Basic information

2012/0192(COD) COD - Ordinary legislative procedure (ex-codecision procedure) Regulation	Procedure completed
Clinical trials on medicinal products for human use Repealing Directive 2001/20/EC 1997/0197(COD) Amended by 2021/0432(COD) **Subject** 4.20.02 Medical research 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 and Food Safety	WILLMOTT Dame Glenis (S&D)	12/10/2012
	Shadow rapporteur JUVIN Philippe (PPE) PARVANOVA Antonyia (ALDE) AUKEN Margrete (Verts /ALE) CABRNOCH Milan (ECR) SOUSA Alda (GUE/NGL)	

Committee for opinion	Rapporteur for opinion	Appointed
ITRE Industry, Research and Energy	SARTORI Amalia (PPE)	26/09/2012
IMCO Internal Market and Consumer Protection	BUŞOI Cristian-Silviu (ALDE)	18/09/2012
LIBE Civil Liberties, Justice and Home Affairs	LÓPEZ AGUILAR Juan Fernando (S&D)	21/02/2013

Council of the European Union

Council configuration	Meetings	Date
Agriculture and Fisheries	3308	2014-04-14

European Commission	**Commission DG**	**Commissioner**
	Health and Food Safety	BORG Tonio
European Economic and Social Committee		
European Committee of the Regions		

Key events

Date	Event	Reference	Summary
17/07/2012	Legislative proposal published	COM(2012)0369	Summary
11/09/2012	Committee referral announced in Parliament, 1st reading		
29/05/2013	Vote in committee, 1st reading		
10/06/2013	Committee report tabled for plenary, 1st reading	A7-0208/2013	Summary
02/04/2014	Decision by Parliament, 1st reading	T7-0273/2014	Summary
02/04/2014	Results of vote in Parliament		
02/04/2014	Debate in Parliament		
14/04/2014	Act adopted by Council after Parliament's 1st reading		
16/04/2014	Final act signed		
16/04/2014	End of procedure in Parliament		
27/05/2014	Final act published in Official Journal		

Technical information

Procedure reference	2012/0192(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation
Legislative instrument	Regulation
Amendments and repeals	Repealing Directive 2001/20/EC 1997/0197(COD) Amended by 2021/0432(COD)
Legal basis	Treaty on the Functioning of the EU TFEU 168-p4 Treaty on the Functioning of the EU TFEU 114-p1
Other legal basis	Rules of Procedure EP 165
Mandatory consultation of other institutions	European Economic and Social Committee European Committee of the Regions
Stage reached in procedure	Procedure completed
Committee dossier	ENVI/7/10164

Documentation gateway

European Parliament

Document type	Committee	Reference	Date	Summary
Committee draft report		PE504.236	31/01/2013	
Amendments tabled in committee		PE506.158	01/03/2013	
Amendments tabled in committee		PE506.161	01/03/2013	
Amendments tabled in committee		PE506.162	01/03/2013	
Amendments tabled in committee		PE506.159	06/03/2013	
Amendments tabled in committee		PE506.160	06/03/2013	
Committee opinion	ITRE	PE504.167	21/03/2013	
Committee opinion	IMCO	PE500.727	26/03/2013	
Committee opinion	LIBE	PE506.211	09/04/2013	
Committee report tabled for plenary, 1st reading/single reading		A7-0208/2013	10/06/2013	Summary
Text adopted by Parliament, 1st reading/single reading		T7-0273/2014	02/04/2014	Summary

Council of the EU

Document type	Reference	Date	Summary
Draft final act	00002/2014/LEX	16/04/2014	

European Commission

Document type	Reference	Date	Summary
Legislative proposal	COM(2012)0369	17/07/2012	Summary
Document attached to the procedure	SWD(2012)0200	17/07/2012	
Document attached to the procedure	SWD(2012)0201	17/07/2012	
Commission response to text adopted in plenary	SP(2014)471	09/07/2014	

National parliaments

Document type	Parliament /Chamber	Reference	Date	Summary
Contribution	IT_SENATE	COM(2012)0369	04/10/2012	
Contribution	PT_PARLIAMENT	COM(2012)0369	11/10/2012	
Contribution	CZ_SENATE	COM(2012)0369	07/11/2012	
Contribution	EL_PARLIAMENT	COM(2012)0369	26/11/2012	

Other institutions and bodies

Institution/body	Document type	Reference	Date	Summary
EESC	Economic and Social Committee: opinion, report	CES2059/2012	12/12/2012	
EDPS	Document attached to the procedure	N7-0092/2013 OJ C 253 03.09.2013, p. 0010	19/12/2012	Summary

Additional information

Source	Document	Date
National parliaments	IPEX	
European Commission	EUR-Lex	
European Commission	EUR-Lex	

Final act

Corrigendum to final act 32014R0536R(04)
OJ L 311 17.11.2016, p. 0025

Regulation 2014/0536
OJ L 158 27.05.2014, p. 0001 Summary

Delegated acts

Reference	Subject
2017/2710(DEA)	Examen d'un acte délégué
2022/2819(DEA)	Examen d'un acte délégué

Clinical trials on medicinal products for human use

2012/0192(COD) - 10/06/2013 - Committee report tabled for plenary, 1st reading/single reading

The Committee on the Environment, Public Health and Food Safety adopted the report by Glenis WILLMOTT (S&D, UK) on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

The committee recommends that the European Parliament's position at first reading adopted under the ordinary legislative procedure should amend the Commission proposal as follows:

General principle: a clinical trial may be conducted only if : (i) **the rights, safety, physical and mental integrity, dignity and well-being of subjects are protected**, and the ethics

committee has provided assurances thereof; (ii) the data generated in the clinical trial can be expected to be reliable, robust and relevant for improving the prevention and treatment of diseases.

In a clinical trial the safety, rights, health and well-being of subjects should be protected and the data generated should be relevant, reliable and robust and reflect the diversity of the population in terms of age and gender balance. The interests of the participants should always take priority over other interests.

Members insist that it should be ensured that persons assessing the application **do not have conflicts of interest**, are independent of the sponsor, the trial site and the investigators involved, as well as free of any undue influence.

Ethics committee: a clinical trial should be subject to prior authorisation after having been examined by the ethics committee concerned in accordance with the World Medical Association's Declaration of Helsinki.

The Ethics committee shall be an **independent body** in a Member State, consisting of health-care professionals and nonmedical members including at least one well-experienced, knowledgeable patient or patient representative. In cases of clinical trials involving minors, the ethics committee shall include at least one healthcare professional with paediatric expertise.

Vulnerable persons: where the subjects belong to vulnerable population groups including pregnant and breastfeeding women, persons deprived of liberty, persons with specific needs including the elderly, frail people and people with dementia, specific consideration shall be given to the assessment of the application for authorisation of a clinical trial.

Low-risk clinical trials: given that low-risk clinical trials have only a very limited and temporary adverse effect, they should be subject to less stringent rules, such as shorter deadlines for approval. Less stringent rules should not compromise scientific standards and should guarantee the safety of subjects at all times. Those low-risk trials should, however, be subject to the vigilance and traceability rules governing normal clinical practice.

For low-risk trials and when marketing authorisation is not the initial objective of the investigator-initiated trial, the cost of the investigational medicinal product should be borne by the national healthcare system.

Assessment report on clinical trials in the field of rare and ultra-rare diseases: in the specific case of clinical trials in the field of rare or ultra-rare diseases, Members propose that the reporting Member State shall seek the expert opinion of the Scientific Advice Working Party of the European Medicines Agency on the disease or group of diseases concerned by the clinical trial in order to help the reporting Member State and the Member States concerned to provide a well informed assessment of the application.

Transparency: Members propose that the assessment report shall be **submitted through the EU portal, and stored in the EU database**. It shall be made publicly available to foster public confidence in the authorisation process.

The subject shall be informed that within one year from the end of the clinical trial or its early termination, the **summary of the results of the trial and a summary presented in terms understandable to a layperson will be made available in the EU database**, irrespective of the trial outcome, or that he or she can obtain information from the investigator or its representative about the overall results of the trial.

The reasons for early termination of a clinical trial shall be published in the EU database.

Members also propose that Member States should impose **fines** on sponsors that do not meet their responsibilities in terms of transparency.

Informed consent: rules on informed consent are established in detail by the Members in order to ensure access to information and to damage compensation.

Informed consentment should be given **freely and voluntarily**. During the prior interview, the potential subject shall also be informed of the right to refuse to participate in the clinical trial without any resulting detriment. The prior interview with the investigator or a member of the investigating team in order to obtain the subject's informed consent shall include a test of full understanding on the part of the subject and/or his or her de facto representative.

Within the original consent, an option of broad consent should be made available to the patient, whereby his/her data could be allowed to be used at the behest of the treating institution for future research.

Specific measures are also applied to clinical trials on pregnant or breastfeeding women, persons deprived of liberty or subjects with specific needs.

Reporting on efficacy defects of authorised investigational medicinal products: efficacy defect on an authorised medicinal product could represent a serious risk for patient safety and should therefore be added as a reporting obligation under this regulation.

Clinical trial master file: although the Commission proposed that the sponsor shall archive the content of the clinical trial master file for at least five years, Members are of the opinion that should a sponsor come under investigation for misconduct, the clinical trial master file would be vital. Therefore the master file should be **archived indefinitely** unless national legislation states otherwise. The master file can be stored in the EU database if necessary.

In order to follow a given clinical trial from initial ethical approval to final publication, Members proposal that a **Universal Trial Registration Number (UTRN)** should be assigned to each trial to be conducted in the Union.

Clinical trials on medicinal products for human use

2012/0192(COD) - 19/12/2012 - Document attached to the procedure

Opinion of the European Data Protection Supervisor (EDPS)

The EDPS welcomes the fact that the Commission has made an effort to guarantee the correct application of EU rules concerning the protection of personal data in the proposed Regulation on clinical trials on medicinal products for human use.

The EDPS considers, however, that **clarifications are necessary** with regard to where **sensitive data** regarding health might be processed and stored, regarding the authorisation procedure in the EU Portal and database and the reporting of adverse effects in the European Medicines Agency (EMA) database.

The EDPS recommends in particular, that the proposal:

- explicitly refers to Article 8 of Directive 95/46/EC and Article 10 of Regulation (EC) No 45/2001 regarding the processing of personal data concerning health;
- clarifies whether personal data concerning health will be processed in the EU database, and if so, for what purpose;
- refers to the right of the data subjects to block their personal data;
- ensures, for the EMA database, a provision which more clearly defines in what situations and subject to what safeguards information containing patient data will be processed and stored;
- explicitly mentions that the annual reports should only be using anonymous data;
- replaces or complements the minimum retention period of 5 years by a maximum retention period.

Clinical trials on medicinal products for human use

2012/0192(COD) - 02/04/2014 - Text adopted by Parliament, 1st reading/single reading

The European Parliament adopted by 594 votes to 17, with 13 abstentions, a legislative resolution on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

Parliament adopted its position at first reading following the ordinary legislative procedure. The amendments adopted in plenary are the result of an agreement negotiated between the European Parliament and the Council. They amend the proposal as follows:

General principle: a clinical trial may be conducted only if: (i) the rights, safety, dignity and well-being of subjects are protected and prevail over all other interests; and (ii) it is designed to generate reliable and robust data.

A clinical trial shall be subject to **scientific and ethical review** and shall be authorised in accordance with this Regulation. The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned.

Simplified procedures: application dossiers for clinical trials should be submitted by means of a single submission portal. In order to avoid administrative delays for starting a clinical trial, the **procedure to be used should be flexible and efficient**, without compromising patient safety or public health.

According to the new text, Member States should **efficiently assess all clinical trials applications within the given timelines**. A rapid yet in-depth assessment is of particular importance for clinical trials concerning **medical conditions which are severely debilitating** and/or life threatening and for which therapeutic options are limited or non-existent, as in the case of rare and ultra-rare diseases.

Vulnerable persons: the assessment of applications for the authorisation of clinical trials should be conducted on the basis of appropriate expertise. Specific expertise should be considered when assessing clinical trials involving subjects in emergency situations, minors, incapacitated subjects, pregnant and breastfeeding women and, where appropriate, other identified specific population groups, such as elderly people or people suffering from rare and ultra rare diseases.

The text underlines that in order to improve treatments available for vulnerable groups such as frail or older people, people suffering from multiple chronic conditions, and people affected by mental health disorders, medicinal products which are likely to be of significant clinical value should be fully and appropriately studied for their effects in these specific groups.

Conditions for the conduct of a clinical trial: the following conditions should be met:

- the anticipated benefits to the subjects or to public health justify the foreseeable risks and inconveniences and compliance with this condition is constantly monitored;
- the subjects, or where a subject is not able to give informed consent, his or her legally designated representative, have been informed;
- the subjects, or where a subject is not able to give informed consent, his or her legally designated representative, have given informed consent;
- the rights of the subjects to physical and mental integrity, to privacy and to the protection of the data concerning them are safeguarded;
- the clinical trial has been designed to involve as little pain, discomfort, fear and any other foreseeable risk as possible for the subjects and both the risk threshold and the degree of distress are specifically defined in the protocol and constantly monitored;
- the medical care provided to the subjects is the responsibility of an appropriately qualified medical doctor or, where appropriate, a qualified dental practitioner;
- the subject or, where the subject is not able to give informed consent, his or her legally designated representative has been provided with the contact details of an entity where further information can be received in case of need;
- no undue influence, including that of a financial nature, is exerted on subjects to participate in the clinical trial.

Informed consent: information given to the subject or his or her legally designated representative shall enable an understanding of:

- the nature, objectives, benefits, implications, risks and inconveniences of the clinical trial;
- the subject's rights and guarantees regarding his or her protection, in particular his or her right to refuse to participate and the right to withdraw from the clinical trial at any time without any resulting detriment and without having to provide any justification;

- the conditions under which the clinical trial is to be conducted, including the expected duration of the subject's participation in the clinical trial; and
- the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical trial is discontinued.

Information should be: (i) be kept **comprehensive, concise, clear, relevant, and understandable** to a layperson; (ii) be provided in a **prior interview** with a member of the investigating team who is appropriately qualified according to the law of the Member State concerned; (iii) include information about the applicable **damage compensation system**.

The sponsor should provide within the time limits a summary of the results of the clinical trial and a summary presented in terms understandable to a layperson and, if appropriate, the clinical trial report.

Subject safety: in addition to serious adverse events and reactions, the new text stipulates that all unexpected events that might materially influence the benefit-risk assessment of the medicinal product or that would lead to changes in the administration of a medicinal product or in overall conduct of a clinical trial are **notified** to the Member States concerned.

Transparency: Members amended the legal text in order to increase transparency, requiring that detailed summaries of the trial be **published on a European database that is accessible to the public**.

Penalties may be imposed in the cases of non-compliance with the provisions laid down in the Regulation on submission of information intended to be made publicly available to the EU database and non-compliance with the provisions on subject safety.

Clinical trials on medicinal products for human use

2012/0192(COD) - 16/04/2014 - Final act

PURPOSE: to promote public health and research throughout the European Union (EU) by establishing harmonised rules concerning the authorisation and the conduct of clinical trials.

LEGISLATIVE ACT: Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

CONTENT: the new Regulation replaces **Directive 2001/20/CE and applies to all clinical trials conducted in the Union**. It relies on the general principle according to which a clinical trial may be conducted only: a) if the rights, safety, dignity and well-being of subjects are protected and prevail over all other interests; and b) if it is designed to generate reliable and robust data.

According to the Regulation, any clinical trial shall be subject to a **scientific and ethical review** and shall be subject to **prior authorisation**. The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned.

Procedures for authorisation: the procedure to be used should be **flexible and efficient**, in order to avoid administrative delays for starting a clinical trial, without compromising patient safety or public health.

To obtain an authorisation, the sponsor must submit **one application dossier** to all the Member States concerned **through a single EU portal**. The Regulation sets the deadline for authorisation of clinical trials at **60 days**. If no decision is taken within this period, the autorisation shall be deemed to have been given (tacit approval). Decisions on requests for substantial changes to clinical trials should be taken within **49 days**. In the absence of a decision, the authorisation will be taken as given.

Application dossier for authorisation of a clinical trial: it should contain information on: a) the conduct of the clinical trial, including the scientific context and arrangements taken; b) the sponsor, investigators, potential subjects, subjects, and clinical trial sites; c) the investigational medicinal products and, where necessary, the auxiliary medicinal products, in particular their properties, labelling, manufacturing and control; d) measures to protect subjects; e) justification as to why the clinical trial is a low-intervention clinical trial, in cases where this is claimed by the sponsor.

V**ulnerable people**: clinical trials involving subjects in emergency situations, minors, incapacitated subjects, pregnant and breastfeeding women and, where appropriate, other identified specific population groups, such as elderly people or people suffering from rare and ultra rare diseases, will be strictly supervised and their evaluation subject to **specific expertise**.

Protection of participants: the Regulation stipulates that a clinical trial may be conducted only where certain conditions are met. In particular:

- the anticipated benefits to the subjects or to public health justify the foreseeable risks and inconveniences and compliance with this condition is constantly monitored;
- the subjects have been informed and given their informed consent;
- the rights of the subjects to physical and mental integrity, to privacy and to the protection of the data concerning them are safeguarded;
- the clinical trial has been designed to involve as little pain, discomfort, fear and any other foreseeable risk as possible for the subjects;
- the subject has been provided with the contact details of an entity where further information can be received in case of need;
- no undue influence, including that of a financial nature, is exerted on subjects to participate in the clinical trial.

Informed consent: informed consent must be written, dated and signed by the person conducting the interview and the participant, or if he is not able to give his consent, **his legally designated representative**.

Information given to the subject or his legally designated representative should allow them to understand: i) the nature, objectives, benefits, implications, risks and inconveniences of the clinical trial; ii) the subject's rights and guarantees regarding his or her protection; iii) the conditions under

which the clinical trial is to be conducted, including the expected duration of the subject's participation in the clinical trial; iv) the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical trial is discontinued.

In addition, the information should be: i) **comprehensive and understandable** to a layperson; ii) provided in a **prior interview** with a member of the investigating team who is appropriately qualified according to the law of the Member State concerned; iii) include information about the applicable damage compensation system.

Transparency: in order to allow patients to assess possibilities to participate in a clinical trial, and to allow for effective supervision of a clinical trial by the Member State concerned, the start of the clinical trial, the end of the recruitment of subjects for the clinical trial and the end of the clinical trial should be **notified**. In accordance with international standards, **the results** of the clinical trial should be reported **within one year** from the end of the trial.

The European Medicines Agency shall set up and maintain an electronic database for the **reporting** provided for in the clinical trial framework.

Supervision, Union inspections and controls: where a Member State concerned has justified grounds for considering that the requirements set out in this Regulation are no longer met, it may: a) revoke the authorisation of a clinical trial; b) suspend a clinical trial; c) require the sponsor to modify any aspect of the clinical trial. Qualifed **inspectors** shall be designated by the Membe States to supervise compliance with this Regulation.

The Commission should be able to control whether Member States correctly supervise compliance with this Regulation. Moreover, the Commission should be able to control whether regulatory systems of third countries ensure compliance with the specific provisions of this Regulation and Directive 2001/83/EC concerning clinical trials conducted in **third countries**.

Union database: in order to streamline and facilitate the flow of information between sponsors and Member States as well as between Member States, the Agency should, in collaboration with Member States and the Commission, set up and maintain an EU database, accessed through an EU portal. In order to ensure a sufficient level of transparency in the clinical trials, the EU database should contain **all relevant information** as regards the clinical trial submitted through the EU portal.

ENTRY INTO FORCE: 16.06.2014. The Regulation shall apply no earlier than 28.05.2016.

DELEGATED ACTS: the Commission may adopt delegated acts in order to supplement or amend non-essential aspects of the Regulation. The power to adopt such acts shall be conferred on the Commission for a period of **five years** from the date of the implementation of the Regulation. The European Parliament or the Council may object to a delegated act within a period of two months from the date of notification (this period can be extended for two months). If the European Parliament or the Council make objections, the delegated act will not enter into force.

Clinical trials on medicinal products for human use

2012/0192(COD) - 17/07/2012 - Legislative proposal

PURPOSE: to promote public health and research in the EU by laying down harmonised rules on the authorisation and conduct of clinical trials.

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

BACKGROUND: clinical trials are an indispensable part of clinical research which, in turn, is essential to develop medicinal products and improve medical treatment. In the EU/EEA, approximately 4 400 clinical trials are applied for every year. Approximately 24 % of all clinical trials applied for in the EU are multinational clinical trials, i.e. clinical trials intended to be performed in at least two Member States. These 24% clinical trials involve approximately 67% of all subjects enrolled in a clinical trial.

Directive 2001/20/EC aimed to simplify and harmonise the administrative provisions governing clinical trials in the European Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a clinical trial in several Member States.

Directive 2001/20/EC has brought about important improvements in the safety and ethical soundness of clinical trials in the EU and in the reliability of clinical trials data. However, it is criticized by all stakeholders in the pharmaceutical sector for the following reasons: (i) the number of applications for clinical trials fell by 25 % from 2007 to 2011; (ii) the costs for conducting clinical trials have increased; (iii) the average delay for launching a clinical trial has increased by 90 % to 152 days.

It would be wrong to attribute the fall in clinical trial activity solely and exclusively to the Directive 2001/20/EC. However, the Directive has had many direct effects on the cost and feasibility of conducting clinical trials, which, in turn, have led to a decline in clinical trial activity in the EU. The Commission considers it necessary, therefore, to take new measures.

IMPACT ASSESSMENT: the Commission has carried out an impact assessment in accordance with its guidelines and published the results.

LEGAL BASIS: Articles 114 and 168(4)(c) of the Treaty on the Functioning of the European Union (TFEU.) The Regulation aims at achieving an internal market as regards clinical trials and medicinal products for human use, taking as a base a high level of protection of health. At the same time, the Regulation sets high standards of quality and safety for medicinal products to meet common safety concerns as regards these products.

CONTENT: the proposed legislation takes the form of a Regulation and replaces Directive 2001/20/EC. This legal form ensures that Member States base their assessment of an application for authorisation of a clinical trial on an identical text, rather than on diverging national transposition measures. This holds not only for the entire authorisation process, but also for all other issues addressed in the Regulation, such as safety reporting during clinical trials, and the requirements for labelling of the medicinal products used in the context of a clinical trial.

A Regulation also allows actors to plan and conduct clinical trials, including multi-national clinical trials, on the basis of one regulatory framework.

The main points of the proposal are as follows:

New authorisation procedure for clinical trials: this based on the following:

- a harmonised authorisation dossier;
- a 'single portal' to submit an application for conducting a clinical trial linked to an EU database;
- a flexible and swift assessment procedure;
- a clear mechanism to appoint a 'reporting Member State';
- clear timelines with a concept of tacit approval in order to ensure compliance;
- a coordination and advisory forum to address issues which may arise in the authorisation procedure;
- a clear distinction between aspects where Member States cooperate in the assessment and aspects of an intrinsic ethical or national/local nature where the assessment is made by each Member State individually;
- the option for a Member State to 'opt-out' of the conclusions of an assessment of an application for conducting a clinical trial ('qualified opt-out');
- a swift procedure to 'extend' a clinical trial to additional Member States;
- where a clinical trial is modified after it has been authorised, this modification is subject to authorisation if, and only if, the modification has a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial.

Simplified safety reporting: compared to Directive 2001/20/EC, the rules have been streamlined, simplified and modernised as follows:

- the option to exclude reporting by the investigator to the sponsor of adverse events, if this is provided for in the protocol;
- direct reporting of suspected unexpected serious adverse reactions by the sponsor to the European database EudraVigilance;
- simplified submission of the annual safety report by the sponsor.

Protection of subjects and informed consent: Directive 2001/20/EC does not address the specific situation where, because of the urgency of the situation, it is impossible to obtain free and informed consent from the subject or the legal representative ('clinical trials in emergency situations'). To address this, specific provisions on clinical trials in emergency situations have been added in line with existing international guidance documents on this issue.

Furthermore, as regards the protection of personal data, provisions of Directive 95/46/EC and Regulation (EC) No 45/200110 apply.

No personal data of data subjects participating in a trial will be collected in the EU database. Personal data of investigators, which may be collected in the EU database, are kept in accordance with the exception provided in the text.

Compensation for damage: where there is no additional risk, or where that additional risk is negligible, the Regulation does not provide a specific damage compensation (be it an insurance or an indemnification) for the clinical trial. However, in cases where a clinical trial does pose an additional risk, the proposed Regulation obliges the sponsor to ensure compensation – be it through insurance, or through an indemnification mechanism.

Sponsors, co-sponsorship, EU contact person: every clinical trial must have a 'sponsor', i.e. a legal or natural person responsible for initiating and managing the clinical trial. Clinical trials are increasingly initiated by loose networks of scientists or scientific institutions within one Member State or across several Member States. The proposed Regulation introduces the concept of 'co-sponsorship'. At the outset, all co-sponsors are responsible for the entire clinical trial. However, the proposal allows co-sponsors to 'split' the responsibility for the clinical trials amongst themselves.

If the sponsor is established in a third country, an EU contact person must be provided in order to ensure an effective supervision of a clinical trial.

Inspections: the proposed Regulation provides the legal basis for Commission staff to perform controls in Member States and in third countries in the context of the EU acquis for medicinal products for human use and clinical trials.

BUDGETARY IMPLICATIONS: **EUR 4 144 000 in commitment appropriations for the period 2014-2020.**

The budgetary implications of this proposal are as follows:

- costs for databases (one-off costs and maintenance);
- Commission staff to manage the functioning of the Regulation;
- costs for meetings of Member States to ensure that the authorisation procedure set out in this Regulation functions properly;
- Commission staff and other costs to conduct Union controls and Union inspections.

The costs will be covered with the envelope of the Health for Growth Programme 2014-2020 2014-2020.