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Table of content

Research Ethics Commissions Legal Framework in Romania

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Abstract: *The research on human beings has been essential for the progress of science [1]. At the same time, the cases of un-ethical research on humans showed that research conducted outside of a well-defined legal and ethical framework becomes harmful for participants and for society in general. Research on human subjects in Romania is regulated by national legislation and international regulations ratified by our country. However, in order to become effective in practice the legal and ethical regulations require, formal enforcement tools which are currently represented by the research ethics commissions at national and local level. In this paper the authors performed an analysis of the Romanian legislation governing the organization and functioning of the research ethics commissions in Romania. The authors noted that the Romanian law on research on human beings is consistent with international norms. However, in Romania there is no centralized record of research ethics committees and projects under evaluation, and no consistent concern for educating members of research ethics committees and updating their knowledge on the evolution of the field of research ethics.*

Keywords: *research, ethics commission, law*

Conditioning the beginning of a research on human beings by a favourable opinion from a research ethics commission was regulated for the first time internationally in the 1975 revision of the Declaration of Helsinki which states: "The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins" [2]. The same requirement is also stipulated in other international documents developed by organizations such as the Council of International Organizations of Medical Sciences (CIOMS) and the Council of Europe [3, 4].

In Romania, research on humans can begin only after obtaining a favourable opinion of the ethics commission and the approval by the director of the institution where research will be conducted [5-9].

The principal main investigator is obliged to provide the members of the research ethics commission with the necessary information for the evaluation process, namely: the description of the relevance of the clinical trial, describing the procedure for the recruitment of the participants, the information to be provided to potential participants, the justification of enrollment of vulnerable populations and the way of obtaining their informed consent for inclusion in the research, how they will be informed of the study, and the assessment of risks and benefits of the research [7, 10].

After receiving a favourable opinion of the research ethics commission of research, research must be conducted in accordance with the protocol that has been assessed and approved. Any change of the protocol approved by the ethics committee must be justified and documented [6, 7, 11], except for those changes that are necessary to reduce risks to participants. In the latter situation, however, research ethics committee must be informed of the change made and the justification for it as soon as possible [6, 7].

Organization of research ethics commissions in Romania

In Romania, research ethics commissions are organized at national and local/institutional levels.

The *National Bioethics Commission of Medicines and Medical Devices* is an independent body consisting of healthcare professionals and non-medical members, which operates under the coordination of the Ministry of Health and Medical Sciences Academy. The National Bioethics Commission of Medicines and Medical Devices has a consultative role and the responsibility "to protect the rights, safety and comfort of a clinical trial and ensuring the public of this protection." To this end, the Commission formulates an opinion on the trial protocol under evaluation, the investigator's appropriate qualification, the adequacy of the facilities where the study will be conducted and on the information to be provided to potential participants in order to obtain their informed consent for participation. The rules of organization and operation of the commission are proposed by the Scientific Council of the Academy of Medical Sciences and approved by the General Assembly of the Academy [12- 14].

At the Romanian College of Physicians the *Bioethics Commission* operates, being composed of 7 members (president, vice president, secretary and four members). The Commission is appointed and approved by the National Council of the Romanian College of Physicians.

This commission evaluates the multicenter non-interventional clinical trials with medical devices and the multi-center non- therapeutic clinical trials (e.g. epidemiological studies). For the approval of a clinical at least 5 members need to express a positive opinion [15].

In the facilities and institutions that carry out research activities, the *institutional ethics commissions operate*. The institutional research ethics commissions are designed to ensure on the one hand the ”rights, safety and comfort of all participants", and secondly to protect vulnerable subjects [6, 8].

Research ethics commissions evaluate, approve and monitor the clinical trial protocol, its amendments as well as the procedure of informing the research participants and obtaining their informed consent [6].

Research ethics commissions are composed of at least 5 members of the medical field and in other fields who have the necessary qualifications to assess the proposed clinical trials from both scientific and ethical perspectives [6]. For example, for the assessment of the clinical trials on children, it is recommended to hire someone with experience in clinical, ethical and psychosocial particularities of children [16].

The independence of the research ethics commissions is essential for their impartiality. Therefore, at least one member of the research ethics commission must be outside the scientific field and at least one member outside the institution where the study runs. Also, the research ethics commissions must have no connection to the investigator and sponsor [6].

In the medical facilities where biomedical research involving ionizing radiation takes place, *ethics commissions* operate, whose members are not involved in research activities and have no connection to researchers. The Ethics Commission meets when its opinion is requested. The decision of the commission, either in the form of approval or rejection, must be issued in maximum 30 days and it must be provided in written. Also, the ethics commission is required to monitor the research throughout its deployment, receiving reports on the results. If the commission finds violations of specific regulations regarding medical exposures to ionizing radiation it may withdraw its approval, and it has the obligation to report those cases yearly to the Ministry of Health, the National Authority for Scientific Research and the National Commission for the Control of the Nuclear Activities [17].

Functioning of the research ethics commissions

The principles guiding the work of research ethics commissions are transparency and independence of the investigator, sponsor or any other undue influence [11].

The research ethics commissions must operate on the basis of written procedures in accordance with good clinical practice in clinical studies and legal regulations in force.
In the evaluation of the research proposals, the ethics commissions should pursue the following elements: qualifications of the investigator for the proposed trial [6, 8]; adequacy of facilities for carrying out the study [8]; compliance with the legal and ethical requirements for the studies without specific therapeutic benefit and studies in which the consent of the participants or of their legal representatives cannot be obtained; the reward for participation and way of payment of the subjects and the information to be provided to the potential participants [6].

The investigator does not have the right to attend the meetings of the research ethics commission that evaluates research studies which he/she has proposed.
The decisions of the research ethics commissions can be made only if a quorum is present. Only those members who participated in the discussions and are independent of the investigator and sponsor may vote or express their opinion on the study. After analyzing the documentation received, the research ethics commission may decide: approval/ favorable opinion; formulating amendments necessary for approval; disapproval/ negative opinion; study closure/ suspension of any approval. The opinion of the research ethics commission is made in writing and communicated to both the investigator and the facility/institution where the study is to be conducted [6].

The research ethics commissions must keep written records of their meetings. All relevant records (written procedures, membership lists, affiliation of members, submitted documents, minutes of meetings and correspondence) are kept for at least three years after the completion of the study. They can be submitted to the National Agency of Medicines and Medical Devices by request. Written procedures and list of members of the ethics commission may be submitted to the investigator, sponsor or National Agency of Medicines and Medical Devices upon request [6, 18].

Control and monitoring of the rules of good conduct in scientific research

Law 206/2004 creates the mechanism of control for compliance

with the rules of good conduct in research and sanctioning violations. This law sets up the *National Council for Ethics Research, Technological Development and Innovation* (*National Ethics Council*) affiliated to the State Authority for Research and Development. The National Ethics Council is an advisory body without legal personality. Its members are ”persons with recognized activity in research and/ or specialists in the field of law, ethics in research and science". In addition, the Council can collaborate with external experts for carrying out its activities [19].

The National Ethics Council advises on the rules of good practice in research; observes the implementation of the legal provisions on rules of conduct and professional ethics by the establishments, institutions and research staff; formulates opinions and recommendations on ethical issues raised by the developments in science and knowledge and analyzes the situations of any breach of conduct.

In the institutions that carry out research activities, operate *ethics commissions*, which are designed to track the application of codes of ethics specific to their fields of activity and to analyze the complaints concerning the infringement of the rules of good practice in research. The members of these commissions are proposed by the scientific or administrative councils of the institutions and their membership is approved by the directors of the institutions referred to[19].

In each university there is a *commission of university ethics*, made up of prominent members who do not hold management positions. These commissions are designed to ensure compliance by teachers, students and doctoral candidates of the rules of good practice in research and teaching and they can apply sanctions in cases of violations of these rules[19, 20].

The investigation of complaints begins at the level of the institutional ethics commission, whose decision is communicated in writing to the person who formulated the complaint and made public on the institution's web site within 45 days. The report of the analysis made by the ethics commission may be appealed to the National Ethics Council within 15 days of the communication of its provisions. Otherwise, the persons running the institution will implement the sanctions [19].

Referral is directly observed by the National Ethics Council if: the offense was committed by the manager of the institution, a member of the board of directors or of the scientific board or of the ethics commission [19] or if a

serious misconduct (i.e. plagiarism, making scientific data or entering false data in requests for grants) has been committed [20].

Monitoring of research

The role of the research ethics commission continues throughout the research with responsibility for monitoring trials approved at varying intervals, depending on the level of risk but not less than one year. The monitoring of research is a mechanism meant to monitor the development of the clinical trial conducted in order to ensure that it is conducted, recorded and reported in accordance with the protocol, standard operating procedures, rules of good clinical practice and legal regulations in the field.

The investigator has the obligation to submit the research ethics commission of regular reports on the conduct of the study, at intervals established by it. The investigator must report to the ethics commission any significant change that may influence the conduct of the study or may increase the risk for subjects, the serious and unexpected side effects or deaths and the suspension or premature closure of the study. In turn, the research ethics commission has the possibility to decide premature closure or suspension of the trial if the risk to participants becomes disproportionate compared to the benefits and unjustifiable [6, 8].

After completing the study, the investigator is required to submit a summary of the results to the research ethics commission. Also, the investigator is obliged to provide the ethics commission at its request with all the records of study. These must be kept for at least 7 years from the initial commercial use of the drug, but no more than 15 years [6, 11, 21].

During the development of the clinical trial, the National Agency for Medicines and Medical Devices may carry out inspections consisting of checking the documents, facilities, records, quality assurance systems and any other item that is related to the clinical trial. Inspection is carried out by a qualified person designated by the National Agency for Medicines and Medical Devices, which operates in accordance with specific procedures provided by the legislation [6, 18, 22].

Deficiencies found during inspections can cover various aspects of the clinical trial: legal, ethical, the manner and place of study, the personnel involved, the quality of the collected data or investigational drugs.

The deficiencies may be of varying severity: critical deficiencies requiring immediate action; major, requiring

intensive tracking or minor, which might require tracking.

The critical deficiencies regarding ethical issues are: providing incorrect information to research participants, failure to sign the consent forms by the participants, breach of confidentiality of personal data of the subjects, malfunctions of the ethics commission, the lack of assurance for offering compensation of redress in the event of injury or death suffered by the participants.

The major ethical deficiencies are: inadequate procedures for recruitment of the subjects, un-signed consent forms, date not mentioned on the consent form and failure to state the version number, lack of a document attesting the delegation by the principal investigator of responsibility to obtain the consent of the participants, shortcomings concerning the activity of the resesrch ethics commission (lack of working procedures, inadequate documentation of the work, lack of documents certifying commission), failure to indicate the documents approved by the ethics commission [23].

Conclusions

The Romanian legislation on research on human subjects research is coherent with the international ethical standards in this field. The legal framework is backed by an institutional mechanism which intends, on one hand, to implement the legal and ethical principles in the context of research on human subjects, and on the other hand to ensure compliance with them during the clinical studies.

Although conducted in a proper legal framework, the work of the research ethics commissions could be facilitated by the creation of a centralized record of all the research ethics commissions operating in Romania, the evaluated research projects and the respective decisions. It would also be useful to create training programs for the members of the research ethics commissions and regularily update their knowledge in accordance with the development of research ethics atinternationallevel.

The analysis of the legislation on human subjects research conducted in this paper may be the starting point for an indepth analysis of specific aspects of organization and operation of research ethics commissions with a view to providing information meant to facilitate and improve their work.

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