

Clinical Trials Directive (2001/20/EC)

Publication on 1 April 2001, Implementation on 1 May 2004

In Germany 12. AMG-Novelle since August 2004

Purpose

- to simplify and harmonise the administrative provisions governing clinical trials in the European Community
- to design, conduct, record and report clinical trials according to internationally recognized principals of Good Clinical Practice (GCP)
- to protect clinical trial participants
- to generate accurate and verifiable data from trials

What kind of clinical trials will be included by the Directive?

- investigations / studies which are undertaken to ascertain the efficacy or safety of a medicinal product in human subjects; non-interventional trials are excluded (e.g. studies that involve products with a marketing authorisation)
- the comments to the Directive specifically mention non-commercial clinical trials conducted by researchers without participation of the pharmaceutical industry

The Regulations provide a statutory basis for

- standardisation of procedures for ethical and competent authority consideration and authorisation
- Good Clinical Practice (GCP) standards for commencing and conducting clinical trials
- Good Manufacturing Practice (GMP) standards for medicines used in clinical trials
- inspections against internationally accepted principles and standards of GCP and GMP, supported by enforcement powers

Important definitions

- **Investigational medicinal product:** a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an

unauthorised indication, or when used to gain further information about the authorised form.

- Investigator: a doctor or person following a profession agreed in the Member State for investigations due to of the scientific background and the experience in patient care it requires. The investigator is responsible for the conduct of the clinical trial at a trial site.
- Sponsor: an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.
- In investigator initiated studies the investigator is also sponsor of the trial!

Some important changes according to the Directive

- Interventional clinical trials have to be entered into EudraCT: EudraCT is a database of all interventional clinical trials of medicinal products in the Community, where both the submission to the Ethics Committee and to the Competent Authority occur on or after 1 May 2004. A sponsor portal is available which gives the sponsor access to the EudraCT application in order to get a EudraCT number as well as access to supporting documentation. The sponsor portal is available at <http://eudract.emea.eu.int>.
- The sponsor may not start a clinical trial until the Ethics Committee has issued a favourable opinion and until the competent authorities gave their acceptance for the trial. For multicenter clinical trials the approval of a single Ethic Committee per Member State is necessary.
- After the commencement of the clinical trial, the sponsor shall notify the competent authorities and inform the Ethics Committee about any amendment to the protocol.
- All manufacturers of investigational medicinal products (IMPs) used in clinical trials must hold a manufacturer`s authorisation. The new manufacturer`s authorisation is required for any relating clinical trial materials including assembling, blinding, and importation. Each medicinal product has to be manufactured in accordance with Good Manufacturing Practice (GMP).
- All adverse events have to be recorded by the investigator, and all suspected serious unexpected adverse events have to be reported to the Ethics Committee and the competent authorities by the sponsor.

- To verify compliance with good clinical and manufacturing practice, inspections of the clinical trial and manufacturing sites shall be conducted by the competent authorities.

Links for detailed information

- The rules governing medicinal products in the European Union:
<http://pharmacos.eudra.org/F2/eudralex/index.htm>
- Implementing texts for Directive 2001/20EC:
<http://pharmacos.eudra.org/F2/pharmacos/dir200120ec.htm>
- Good Clinical Practice Guidelines:
<http://www.emea.eu.int/pdfs/human/ich/013595en.pdf>
- Sponsor portal for EudraCT application:
<http://eudract.emea.eu.int>