ISTINYE UNIVERSITY
SENATE MEETING

MEETING DATE	MEETING HOUR	SESSION NO
05/07/2018	10.00	13

ISTINYE UNIVERSITY
DIRECTIVE ON THE OPERATING PRINCIPLES OF THE ETHICS COMMITTEE FOR CLINICAL RESEARCH

SECTION ONE
Purpose, Scope, Legal Basis and Definitions

Purpose

Article 1 - (1) The purpose of the Ethics Committee is to protect the rights, safety and well-being of the volunteers involved in clinical trials, taking into account the scientific aspect of the research and the concerns of the society. The Ethics Committee provides timely, comprehensive and independent reviews of the ethical and scientific characteristics of the presented research by following the standards and the relevant legislation on good clinical practices, in accordance with the current Declaration of Helsinki. The Ethics Committee has the responsibility to act in accordance with the relevant regulatory authorities, the requirements of the relevant legislation, the applicants and the society.

Scope

Article 2 - (1) This Directive covers any type of invasive and non-invasive scientific research and activities presented to the Istinye University Ethics Committee.

Basis

Article 3 - (1) This Directive was prepared taking into account the general principles identified in accordance with the national and international legislation and agreements, the details of which are provided below:

a) Good Clinical Practice (GCP) Guidelines and the related European Union Directives.

b) World Medical Association Declaration of Helsinki.

c) Law on the Approval of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine.

d) Article 90 of the Turkish Penal Code No. 5237 which is published in the Official Gazette No. 25611 dated 12/10/2004.

e) Basic Law of Health Services No. 3359 which is published in the Official Gazette No. 19461 dated 15/05/1987.

f) Higher Education Law No. 2547 which is published in the Official Gazette No. 17506 dated 06/11/1981.

g) Regulation on the Clinical Trials of Pharmaceutical and Biological Products which is published in the Official Gazette No. 28617 dated 13/04/2013.

Definitions

Article 4 - (1) In this Directive,

a) Research protocol/plan: refers to the document detailing the purpose, design, methodology, statistical methods and organization of the research,

b) Sponsor: refers to the individual, institution or organization responsible for funding a research: refers to TUBITAK, SPO or the BAP units of universities or other non-commercial institutions and organizations,

c) Ethics Committee: refers to Istinye University Ethics Committee for Clinical Research,

d) Volunteer: refers to sick or healthy individuals taking part in the study upon the receipt of their or their legal representative's written consent,

e) Rector: refers to the Rector of Istinye University,

f) Secretariat: refers to the Secretariat of the Istinye University Ethics Committee for Clinical Research,

g) Senate: refers to the Istinye University Senate,

h) Lead researcher: refers to the person who has completed a residency training or doctorate degree in the field related to the research subject and is responsible for the execution of the research,

i) University: refers to Istinye University.

SECTION TWO
The Structure and Operating Procedures and Principles of the Istinye University Ethics Committee for Clinical Research

The method to be followed in the establishment of an Ethics Committee

Article 5 - (1) The following procedure shall be followed in the establishment of the Ethics Committee:

a) The Ethics Committee is established in line with the relevant legislation and the good clinical practices to perform a proper review of the submitted research protocols from an ethical and scientific point of view, ensuring that its members stay away from any prejudices and influences that may affect their impartiality.

b) The Ethics Committee is established upon the proposal of the rector and the approval of the Pharmaceuticals and Medical Devices Agency of Turkey, and begins its activities as of the date of this approval.

c) The application for establishing an Ethics Committee shall be made in accordance with the required information and documents published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey.

d) The Ethics Committee consists of a minimum of seven and a maximum of fifteen members, the majority of whom are healthcare professionals who are educated at a PhD or residency level.

e) Members who are healthcare professionals must have received basic training on good clinical practices and clinical research in accordance with the current legislation, before joining the Ethics Committee. Members who are not healthcare professionals must complete the basic training on good clinical practices and clinical research in accordance with current legislation as soon as possible after their appointment as an Ethics Committee member. These trainings must be repeated at appropriate intervals, and the certificates of achievement which are received at the end of the trainings must be renewed if that is requested by the Pharmaceuticals and Medical Devices Agency of Turkey.

(2) The Ethics Committee for Clinical Research has the following members whose minimum qualifications are stated below:

a) Specialist physicians/physicians who participated in international clinical trials that were ideally organized in accordance with the rules of good clinical practices, as researchers and who ideally have a diverse range of specialties.

b) A person who has a PhD in Pharmacology or received a medical specialty training in this field,

c) A person who has a PhD in biostatistics or a public health specialist or a medical doctor who has a PhD in this field,

d) A biomedical engineer or specialist, if such a person is not available, a biophysicist or physiologist,

e) A lawyer,

f) A person who is not a healthcare professional,

g) A person, if any, who has a PhD or received specialist training in medical ethics or deontology,

(3) In addition to the minimum level of members who are required to be in the Ethics Committee for Clinical Research, there may also be individual(s) who have completed a PhD degree in healthcare professions:

Conditions of appointment of the Ethics Committee members and the rules they must follow

Article 6 - (1) The conditions of appointment of the Ethics Committee members and the rules they must follow are as follows:

a) The term of office of the members of the Ethics Committee is two years.

b) Memberships are renewed every two years.

c) The memberships of those who do not attend three meetings in a row or five meetings in total without an excuse within their membership period shall automatically be terminated. In place of a member whose term of office expires or whose membership is terminated, a member with ideally the same qualifications shall be appointed.

d) If the term of office of any of the members who are required at a minimum level to be present in the Ethics Committee as per the relevant legislation, expires or if that member resigns from his post, a new member with the same qualifications must be appointed as of the date of the expiry or resignation. The Ethics Committee cannot operate and take decisions until the appointment is approved by the Pharmaceuticals and Medical Devices Agency of Turkey.

e) A person cannot be a member of more than one ethics committee.

f) At least three members of the Ethics Committee should have no affiliations with Istinye University.

g) The senior executives of the organization where the clinical research is conducted (Rector, Vice Rectors, Dean, the relevant Institute Manager or Center Manager, Chief Physician, Hospital Manager) cannot serve in the Ethics Committee.

(2) Membership of the Ethics Committee ceases when:

a) The term of office is completed.

b) A written statement of resignation is submitted.

c) It is understood and/or the member declares that s/he won't be able to attend any of the Ethics Committee meetings for a period over six months due to reasons such as overseas appointments and health problems.

d) The member does not attend three meetings in a row or five meetings in total without any excuses.

e) It is confirmed that the code of ethics is violated.

(3) If the Ethics Committee membership of a member expires or if the member resigns from his/her post, the document indicating the date that the relevant membership ended should be sent to the Pharmaceuticals and Medical Devices Agency of Turkey.

(4) The Ethics Committee members may serve more than one term if it is deemed appropriate.

(5) The Ethics Committee members should pay attention to the issue of conflict of interest.

(6) The Ethics Committee members are required to comply with the confidentiality principle for any information that they acquire and before they take office, they sign the confidentiality agreement and the covenant document which are published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey, and which are renewed every year and in case of any changes in the submitted statement, and sent to the Pharmaceuticals and Medical Devices Agency of Turkey.

(7) The records of the trainings that the Ethics Committee members received on good clinical practice and clinical trials in accordance with the current legislation should be stored.

Working procedures and principles of the Ethics Committee

Article 7 - (1) The working procedures and principles of the Ethics Committee are listed below;

a) The members of the Ethics Committee convene with a two-thirds majority of the total number of its members and decide by an absolute majority of the total number of members.

b) Following the establishment of the Committee upon the approval of the Pharmaceuticals and Medical Devices Agency of Turkey, members shall convene within

fifteen days, and elect a president, vice president and a member who shall serve in evaluations where notification is sufficient according to the relevant legislation, through a secret ballot from among themselves, and shall notify the election to the Pharmaceuticals and Medical Devices Agency of Turkey.

c) The vice president shall serve as the acting president in his/her absence.

d) Where required, the Ethics Committee shall receive the written opinions of individuals who are experts in the related field or the sub-field and may invite these individuals to the meeting as advisors. These individuals are also required to sign the confidentiality agreement and the covenant document which are published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey.

e) For any clinical trial to be conducted on children, the Ethics Committee cannot approve such trials without the positive opinion of a pediatrician for the research to be carried out on children. If deemed necessary for these studies, the opinion of the physician or dentist who has a PhD degree or received residency training in the related discipline is taken and the decision with regards to whether the research shall be approved or not is made based on this opinion. In addition, if there is a change in the research protocol or the consent form of the informed volunteer during these investigations, the Ethics Committee cannot approve such changes to be applied on children without the positive opinion of a pediatrician.

f) The Ethics Committee is informed by a physician who received his/her residency training in the area of the research, on clinical, ethical, psychological and social problems related to the research, particularly in terms of fetus or infant health, and the protocol is assessed accordingly.

g) A member of the ethics committee who is involved in or has a role in the research that is under review cannot participate in the discussions and voting related to this research in the Ethics Committee and cannot sign the related decision.

SECTION THREE
Ethics Committee Office and Secretariat

Ethics Committee Secretariat

Article 8 - (1) The Ethics Committee secretariat carries out its activities as follows:

a) The Ethics Committee corresponds directly with the Pharmaceuticals and Medical Devices Agency of Turkey or the sponsor or the sponsor's legal representative through its own secretariat on issues other than the change of members.

b) The receipt of applications to the Ethics Committee, informing the sponsor, the legal representative of the sponsor or the lead researcher, archiving the documents, conducting the necessary correspondences, organizing the meetings and other similar tasks are carried out by the secretariat of the Ethics Committee.

c) The personnel working for the Ethics Committee secretariat are required to comply with the confidentiality principle for any information that they acquire and before they take office, they sign the confidentiality agreement and the covenant document which the Pharmaceuticals and Medical Devices Agency of Turkey publishes on its website, and which are renewed every year and in case of any changes in the submitted statement, and sent to the Pharmaceuticals and Medical Devices Agency of Turkey.

d) The personnel working for the secretariat of the Ethics Committee should receive the necessary trainings, such as the training on fire extinction equipment, and keep records of such training.

e) If there are sufficient human resources at the University, the people working for the secretariat of the Ethics Committee are recommended to be dedicated personnel of the secretariat.

SECTION FOUR
Duties and Powers of the Ethics Committee; Acceptance of Applications and Decision

Duties and powers of the Ethics Committee

Article 9 - (1) The Ethics Committee carries out its activities as follows:

a) The Ethics Committee for Clinical Research informs the applicant on their opinion within the period specified in the relevant legislation for the concerned type of research.

b) For research to be conducted using products including genetically modified organisms and cellular therapies or gene therapy, the fifteen-day period identified for the ethics committee approval may be extended by an additional thirty-day period.

c) If additional information and clarifications are required during the review process of the Ethics Committee, all the required requests are forwarded to the applicant as a whole. The review process is suspended until the required information and documents are submitted to the ethics committee.

d) The Ethics Committee may monitor any clinical trial that it approved, with or without prior notice. In addition, the Pharmaceuticals and Medical Devices Agency of Turkey may also request the Ethics Committee to monitor a clinical trial. The Ethics Committee shall send its monitoring report to the Pharmaceuticals and Medical Devices Agency of Turkey within fifteen days. These reports are assessed by the Pharmaceuticals and Medical Devices Agency of Turkey.

e) The Ethics Committee may request the termination of a trial in which a non-compliance is identified, by providing its rationale.

f) The Ethics Committee is obliged to comply with and fulfill the requirements of the relevant legislation.

g) The Ethics Committee shall submit examples of their approval and rejection decisions for research that they reviewed for the first time, which are included in the relevant legislation, to the Pharmaceuticals and Medical Devices Agency of Turkey on a quarterly basis.

h) The Ethics Committee shall submit the annual activity report which is published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey, regularly and on an annual basis to the Pharmaceuticals and Medical Devices Agency of Turkey.

Application to the Ethics Committee and the procedure for processing the application Article 10 - (1) The procedure for applications to the Ethics Committee are as follows:

a) The application files shall be submitted as one copy and in red for Phase I clinical trials, in yellow for Phase II clinical trials, in blue for Phase III clinical trials, in black for Phase IV clinical trials, in white for observational studies, in orange for bioavailability and bioequivalence studies, and in gray for non-pharmacological research.

b) An application fee identified by Istinye University, which shall not exceed the application fee identified and published by the Pharmaceuticals and Medical Devices Agency of Turkey on their website shall be deposited to the account of Istinye University, in the first application to the Ethics Committee, if the Ethics Committee deems it to be necessary, and original or a certified copy of the bank receipt shall be attached to the application file. No application fee is required for dissertations or research for academic purposes.

c) The application is made by the sponsor or the legal representative of the sponsor and the Ethics Committee secretariat conducts all the correspondence with the sponsor or the legal representative of the sponsor.

d) In applications to the Ethics Committee, the appropriate application form based on the type of the research, which is published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey must be used.

e) In applications to be made to the Ethics Committee, the relevant legislation must be followed.

f) The applications to be made to the Ethics Committee should be submitted in accordance with the order specified in the application form, with section headings indicated in brackets.

g) Following the preliminary review of the application by the Ethics Committee secretariat in terms of format, the applications that are in compliance with the relevant legislation and are made in accordance with the application forms are processed.

Review method

Article 11 - (1) The Ethics Committee reviews the files on its agenda within the following framework:

a) All applications that are properly processed must be reviewed in a timely manner and in accordance with the specified review method.

b) The members of the Ethics Committee must convene in accordance with the regularly scheduled meeting dates that are announced by the Ethics Committee secretariat.

c) The Ethics Committee may declare a holiday for a period of fifteen days or less during the year, provided that it is announced in advance.

d) Meetings follow the agenda which is pre-scheduled by the Ethics Committee secretariat and prepared in accordance with the dates of applications, provided that changes are made, where required.

e) Where required, the applicant or the lead researcher is invited to the Ethics Committee meeting to obtain information about the application.

f) Where necessary, representatives of special patient groups or groups related to specific issues are invited to the meeting to assist in the studies and investigations.

g) The existing applications, including applications made at least three business days before the meeting date, are included in the agenda. However, applications that cannot be evaluated at the meeting should be prioritized in the next agenda.

h) The evaluation of seasonal studies and studies on rare diseases shall be prioritized.

(2) In addition to the issues specified in the relevant legislation, the Ethics Committee should
consider the following points in their reviews:

a) The adequacy of the presented information and its ability to respond to ethical questions that arise during the research,

b) The relevance of the research protocol/plan and data collection forms as well as the sample size in relation to the objectives of the research,

c) Statistical analysis and scientific effectiveness, i.e. the potential to achieve sound results with the smallest possible exposure of the volunteer, and the determination of the acceptability of the anticipated risks and distress against the expected benefits for the volunteers or other individuals,

d) The adequacy of the medical monitoring of the research,

e) The adequacy, completeness and clarity of the written and oral information that should be provided to the volunteers and their legal representatives, if necessary,

f) Measures to ensure the confidentiality and protection of the personal information of volunteers,

g) Payments for volunteers, if any.

Decision-making method

Article 12 - (1) The decision-making process of the Ethics Committee is as follows:

a) The decision of the Ethics Committee regarding the reviewed applications can only be made after an evaluation by taking enough time for a review and discussion after any third parties leave the meeting.

b) The Ethics Committee should ensure that the information and documents to be submitted in the application form are complete and that they are addressed before a decision is made.

c) The Ethics Committee may attach non-coercive advice to the decision.

d) In cases where the decision is taken by an absolute majority of the total number of members, members who do not agree with the decision shall sign the Ethical Committee decision by stating the issues that they don't agree with.

e) A negative opinion for a practice should be supported by clearly stated reasons.

f) The Ethics Committee members shall write the date, their names and surnames, the full name of the research, the issue and their decisions on the review form clearly and intelligibly, and sign the form. The form is signed during the meeting.

g) If authorized by the Ethics Committee, a member who shall be appointed by the Ethics Committee may decide on issues identified in a previous meeting/may express his/her opinions in urgent cases.

h) The assessment of cases where notification is sufficient as per the relevant legislation may be agreed on through the signatures of a member who shall be appointed by the Ethics Committee and the President of the Ethics Committee.

i) The assessment of the statements of reliability can be agreed on through the signature of the President of the Ethics Committee.

Method for the communication of the decision

Article 13 - (1) The Ethics Committee shall take its decisions as follows:

a) After the meeting in which the decision is established, the decision must be forwarded to the applicant by the secretariat of the Ethics Committee within a period of time that should not exceed the period specified in the relevant legislation.

b) The applicant is responsible for communicating the decision to all centers in research projects with multiple centers.

c) The format of the Ethics Committee decision form must be in compliance with the format published on the website of the Pharmaceuticals and Medical Devices Agency of Turkey, and the relevant fields of the form must have been filled out completely.

d) The Ethics Committee decision form should be approved by the president of the ethics committee or the Ethics Committee Secretariat, with the indication that it is a "true copy of the original".

e) The cover letter in which the decision is informed must state whether the reviewed research requires the permission of the Pharmaceuticals and Medical Devices Agency of Turkey as per the relevant legislation.

Method of documentation and archiving

Article 14 - (1) All documents and correspondence of the Ethics Committee should be dated, filed and archived.

(2) various documents, files and archives should only be accessed and used by the members and secretariat of the Ethics Committee, and the individuals specified in the relevant legislation.

(3) Documents to be filed and archived should include, but are not limited to:

a) Establishment of the Ethics Committee, historical documents,
b) Resumes of all Ethics Committee members,
c) Resumes of the personnel working for the secretariat of the Ethics Committee,
d) Signed confidentiality agreements and covenants,
e) Announcements that are identified and published by the Ethics Committee,
f) All information and documents submitted by applicants,
g) All correspondence regarding the application, decision and follow-up between the members of the Ethics Committee and the applicant or the other relevant parties,
h) Agenda of the Ethics Committee meetings,
i) One copy of each of the Ethics Committee decisions and all the information that is sent to the applicant,
j) All the documentation and communication records that are sent to the Ethics Committee or created during the audit,
k) All archived files shall be stored for the period specified in the relevant legislation.

SECTION FIVE

Miscellaneous and Final Provisions

Article 15 - (1) Confidentiality of the documents related to the research is essential. These documents shall only be submitted to authorized individuals upon the request of legally authorized individuals or authorities.

(2) Where the research is transferred to another individual/organization by the lead researcher for any reason, the Ethics Committee shall be informed. The Committee shall approve the transfer if it deems it to be appropriate. In case of the transfer of the research, the new owner of the research shall be responsible for the storage of all data and/or documents.

(3) It is appropriate to specify the research budget in detail in the application file.

(4) The receipt of the Informed Volunteer Consent Form from the volunteer who participates in the trial does not terminate the volunteer's right to compensation for the damages s/he suffered by the trial.

(5) Any changes made in the trials after the approval of the Ethics Committee should be notified to the Ethics Committee.

(6) If one or more of the researchers leaves the study or new researchers are involved in the study, the Ethics Committee must be notified of the written consent of the leaving individuals and/or the new participants.

Cases which are not regulated

Article 16 - (1) In cases for which there are no relevant provisions in this Directive; the provisions of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, the Medical Deontology Ordinance which was put into force by the Cabinet Decree No. 4/12578 dated 13/1/1960, the Patient Rights Regulation in relation to the rights of the volunteers who participate in the research, which was published in the Official Gazette No. 23420 dated 1/8/1998, the Regulation on Clinical Trials of Pharmaceuticals and Biological Products which was published in the Official Gazette No. 28617 dated 13/04/2013, and the provisions of other relevant legislation shall apply.

(2) In case of any conflict between the provisions of this Directive and the Regulation on Clinical Trials of Pharmaceuticals and Biological Products, the provisions of the Regulation shall prevail.

Effective Date

Article 17 - (1) This Directive shall enter into force on the date of its adoption by the University Senate.

Execution

Article 18 - (1) The provisions of this Directive shall be executed by the Rector.