1. INTENT

The procedure establishes the rules that guide the activities of analysis and elaboration of the response of the Scientific Research Ethics Commission.

2. FIELD OF APPLICATION

The procedure applies to all studies/projects subject to the approval of the Scientific Research Ethics Commission.

3. DEFINITIONS

Scientific Research Ethics Commission (CECS): independent body, made up of members from the medical, scientific and non-medical fields whose responsibility is to ensure the protection of the rights, safety and comfort of the subjects involved in the study;

Human subject: Participant in a study for whom the rights, benefits and risks associated with inclusion have been explained, followed by the signing of an inclusion agreement in accordance with applicable legislative regulations.

Experimental animals: live non-human vertebrate animals, including self-feeding larval forms and mammalian fetal forms from the last third of their normal developmental stage; living cephalopods.

Clinical study: any investigation carried out on human subjects, to discover or confirm the clinical, pharmacokinetic/pharmacodynamic/pharmacotoxicological effects associated with their exposure within therapeutic interventions, carried out at an institutional level.

Protocol: document describing the objective(s), design, methodology, statistical aspects and organization of the study; the term "protocol" covers the protocol, its successive versions and its amendments.

Project: a work program with defined scientific objectives, which involves the use of one or more procedures.

Procedure (experimental): any use, invasive or non-invasive, of the animal for experimental or other scientific purposes, with known or unknown results or for educational purposes, which may cause the animal a certain level of pain, suffering, stress or lasting injury equivalent to or even stronger than that caused by the insertion of a needle, in accordance with good veterinary practice; any action aimed at or likely to result in the birth or hatching of an

animal or the creation and maintenance of a line of genetically modified animals under any of these conditions is included, but the killing of animals for the sole purpose of using their organs or tissues is excluded.

Amendment to the protocol: - a written presentation of the amendment/amendments to the protocol or an official explanation thereof.

Opinion: - the affirmative decision of the Ethics Commission by which it confirms that the necessary documents have been analyzed and that the clinical study can be carried out in the proposed institution because there are appropriate conditions, the rules of good practice in the clinical study and the legal regulations in force are respected.

Investigator's brochure: set of clinical or non-clinical data on the drug or drugs for clinical investigation and which are relevant to the study of the effect of these drugs in humans.

Informed consent: the decision to participate in a clinical trial, which must be written, dated and signed, made voluntarily, after receiving all necessary information about the nature, significance, consequences and possible risks, such as and the necessary documentation, of a person capable of giving consent or, in the case of a person who is unable to do so, by his legal representative; if the person involved is not able to write, he can, in exceptional cases provided by national legislation, give his consent verbally in the presence of at least one witness.

The investigator: a doctor or a person practicing an approved profession in Romania in order to conduct clinical trials according to the legislation in force, based on the scientific knowledge and experience in the field of patient care that this requires; the investigator is responsible for the conduct of the clinical trial in a center, and if, in a center, the trial is conducted by a team, the investigator is the team leader and may be named the principal investigator.

Applicable legal regulations: any laws and regulations that relate to the conduct of clinical trials for the investigation of a medicine.

Clinical trial best practice: a standard by which the clinical trial is designed, conducted, conducted, monitored, audited, recorded, analyzed and reported, which guarantees both the credibility and correctness of the data and results reported, and the fact that the rights and integrity of the subjects as well as their confidentiality are protected.

Non-interventional study: the study in which the medicinal product or medicinal products are routinely prescribed in accordance with the terms of the marketing authorization; the patient's use of a given therapeutic strategy is not fixed in advance by a study protocol, but is subject to current practice, and the decision to prescribe the drug is clearly separated from that of including the patient in the study; no additional diagnostic or surveillance procedures should be applied to patients, and epidemiological methods are used to analyze the collected data.

Non-clinical study: biomedical study that is not conducted on human subjects.

4. REFERENCE DOCUMENTS

European Charter of Human Rights (2010);

Law no. 206/2004 on good conduct in scientific research, technological development and innovation, updated;

The European Charter of the researcher and the Code of Conduct for the recruitment of researchers (Recommendation 2005/251/EC);

Law no. 95/2006 regarding health reform, with subsequent amendments and additions;

Order of the Minister of Public Health no. 905/25.07.2006 on the approval of the Principles and guidelines of good manufacturing practice for medicinal products for human use, including those for clinical investigation

Order of the Minister of Public Health no. 904/25.07.2006 for the approval of the Norms relating to the implementation of the rules of good practice in the conduct of clinical trials conducted with medicinal products for human use

Order of the Minister of Public Health no. 903/25.07.2006 for the approval of the Principles and detailed guidelines on good practice in the clinical trial for medicinal products for human use for clinical investigation, as well as the requirements for the manufacture and import of these medicinal products;

Declaration of Helsinki (2013);

Law no. 43/2014 on the protection of animals used for scientific purposes, with subsequent amendments and additions transposing the provisions of Council Directive 63/2010/EU on the protection of animals used for scientific purposes

ANSVSA Guide 2017 – regarding the method of sanitary and veterinary authorization of projects involving the use of animals in procedures

Order no. 143/400 of the Ministry of Agriculture, Food and Forests and of the Ministry of Water and Environmental Protection, for the approval of the Instructions regarding the housing and care of animals used for scientific or other experimental purposes;

Law no. 319/2003, with subsequent amendments and additions, regarding the Statute of the researcher;

National Education Law no. 1/ 2011, with subsequent amendments and additions.

5. PROCEDURE DESCRIPTION

5.1. Overview

5.1.1. The Scientific Research Ethics Commission (CECS) has as its main objective the supervision of the observance of ethical principles in scientific research carried out on human subjects and experimental animals and the promotion of scientific research in this spirit.

5.1.2. The Scientific Research Ethics Commission has the role of monitoring good conduct in scientific research.

5.2. Obtaining the approval of the Scientific Research Ethics Commission

5.2.1. Before starting a research, the investigator must have the favorable, written opinion of the CECS, specifying the date of issuance of the opinion, for the study in question.

5.2.2. In order to analyze for issuing an opinion, the Scientific Research Ethics Commission of UMF "Carol Davila" must receive the following:

I. Human subjects

a) Application for issuing the opinion of the Scientific Research Ethics Commission;

b) the study protocol and any amendments;

c) the informed consent form;

d) procedures for recruiting subjects;

e) the written information that will be provided to the subjects;

f) the investigator's brochure;

g) the available information regarding the safety of the methods and products to be used (e.g. the administration of some medicines);

h) information about the payments and compensations available to the subjects (if applicable);

i) updated curriculum vitae of the investigator or investigators and/or other documents proving his/her qualification;

j) any other documents necessary for the CE to fulfill its responsibilities and to be able to carry out the analysis in the shortest possible time.

II. Experience animals:

a) the request for issuing the opinion of the Scientific Research Ethics Commission;

b) the use of animals, including the origin of the animals needed, the estimated number, species and life stages;

c) experimental procedures;

d) Application of replacement, reduction and improvement methods in the case of procedures on animals;

e) Planned use of anesthesia, analgesia and other pain relief methods;

f) Reducing, avoiding and alleviating any form of animal suffering from birth to death, as the case may be;

g) Use of human endpoints;

h) Experimental or observational strategy and statistical design in order to minimize the number of animals, pain, suffering, stress and impact on the environment, where appropriate;

i) The reuse of animals and the cumulative effect on animals;

j) The proposed classification of the severity of the procedures;

k) Avoiding unjustified duplication of procedures, where applicable;

l) Housing, breeding and care conditions for animals;

m) Methods of euthanasia;

n) Competence of the people involved in the project.

5.2.3. The application for analyzing the file will be registered at the university registry.

5.2.4. The application and the documents mentioned above can be submitted as such or can be scanned and sent by email to the address: etica.cercetare@umfcd.ro.

5.2.5. From the moment of receipt of the documentation, it will be initially analyzed as completeness, in an interval of no more than 30 days.

5.2.6. The documentation will be sent to the members of the research ethics committee for analysis and the expression of opinion regarding the documents presented and the Checklist of meeting the conditions of the Scientific Research Ethics Committee will be used;

5.2.7. If the documents are complete and no other documents and clarifying explanations are requested, their analysis must take place within a maximum of four weeks.

5.2.8. Approval of the study is achieved if half plus one of the members give a positive vote. The vote can be expressed directly, in the meeting, or by email.

5.2.9. The investigator will be able to receive the opinion as a scanned document, by email, or in the way he needs to have it in the records of the project file. The investigator will ensure that at the moment of the appearance of any changes to the documents submitted to obtain the opinion of the scientific research ethics committee, they will be brought to the notice of the committee, with speed.

6. RESPONSIBILITIES

6.1. Scientific Research Ethics Commission

6.1.1. Supervision of compliance with ethical principles in scientific research carried out on human subjects and experimental animals and promotion of scientific research in this spirit;

6.1.2. Protecting the rights, safety and well-being of study participants and assuring the public of this protection, in particular by formulating an opinion on the study protocol, the skills of the investigators and the adequacy of the facilities, as well as

on the methods and documents that should be used to informing study participants, in order to obtain their informed consent;

6.1.3. Monitoring good conduct in scientific research;

6.1.4. Approval based on the regulations in force of projects, studies, procedures involving human subjects and/or experimental animals;

6.1.5. Ensuring the support related to the documentation necessary for the approval of projects, studies, procedures involving human subjects and/or experimental animals;

6.1.6. Monitoring the implementation of positively approved projects, studies, procedures involving human subjects and/or experimental animals. Analyzes the initial documentation received in no more than two weeks and the complete one in no more than four weeks;

6.1.7. Formulating a response based on the documentation received/requested completions, with clear identification of the study. The resolution may fall into one of the following categories:

- Approved
- Approved, after making the changes proposed by the Commission;
- Not approved.

6.1.8. CECS grants you the right to decline its issued opinion, in case of non-compliance with the ethical principles and/or the legislative norms in force.

6.2. The investigator

6.2.1. Must have the written favorable opinion, specifying the date of issue for the study;

6.2.2. Responds to the commission's requests and submits to it all the additional documents requested, in order to obtain the opinion.

6.2.3. He must bring to the attention of the Scientific Research Ethics Commission any changes to the documents submitted to obtain the opinion of the Scientific Research Ethics Commission.

6.3. Registry office

6.3.1. Register the Request for issuing the opinion of the Scientific Research Ethics Commission

6.3.2 Record the Opinion of the Scientific Research Ethics Commission

7. FINAL PROVISIONS

The CECS meets for specific issues, without having an established periodicity, whenever necessary, at the call of the president or any member and is legally constituted if half plus one of the total number of commission members are present. Communication between committee members is usually done by e-mail.

8. APPENDICES AND RECORDS

ANNEXES

a) Annex 1 – Distribution list of the procedure;

RECORDS

a) Application for the issuance of the opinion of the Scientific Research Ethics Commission code PO-35-F-01;

b) Checklist for meeting the conditions of the Scientific Research Ethics Commission code PO-35-F-02;

c) The opinion issued by the Scientific Research Ethics Commission code PO-35-F-03.

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