Legal aspects of clinical research

15 May 2021

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Summary

- Applicable legislation
- Terms and definitions
- Involved actors
- Main principles for experiments under the law of 2004
- Other studies

Applicable legislation

Law of 7 May 2004 concerning experiments on the human person (LEHP)

> Directive 2001/20/EG → **Clinical Trials Regulation** EU536/2014

Law of 7 May 2017 concerning experiments with Investigational Medicinal Products (IMP) in humans

Law of 22 december 2020 concerning medical devices

Law of 19 december 2008 concerning Human Bodily Material

2013: art 22 concerning biobanks

RD 8 january 2018 concerning biobanks

GDPR: Regulation EU2016/679

Terms and definitions

‘Experiment’: each trial, study or research which aims to obtain knowledge about the execution of health care professions as set out in the RD nr 78 (now law on health care professions of 10 May 2015)

Knowledge of health care professions → in HUMAN

→ **'the human person'** :

the person born, living and viable.

Experiments with embryos in vitro, with body material or corpses do not fall within the scope of the Law of 7/5/2004.

Terms and definitions

‘clinical trial’: any investigation in **human subjects** intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more **investigational medicinal product(s),** and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. (art 2, 7° LEHP)

Subcategory: clinical trials with IMP

Fase I – II – II - IV

Terms and definitions

Investigational medicinal product (IMP): a pharmaceutical form of an active substance or a placebo examined or used as a reference in a clinical trial, including a medicinal product authorised for placing on the market but used or formulated (formulated or packaged) in a manner other than the authorised form, used for an unauthorised indication or used to obtain further information on the authorised application

Retrospective (existing data) vs **prospective** (collection of new data)

→ The law of 7 May 2004 is NOT applicable on retrospective studies

Terms and definitions

Interventional vs non-interventional:

‘non-interventional trial’: a study where the medicinal product(s) is (are) **prescribed in the usual manner** in accordance with the terms of the marketing authorisation. The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within **current practice** and the prescription of the medicine is clearly separated from the decision to include the patient in the study. **No additional diagnostic or monitoring procedures shall be applied to the patients** and epidemiological methods shall be used for the analysis of collected data;

Terms and definitions

‘mono-center vs multi-center:

‘multi-centre clinical trial’: a clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator

‘mono-centre clinical trial’: a clinical trial conducted in one single site

Actors

‘investigator’: a health care worker (cfr law HCP) who is **responsible** for the conduct of a study at a study site.

If a trial is conducted by a **team** of individuals, the investigator is the leader responsible for the team and may be called the **principal investigator** – other investigators can be called **subinvestigators**

‘subject’: the human person who participates in the study

Actors

'sponsor': an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a study

→ **Commercial trial:** the Sponsor is a commercial company (mostly pharmaceutical companies)

→ **Non-Commercial trial:**

- → the Sponsor is an academic institution
- → the holder of the patent of a medicinal product or of a registered trade mark of a medical device to which the experiments relate is neither directly nor indirectly the sponsor of the experiment;
- → the sponsor exercises intellectual property rights over the concept of an experiment, its implementation and the resulting scientific data;

Which law applies?

Depending on the type of the study:

- all experiments on the human person, except retrospective research on pre-existing data → Law of 7/5/2004
- IMP-studies ('clinical trials') → Law of 7/5/2004 and 7/5/2017 + **Clinical Trials Regulation** EU536/2014
- device-studies → Law of 20/12/2020
- Study on HBM without any impact for the donor → Law of 19/12/2008 conc. HBM
- any study or experiment with not anonymized personal data → GDPR

Main principles for experiments (law 2004)

Requirements for the conduct of an experiment (art 5):

1° the experiment is **scientifically justified** and based on the latest state of scientific knowledge and on an adequate preclinical experiment;

2° the aim of the experiment is to **increase the knowledge** of the human person or of the means which can improve his condition;

3° there is **no alternative method** whose effectiveness is comparable and which makes it possible to achieve the same results;

Main principles for experiments (law 2004)

4° the **foreseeable risks and disadvantages**, in particular of a physical, psychological, social and economic nature, were **weighed** against the individual **benefit** to the participant as well as to other human persons, including their right on **physical and psychological integrity**, as well as their right on respect for their privacy and the **protection of personal data**;

→ Reference to ICH/GCP

→ Reference to privacy laws (GDPR)

Main principles for experiments (law 2004)

5° the evaluation leads to the decision that the **expected therapeutic and public health benefits outweigh the risks**. The experiment may be continued only in so far as compliance with that requirement is continuously **monitored**; **the interests of the participant always take precedence** over the interests of science and the community;

→ Constant monitoring and follow-up of side effects

Main principles for experiments (law 2004)

Serious Adverse Events (SAE's) and Suspected Unexpected Serious Adverse Reactions (SUSAR's).

SERIOUS:

- → deadly or
- → life-threatening or
- → requires (prolongation of) hospitalization or
- → permanent or significant disability or incapacity for work

UNEXPECTED:

a side effect whose nature or severity does not correspond to the information on the experiment and, in the case of a test, to the information on the product

→ mandatory notification to EC and FAHMP

Main principles for experiments (law 2004)

6° the Protocol was subject of a favorable opinion of a fully recognized Ethics Committee and, where required by Law, of the minister's admission in accordance with the provisions of Article 12;

- → Written Protocol
  - → Methodology
  - → Statistic analysis
  - → Organization of the experiment
- → EC Review (‘favorable opinion’)
- → FAHMP: IMP + devices

Main principles for experiments (law 2004)

Review by the EC:

- the relevance of the experiment and its design;
- the adequacy of the assessment of the expected benefits and risks as well as the merits of the conclusions, in particular at therapeutic level and on public health;
- the Protocol;
- the competence of the investigator and his staff;
- the investigator's file;
- the suitability of the facilities;

Main principles for experiments (law 2004)

- *ICF*
- *Compensation of damage suffered by the participants*
- *Insurance of Sponsor*
- payment and compensation of the researchers and participants, as well as the relevant elements of each agreement between the client and the location;
- the method of selection of the participants;
- If applicable: the objectives and activities of the biobank associated with the experiment

Review within strict timelines

Law 2004 vs 2017

Main principles for experiments (law 2004)

7° without prejudice to the application of the provisions of Articles 6 to 9, the person taking part in the experiment, or his representative, has given his **consent** and has a contact point where he can obtain more information;

→ Informed consent

- Informed:
  - Clear and understandable (language!)
  - Oral explication and answers on questions
  - By investigator or member of the research team
- Free:
  - Without any pressure
  - Withdrawal at any moment without disadvantages
- Prior to start - In writing
- signed by participant or legal representative

Main principles for experiments (law 2004)

8° the concerns provided to participants and the decisions taken concerning them are the responsibility of a **qualified practitioner** in accordance with the provisions of Royal Decree No 78 of 10 November 1967 on the exercise of the **healthcare professions**;

→ RD nr 78 → Law 2015 concerning healthcare professions

→ PI = healthcare professional

Main principles for experiments (law 2004)

9° the **insurance** and coverage of the **liability** of the investigator and the sponsor shall be organized in accordance with the provisions of Article 29.

→ no-fault liability of Sponsor

→ Insurance coverage

Studies outside the Law of 2004

Devices: law of 2020

- Similar principles

Biobanking studies

- On (leftover) human bodily material
- No risks for the patient
- Law 2008 HBM and biobank

Retrospective studies

- Not under law 2004
- Ethics review required for publication
- ICF required for GDPR

???

Questions?

Thank you for your attention!

Good luck with your future research projects!