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.