". The definition selected by the Council differs from that proposed by the Parliament in that it also covers persons who are not in a position to give their consent with full knowledge of the facts; - the definition of "unexpected adverse reaction"; - the extension of the 60-day period for the Ethics Committee to give its opinion in cases where trials involve medicinal products for gene therapy was accepted by the Council and extended to include somatic cell therapy, including xenogenic cell therapy; - the strict observance of the confidentiality of data to be entered in the European databases; - the obligation to inform the sponsor, the competent authorites, the Ethics Committee and the Commission in cases where a suspension of clinical trials must be contemplated; - provisions relating to the manufacture and importation of investigational medicinal products. In relation to the amendments which were partly accepted by the Council, these concern the protection of trial subjects in clinical trials. Moreover, they also concern the trial subject's right to have his mental and physical integrity safeguarded. On the other hand, the amendments not accepted by the Council relate in particular to: - replacing the idea of "person responsible" in the definition of "investigator" by "doctor responsible"; - the deletion of the provision on the arrangements for rewarding or compensating investigators and trial subjects as one of the elements to be considered when the Ethics Committee prepares its opinion; - the indication on the packaging that the medicinal product is being used in the framework of a clinical trial and that it cannot be sold. Lastly, the Council did not accept the amendment whichprovides for the deletion of the indication that inspections for the purpose of verifying compliance with good clinical and manufacturing practice are carried out on "behalf of the Community".?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The Commission supports the common position. The adoption of Community legislation on the application of good clinical practice in the conduct of clinical trials on medicinal products will promote the conduct of such trials in the European Union.?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The committee adopted the recommendation for second reading under the codecision procedure by Hans-Peter LIESE (EPP-ED, D) amending the Council's common position. The committe retabled, sometimes in slightly modified form, many of the amendments tabled at first reading which had not been taken up by the Council. These concerned in particular the need for written, dated and signed consent to take part in clinical trials, the need for the principal investigator always to be a doctor and the need for special protection for persons incapable of giving their informed consent. The committee also added a number of new points, such as allowing oral consent (in exceptional circumstances) in the presence of witnesses for a person unable to write, and making it clear that the task of balancing benefits against risks in the case of a clinical trial belonged to an Ethics Committee. It also wanted a prior interview to be carried out in order to make sure that trial subjects were properly informed. The committee felt that clinical trials on children should be allowed subject to certain restrictions, including the need for informed consent of the child's parents or legal representative, for the child to be properly informed about the issues, in line with its ability to understand them, and for clinical trials to be designed to minimise pain, discomfort and fear. It also wanted similar requirements to apply to psychiatric patients and other types of patient unable to give consent, who should be included in clinical trials only on a restrictive basis. There should be a justified expectation that the medicinal product to be administered would produce benefits for the patient outweighing the risks, and experts in the type of patients concerned should sit on the Ethics Committees examining the studies in question.?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

The European Parliament approved, with a number of compromise amendments, the resolution by Mr Peter LIESE (EPP/ED, D) on the Council's common position. Commissioner Michel BARNIER said he could also accept these compromise amendments. For a long time, the European Parliament and Council positions had been very different but a detailed agreement has been finally reached. Key points of the compromise amendments were that necessary research will be allowed but that 'trial subjects' are ensured maximum protection. In order to implement the agreement, Parliament adopted a large number of compromise amendments. These are mirrored in the decision of the committee responsible. (Refer to the previous document).?

Medicinal products for human use: implementation of good clinical practice in the conduct of clinical trials

PURPOSE : to establish specific provisions regarding the conduct of clinical trials of medicinal products on human subjects, particularly in relation to the implementation of good clinical practice. COMMUNITY MEASURE : Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. CONTENT : This directive obliges Member States to adopt detailed rules to protect from abuse individuals who are incapable of giving their informed consent. This includes minors, and incapacitated adults. Such persons should not participate in trials if the same results would be obtained from persons who are capable of giving consent. The directive sets out the preconditions under which trials may take place. The foreseeable risks and inconveniences must be weighed against the anticipated benefits for the individual trial subject and other patients. A trial may only be initiated by the Ethics Committees, the establishment and duties of which are set out in the directive. The trial subject or his legal representative must be given certain information about the trial, including the right of withdrawal. The directive establishes rules on the commencement and conduct of trials,

suspension of the trials or infringements, the manufacture and import of investigational medicinal products, labelling, and verification of compliance with good clinical and manufacturing practice. ENTRY INTO FORCE : 01/05/2001 DATE OF APPLICATION : Member States shall adopt and publish before 1 May 2003 the laws to comply with the Directive. The provisions will apply at the latest with effect from 1 May 2004.
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