VELFERÐARRÁÐUNEYTIÐ

Ministry of Welfare

REGULATION
on clinical trials of medicinal products in humans, No. 443/2004,
as amended by Regulations No. 907/2004 and No. 1099/2010.

CHAPTER I
General provisions.
Article 1
Scope.

This Regulation shall apply to clinical trials in humans.

It shall not apply to medical experiments on individual patients or non-interventional trials.

This Regulation lays down specific provisions concerning the implementation of clinical trials of medicinal products, including multi-centre trials in humans, in particular concerning the implementation of Good Clinical Practice (GCP) in studies on medicinal products.

Concerning processing of personal data in connection with clinical trials, Act No. 77/2000, on the Protection of Privacy as regards the Processing of Personal Data, shall apply insofar as specific provisions of this Regulation do not take precedence.

The arrangements for and implementation and reporting of all clinical trials of medicinal products, including studies of bioavailability and bioequivalence, must comply with the principles of Good Clinical Practice.

[The production and import of medicinal products for clinical trials (investigational medicinal products) shall comply with the provisions of the Regulation on the manufacturing of medicinal products and the Regulation on import and wholesale distribution of medicinal products, as subsequently amended.][1)]

[1)] *Regulation No. 907/2004, Article 1.*

Article 2
Definitions.

For the purposes of this Regulation the following terms shall have these meanings:

a. *Medicinal products:* Medicinal products are substances or compounds covered by the definition of the concept of medicinal products in Article 5 of the Medicinal Products Act, No. 93/1994, as subsequently amended.

[b. *A clinical pharmaceutical study:* A systematic testing of a medicine with the purpose of finding or confirming its effects and/or finding the side effects of the medicine and/or absorption, circulation, metabolism and the excretion of the drug with the purpose of checking its security and functionality.][1)]

c. *Good Clinical Practice (GCP):* A standard for designing, directing, conducting, supervision, recording of data and reporting of results of clinical trials, which ensures that the data and interpretation of results of the trials are credible and accurate and that the rights, safety and welfare of subjects are respected.

d. *Multi-centre clinical trial:* A clinical trial taking place concurrently in more than one location according to the same clinical trial protocol.

e. *Investigator:* a physician or dentist authorised to carry out a clinical trial. If only one investigator is involved in a clinical trial of a medicinal product he/she is also regarded as the principal investigator, *cf.* item f.
f. *Principal investigator:* The investigator responsible for the implementation of a clinical trial of a medicinal product at each research centre. In certain instances the principal investigation may also be a sponsor, *cf.* item i.
g. *Supervisor of the trial:* The principal investigator who co-ordinates implementation of clinical trials on medicinal products in the Icelandic centres involved in a multi-centre trial.
h. *Subject:* an individual participating in a clinical trial of a medicinal product, either as the recipient of the trial product or as part of the control group.
i. *Sponsor:* An individual, company, institution, organisation or enterprise whose role is to initiate, manage and/or finance a clinical trial of a medicinal product. If no sponsor is connected to the study, the principal investigator shall perform this role.
j. *Monitor:* The person who monitors the normal progress of the trial, ensuring that it is carried out in all respects according to the clinical trial protocol, standardised procedures, current guidelines on good clinical practice, and Icelandic laws and regulations.
k. k *Clinical trial protocol:* A document stating the objectives, arrangement, methodology, statistical methods and organisation of a clinical trial of a medicinal product.
l. *Investigator's brochure:* A summary of clinical and pre-clinical data on the trial medicinal product of significance for a clinical trial of the product in humans.
m. *Informed consent:* Written consent give voluntarily after the individual participating in a clinical trial of a medicinal product has been informed, for instance, of its nature, significance, consequences and potential risk. The individual in question must be capable of granting consent or a party who is legally competent to do so must provide this on the person's behalf. If the person is not capable of writing, oral consent given in the presence of witnesses may be provided in exceptional cases.
n. *Inspection:* Action on the part of a public authority consisting of an official review of documents, facilities, records, quality assurance, and all other aspects considered by the public authority to be connected with the clinical trial of a medicinal product and which may be located at a study centre, a sponsor's establishment and/or a laboratory working under contract, or other locations which the public authority deems necessary to inspect.
o. *Adverse event:* Any undesirable medical event experienced by a subject in a clinical trial and not necessarily causally connected with that treatment.
p. *Adverse reaction:* All undesirable, unintentional effects of the dosages of the trial medicinal product used.
q. *Serious adverse event or serious adverse reaction:* A damaging or unexpected reaction or effect where any dosage is fatal, life-threatening, disabling or incapacitating, results in a congenital defect or results in or prolongs hospitalisation.
r. *Unexpected adverse reaction:* An adverse reaction which, in terms of its nature, severity or consequences, is not as mentioned in the investigator's information brochure on the trial medicinal product or the summary of product characteristics (SPC);
s. *Non-interventional trial:* A study where the medicinal product or products are prescribed in a normal manner in accordance with the terms of its marketing authorisation. Treatment of the patient is not pre-determined by a clinical trial protocol, but rather follows current practice. The instructions concerning the medicinal product are clearly separated from the decision that the patient shall take part in the trial. No supplementary analyses or supervision shall be carried out in treating the patient and epidemiological methods used in analysing the data collected.
[*t.* *Investigational medicinal product (test 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 (specially 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.][2)]

[u. *Investigator´s brochure:* A synopsis of clinical and non-clinical data on the investigational medicinal product or the investigational medicinal products, relevant to the study of the its or their functionality in human beings.][1)]

[1)] Regulation No. 1099/2010, Article 1. [2)] Regulation No. 907/2004, Article 2.

Article 3

Multi-centre trials.

Multi-centre trials in Iceland must have a trial supervisor responsible for co-ordinating the centres involved in the trial in question.

When more than one Icelandic centre is involved in an international multi-centre trial, there must be a trial supervisor for the Icelandic centres.

Article 4

Responsibility.

The principal investigator or, as the case may be, the investigator shall be responsible for the trial in question and for the reports and notifications which are to be submitted as provided for in Articles 29–33, as appropriate, *cf.* however Article 30. The principal investigator or, as the case may be, the investigator shall be responsible for the selection, treatment and supervision of subjects. The principal investigator or, as the case may be, the investigator, and the sponsor signing the application for a clinical trial shall be responsible for ensuring that the trial is carried out in accordance with currently applicable rules. The trial supervisor bears this responsibility in multi-centre trials, with the exception of notification of adverse events, for which the investigators and principal investigator shall be responsible.

When a clinical trial is carried out in co-operation with a sponsor, the sponsor is obliged to take part in preparing the reports and notifications which must be submitted.

[A sponsor is authorised to entrust an individual, enterprise, institution or organisation to carry out his/her activity, in whole or in part, that relate to studies. In such instances, he/she will continue to be responsible for ensuring the implementing arrangements of the study and that the final data, the product of the study, are in accordance with the provisions of this Regulation.

A sponsor is required to assess and upgrade the investigator´s brochure at least once a year.][1)]

[1)] Regulation No. 1099/2010, Article 2.

Article 5

Insurance.

Subjects participating in a clinical trial of a medicinal product must be sufficiently insured against conceivable damage to their health resulting from the trial.

The principal investigator or, as the case may be, the investigator shall be responsible for ensuring satisfactory insurance coverage.

Article 6

Ethical assessment.

All clinical trials of medicinal products must be subject to a scientific and ethical assessment before commencing. This assessment shall be entrusted to the National Bioethics Committee, *cf.* Article 2 of the Act on the Rights of Patients, No. 74/1997, and the Regulation on Scientific Research in the Health Sector, No. 552/1999, or the ethics committee of the institution concerned. [Clinical information and other available investigational medicinal product shall be sufficient to endorse scheduled clinical study.][1)]

A request for assessment by the National Bioethics Committee or, as the case may be, the ethics committee of the institution concerned, must be accompanied by the following documentation:

a. A completed application form.
b. The trial protocol, *cf.* Article 9.
c. Additional information on other aspects connected with the trial, *cf.* Article 10.
d. Information on the trial medicinal product and comparable medicinal products, *cf.* Article 11.
e. A copy of the application to the Icelandic Medicines Agency and a copy of the information to participants and informed consent, *cf.* Article 18.

f. A copy of the confirmation of insurance, *cf.* Article 5.

The application must be signed by the principal investigator. If the application is made at a hospital or other health care institution, a head physician or director of the ward or institution must also sign the application. If the trial is carried out in cooperation with a sponsor, the sponsor's representative must also sign the application.

In preparing its assessment, the National Bioethics Committee or, as the case may be, the ethics committee concerned, shall have regard in particular to the following:

a. The value and arrangement of the clinical trial of a medicinal product.
b. Whether the assessment of the intended benefits and risks involved is satisfactory and whether the conclusions are well-founded.
c. The trial protocol.
d. The qualifications of the investigator/principal investigator and his/her assistants.
e. The investigator's brochure. [The information shall be presented in an incisive, simple, impartial and calm way, without an advertising value, so that it is understandable and possible to assess in an unbiased way an advantage in relation to the rightfulness of a scheduled clinical study. If the investigational medicinal product has a marketing authorisation, it is authorised to apply a synopsis of the properties of the medicine instead of an investigator´s brochure.][1)]
f. The quality of the facilities.
g. Whether the written information provided is satisfactory and exhaustive, and whether the procedures to be followed in obtaining informed consent and the grounds given for study of individuals who are incapable of granting their informed consent are satisfactory, having regard to the special limitations prescribed in Article 19.
h. Whether provisions have been laid down for insurance or compensation if the clinical trial results in injury or death.
i. Insurance or compensation to cover the liability of the investigator and sponsor for compensation.
j. The amount and, as applicable, the means of compensation to the investigators and subjects and what conceivable right to compensation they have.
k. Arrangements for enrolment of subjects.

The ethics committee in question shall have a maximum of 60 days from the date it receives a valid application to deliver a reasoned opinion to the applicant and the Icelandic Medicines Agency.

The ethics committee in question may make one request for additional data after it receives a valid application; the application process shall be suspended until the committee receives the data requested.

The 60-day time limit provided for in paragraph 3 may not be extended except in instances concerning medicinal products for gene therapy or somatic cell therapy or medicinal products containing genetically modified organisms. In such instances the time limit may be extended by a maximum of 30 days. If the ethics committee concerned considers it necessary to consult with other groups or committees, it may extend the time limit to as long as 180 days from the receipt of a valid application. In the case of xenogenic cell therapy there shall be no set time limit for an assessment of the application.

If the ethics committee in question intends to extend the afore-mentioned time limit, it must notify the applicant of its intention.

The provisions of paragraph 1of Article 15 shall apply to all modifications which may affect the security of subjects or the results of the trial, or which may be significant in other respects.

[The ethics committee in question shall keep essential instruments in relation to clinical studies for at least 3 years after the end a study.][1)]

[1)] Regulation No. 1099/2010, Article 3.

Article 7

Personal data protection.

Notice of all clinical trials of medicinal products must be sent to the Personal Data Protection Authority before they commence, as provided for in the Act on the Protection of Privacy as regards the Processing of Personal Data, No. 77/2000, as subsequently amended, and rules set by the Personal Data Protection Authority based on this Act concerning notification obligations and authorisation requirement for processing personal data.

CHAPTER II

Application for a clinical trial of a medicinal product.

Article 8

Application for a clinical trial of a medicinal product.

An application for a clinical trial of a medicinal product shall be sent to the Icelandic Medicines Agency and the ethics committee concerned, but does not necessarily need to reach both these parties at the same time.

An application to the Icelandic Medicines Agency for authorisation to conduct a clinical trial must be accompanied by the following documentation:

a. A completed application form.
b. The trial protocol, *cf.* Article 9.
c. Additional information on various aspects connected with the trial, *cf.* Article 10.
d. Information on the trial medicinal product and control medicinal products, *cf.* Article 11.
e. A copy of the application to the ethics committee concerned.
f. A copy of the Information to Participants and Informed Consent, *cf.* Article 18.
g. A copy of the confirmation of insurance, *cf.* Article 5.

The application must be signed by the principal investigator. If the clinical trial is carried out at a hospital or other health care institution, a head physician or director of the ward or institution must also sign the application. If the trial is carried out in cooperation with a sponsor, the sponsor's representative must also sign the application.

A multi-centre trial is regarded as a single trial. In the case of multi-centre trials, a single application shall be sent to the Icelandic Medicines Agency, signed by the trial supervisor. The application shall also be accompanied by supplementary application forms for each centre in Iceland, signed by the principal investigator in each case.

The trial protocol must specify whether the trial is part of an international trial.

The Icelandic Medicines Agency can provide further instructions on completing application forms and accompanying documentation.

The application form must indicate the number assigned to the applicants for registration of the trial in a European database for clinical trials. This number should henceforth be used in all communications with the Icelandic Medicines Agency.

Article 9

Trial protocol.

A trial protocol must be prepared for all clinical trials of medicinal products. The trial protocol shall include the following:

a. The background and objective of the trial.
b. Subjects.
c. Design of the trial.
d. Premises for selection of the sample (admission and exclusion criteria).
e. Treatment programme.
f. Control groups and their treatment.
g. Statistical methods and premises concerning the size of the sample.
h. Registration of the effects of the medicinal product and adverse events.
i. Tests to ensure the safety of subjects.
j. Interpretation of results.
k. Quality assurance of data and methods.
l. Ethical assessment.
m. Control of supplies of the medicinal product.

If the trial is carried out in co-operation with a sponsor, an account must be given as to how this trial fits into the overall development of the medicinal product concerned.

Article 10

Additional information on the trial.

In addition to the documentation already mentioned as part of a trial protocol, the Icelandic Medicines Agency must also be sent information on: