Regulation (EU) on Clinical Trials

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Clinical Trials Regulation: Trilogue Agreement

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- Ethics Committees
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1. The European Commission first initiatives

- **1965**, Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (triggered by the Thalidomide tragedy in the early 1960s).
- **1975**, Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products.
- **2001**, Directive 2001/20/CE of the European Parliament and of the Council of 4 April on the 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.

1. The European Commission first initiatives

The three European Directives draw a path that became clearer each step of the way (and in Directive 2001/20/CE):

- **harmonization** (R1, approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of medicinal products; uniform rules on the compilation of dossiers including their presentation);
- **centralization** (R8, a single opinion for each Member State concerned reduces delay in the commencement of a trial without jeopardising the well-being of the people participating in the trial or excluding the possibility of rejecting it in specific sites).

1. The European Commission first initiatives

The three European Directives deepen the ethical concerns (and in Directive 2001/20/CE):

- **reinforce quality, safety and surveillance at the scientific level, in order to guarantee that the results of the clinical trials are credible;**
- **strengthen the protection of rights, safety and well-being of trial subjects** (persons who are incapable of giving legal consent to clinical trials receive special protection)**;**
- **establish ethics committees that, notwithstanding their number, will produce a single opinion for Member States** (in order to achieve an uniform position and increase the speed of the process);
- **introduce the obligation of insurance or indemnity to cover the liability of the investigator and sponsor.**

2. The European Commission proposal of a Regulation

The European Regulation proposal pursues the path drawn before, through:

- **harmonization** of the legislation in all Member States;
- **simplification** of the legal arrangements applicable to clinical trials;
- **facilitation** of procedures so that the Union becomes more attractive to clinical trials;
- **centralization** of procedures and **decentralization** of competences.

2. The European Commission proposal of a Regulation

The European Regulation proposal raises serious ethical concerns:

- **Ethics Committees** which are no longer considered compulsory neither their advice needed prior to authorization (ethical aspects relate, in particular, to the need to obtain informed consent from the subject or the legal representative);
- **Informed consent**, especially the brand new possibility of skipping informed consent in emergency situations.

3. The Clinical Trials Regulation: an ethical perspective

The European Commission's proposal neglected a significant part of the most relevant bioethical reflection of the last past years.

On the other hand, the Trilogue Agreement succeeded to introduce the right measures that follow from the wide ethical consensus on the present issue, namely in what concerns:

- **the need for Ethics Committees;**
- **and strong requirements for Informed Consent.**

3. The Clinical Trials Regulation: an ethical perspective

In what concerns Ethics Committees

- **definition of an ethics committee** (A2, 10a)**;**
- **Member States are the only responsible to organise the involvement of the ethics committees** (R14)**;**
- **research projects should be reviewed from the ethical point of view before being conducted** (R25aa)**;**
- **ethical review, from ethics committees, becomes a prior requirement for a clinical trial authorization** (A4)**;**
- **the ethics committee advice is binding** (A8, 3a; A14, 9a; A20, 6a; A23, 6a)**;**
- **there are ethical and scientific quality requirements for good clinical practice** (A2, 26)**.**

3. The Clinical Trials Regulation: an ethical perspective

In what concerns Informed Consent

- **Prior to informed consent: information in a prior interview in a clear language, opportunity to ask questions, and time to consider the decision taken** (R24);
- **consideration of specific situations that might affect a free decision making** (R24a);
- **additional requirements in case of minors and incapacitated subjects, an authorisation or agreement from their legally designated representative to include them in the trial** (A2, 19);
- **minimal burden** (A28ea);
- **no undue influence including that of a financial nature** (A28ed);

3. The Clinical Trials Regulation: an ethical perspective

In what concerns Informed Consent

- **special attention paid to the information needs of individual subjects and specific patient populations, as well as to the methods used to give the information** (A28, 2b);
- **confirmation that the information was understood** (A28, 2c);
- **detailed specification of the duly information** (A29,2);
- **involvement of a minor capable of assenting** (A29,3b);
- **CT on incapacitated subjects and on minors the direct benefit outweighing the risks and burdens** (A30,1h(i); A31,1h);
- **enlargement of the vulnerable populations explicitly considered, such as pregnant and breastfeeding women** (A31a) **and others** (A31b);
- **additional safeguards to CT in emergency situations** (A32).

Thanks